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Cardiovascular Risk and Systemic Autoimmune Diseases: A Detailed Review

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Abstract

An autoimmune disease (AD) affects multiple organs or systems and significantly impacts quality of life. Genes and epigenetics, gender disparity, environmental triggers, pathophysiological abnormalities, and subphenotypes are all factors contributing to these conditions. In the past, it was believed that atherosclerosis (AT) was an inevitable consequence of aging. Researchers have found that AT is neither degenerative nor irreversible. It is an autoimmune-inflammatory disease that leads to smooth muscle cell proliferation, narrowing of arteries, and atheroma formation due to infectious and inflammatory factors. The humoral and cellular immune systems are thought to contribute to the onset and progression of AT. There are a number of classic risk factors that have been identified. In patients with ADs, it is interesting to note that these factors do not fully explain excessive cardiovascular (CV) events. The risk factors for premature vascular damage are numerous. In this review, we discuss traditional and nontraditional risk factors for CV disease (CVD) in AD.

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Introduction

Multiple organ systems or specific organs can be affected by chronic ADs. A significant quality of life issue is often associated with ADs. Several factors contribute to autoimmune tautology, including genetic and epigenetic factors, gender disparities, environmental triggers, pathophysiological abnormalities, and certain subphenotypes. AT is a degenerative disease associated with aging. As a result of research conducted during the last three decades, AT is neither a degenerative disease nor an irreversible condition. This autoimmune-inflammatory condition is influenced by inflammatory and infectious factors. As a result of altered lipoprotein metabolism, the immune system is activated and smooth muscle cells are proliferating, arteries become narrow, and atheroma develops. Atheromatous lesions can be influenced by humoral and cellular immune mechanisms [1].

There are several autoimmune pathways shared by AT, and many studies have focused on its immunological background in recent years. An accelerated AT is therefore common in quite a few ADs. According to the Framingham heart study, there are several classic risk factors. Subclinical AT, CV, and endothelial dysfunction, events are the result of these conditions. AD patients' excess CV events are not entirely explained by these factors. Premature vascular damage is associated with a number of novel risk factors. Sarmiento-Monroy et al. [2] classified nontraditional risk factors for ADs, based on a rheumatoid arthritis (RA) model, as AD-related factors, genetic determinants, and miscellaneous factors. When traditional and disease-specific traits interact, AD results. It is possible that all of these pathways share the same proatherogenic phenotype. There are many subphenotypes of CVD in ADs, including coronary artery disease (CAD), cerebrovascular disease, myocardial infarction (MI), arterial hypertension, ischemic heart disease (IHD), angina, congestive heart failure (CHF), transient ischemic attacks, thrombosis, peripheral vascular disease (PVD), and left ventricular diastolic dysfunction (LVDD), such as deep vein subclinical AT, pulmonary embolisms, and thrombosis [3].

This paper presents our understanding of how traditional and nontraditional risk factors contribute to CVD in adolescents [4]. Several ADs share common pathogenic mechanisms and have high mortality and morbidity rates associated with CVDs in recent years. Antiphospholipid syndrome (APS), systemic lupus erythematosus (SLE), and RA are the three rheumatic diseases most likely to suffer from vascular damage due to accelerated AT. A lower CV involvement burden appears to be associated with Sjögren's syndrome (SS) and systemic sclerosis (SSc), as well as specific risks [5].

Methods

Study finding was done using the following medical subject heading terms: RA, or CVD, or APS, or scleroderma, systemic, or SS, and SLE. These terms were used to cross-reference each group: risk factors, traditional risk factors, classical risk factors, nontraditional risk factors, and novel risk factors [6]. There are the most results for each term. Furthermore, human limitations were considered in addition to linguistic limitations (English). Each study was reviewed independently by a blinded team. A predefined eligibility criteria was used to resolve

disagreements from the inception of the project until December 2023 [7].

Process

An abstract search and a review of full-text articles were conducted in search of eligible studies. As criteria for inclusion, the abstract must be available, the original data must be that of the AD, the AD classification criteria must be used, the CV risk factors must be measured, and the clinical endpoints need to be defined. There were no animal models or articles dealing with juvenile pathologies included in the analysis [3, 8]. In addition to reviews and case reports, studies that did not meet the inclusion criteria, studies with insufficient data, and studies with unsignificant results were also excluded. Articles were also categorized according to similarity and duplicates were removed. It must be a new or classic risk factor in order to be statistically significant [9].

Results

The PubMed database identified 12,387 articles. Among them, 7299 were replicas, missing data, or statistically significant. In order to determine eligibility, we assessed 719 full-text articles. The methodological analysis was conducted on only 419 articles. Thus, 94 articles meeting the eligibility criteria and having interpretable data were selected. Traditional CV risk factors include hyperhomocysteinemia, dyslipidemia, smoking, and diabetes. In numerous studies, nontraditional risk factors have been strongly associated with the disease, including genetic markers, autoantibodies, disease duration, markers of chronic inflammation, polyautoimmunity, and familial autoimmunity [3, 10].

APS

Patients with CVD frequency ranging from 1.7% to 6% may be affected by antiphospholipid antibodies (APLAs). Those with asymptomatic APS show a higher CVD prevalence compared to patients with SLE, while healthy controls exhibit a lower prevalence. In the Euro-phospholipid cohort, the MI rate was 2.8%, with 5.5% of patients experiencing MI during the course of their illness [11]. However, only 4% to 6% of patients develop significant cardiac morbidity. Various manifestations of thrombosis affecting coronary circulation or heart valves are thought to contribute to these cardiac symptoms.

SS

SS is linked to an elevated "overall risk" of CV and cerebrovascular events. While CV events are not typically associated with SS, they are a significant concern for those with the condition. Both traditional risk factors and disease-specific mechanisms contribute to this increased CV risk. Research suggests that a complex interplay exists between disease-related factors, endothelial dysfunction, and conventional risk factors. Although various medications are available to manage the systemic manifestations of SS, limited data exist regarding their impact on CV events. However, these treatments have shown improvements in certain outcomes [12]. CV events-such as strokes, MIs, cerebrovascular accidents (CVAs), deep vein thrombosis (DVTs), and arrhythmias occurred in 5 - 7.7% of patients. Other reported complications include tricuspid regurgitation, damage to the mitral and aortic valves, and increased left ventricular mass. This study has also identified a combination of traditional and non-traditional risk factors linked to CVD in older adults [13].

Arthritis rheumaticum

Patients with AD, such as RA, are more susceptible to CVD. Studies suggest that individuals with RA face a 1.5 to 2 times higher risk of CVD compared to the general population of similar age and sex. Accurately evaluating this heightened risk in RA is complicated by the complex interplay of both traditional and emerging CVD risk factors. Various CV conditions have been linked to RA-related CVD. The prevalence of CVD in RA patients is estimated to be between 30% and 50%, as indicated by [14].

SSc

CVD prevalence and mortality rates vary depending on specific subphenotypes in patients. In SSc, the mortality rate for those with CVD is 20 - 30% higher than in patients without CVD. Approximately 10% of SSc patients exhibit CV symptoms, while asymptomatic CAC is present in 33.3% of those with diffuse SSc and 40% of those with limited SSc [15]. Carotid doppler studies reveal carotid stenosis in 64% of patients, compared to 35% in the general population. Additional CV complications observed in SSc patients include LVDD, Mis, coronary spasms, myocardial fibrosis, PVDs, arrhythmias, CVAs, and CAD.

SLE

CVD and mortality rates in individuals with SLE are at least twice as high as those in the general population. Common CVD manifestations in SLE patients include carotid plaques, MIs, angina, CHF, strokes, increased intima-media thickness (IMT), PVD, and pericarditis.

Discussion

CVD is more prevalent in patients with ADs who possess both traditional risk factors, such as dyslipidemia, abnormal body mass index, and male sex, as well as nontraditional risk factors like steroid use, household responsibilities, and the presence of autoantibodies. To reduce the public health burden of these conditions, innovative strategies are needed for the prediction, prevention, and treatment of CVD in AD patients. The review also identified several CVD-related outcomes and contributing factors that highlight the complexity of managing CV risks in this population [16].

APS

It is possible for the APS to be in a prothrombotic state both in the arterial and venous circulations. DVTs usually occurs in the legs and cerebral arterial thrombosis usually occurs in the brain. The heterogeneity of APS clinical manifestations is likely due to the induced effects of APLA on endothelial cells [17]. The venous and arterial circulations are both affected by thrombotic events in APS. An AT or thrombus can cause CVD, CAD, and PVD. Vegetation and valve dysfunction can also result from irregular thickening of valve leaflets as a result of immune complex deposition. APS and CVD risk factors are also discussed in the paper [18]. By diagnosing APS early, implementing lifestyle modification, pharmacology, anti-inflammatory treatment, and keeping close track of patients, CV risk may be reduced. A judicious and careful use of anticoagulants and antiaggregant is necessary in the treatment of patients with APS coagulopathy. The treatment of APS requires targeted immunomodulatory or inflammatory therapies. APLA's pathogenic effects must be targeted by these drugs in order to be effective. As a result of this pathology, atheroma is a major cause of CV mortality [19]. In AM drugs, for example, it may be evident that they have antiatherogenic properties. Anti-atherosclerotic (i.e., preventing calcification of the endothelium), anti-inflammatory (i.e., lowering C-reactive protein levels), antioxidant, immunomodulatory, and antithrombotic properties are among the pleiotropic properties of statins. It has been found that aspirin inhibits platelet aggregation, making it a useful tool for both primary and secondary prevention in APS patients [20]. Heparins are both anticoagulants and anti-

inflammatory agents, in addition to being anticoagulants. There is a possibility that heparin can be used as a therapeutic tool to alleviate inflammation, even though the mechanisms by which it works are not fully understood. Through a better understanding of pathogenic mechanisms, new immunomodulatory approaches have been identified for APS and CVD. The list includes B-cell targeted therapies, complement inhibitors, co-stimulation inhibitors, intracellular pathway inhibitors, and anticytokine therapies [21].

SS

Dryness of the eyes and mouth is usually caused by this autoimmune epithelitis that affects exocrine glands. An autoimmune exocrinopathy and extraglandular manifestations are common in 40 – 50% of patients. As previously mentioned, CVD also falls into this category, but with a lower prevalence. Chronic systemic inflammation is a risk factor for AT, but it does not appear to increase CVD prevalence in SS patients. Inflammation of milder severity has been shown to be associated with this disease by Ramos-Casals et al. [22]. However, it is found endothelial dysfunction in SS patients despite comparable carotid IMT. The CV risk in patients with SS is increasing due to the rising number of women suffering from this disease (postmenopausal women). The carotid arterial wall was found to be significantly changed by Nowak et al. [23] based on femoral and carotid ultrasound findings. As a result of functional impairments in the arterial wall, SS may suffer early stages of AT. There seems to be an association between chronic inflammation and immunological factors and endothelium dysfunction. The paper discusses traditional and nontraditional CVD and SS risk factors. When it comes to the management of CVD in SS patients, it is imperative to aggressively intervene on modifiable and nontraditional risk factors, including the evaluation of autoantibodies and other SS-related factors. Due to the lower frequency of HTN, diabetes, and dyslipidemia that AMs are associated with, these drugs are believed to have a protective effect on CVD and SS patients. A prospective study of the incidence of CVD and the different risk factors is needed in the future (Figure 1) [24].

AD-AT Physiopathology

Since AT is multifactorial, chronic, and inflammatory, it has traditionally been viewed as a lipid-based disorder. However, recent advancements in our understanding now reveal that atheroma formation involves all aspects of the immune system. The role of proinflammatory pathways in the development and progression of vascular damage has gained increased attention as we uncover the underlying mechanisms contributing to vascular injury. While multiple ADs may share common pathways that promote AT and CVD, each AD may also exhibit distinct immunological abnormalities that influence proatherogenic processes. These mechanisms lead to the accumulation of lipid particles, immune cells, autoantibodies, autoantigens, and the production of inflammatory cytokines such as tumor necrosis factor (TNF). Over time, these factors cause thickening of the intima layer, loss of arterial elasticity, narrowing of the lumen, reduced blood flow, plaque rupture, and eventually CV events. Acute-phase reactants like erythrocyte sedimentation rate and C-reactive protein also play a crucial role in the systemic inflammatory response observed in AT [25].

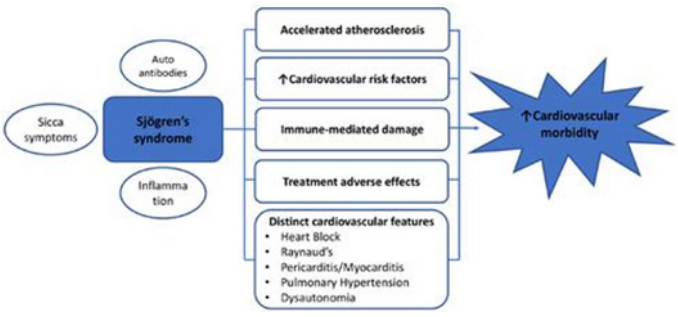

Figure 1: Representation of SS to CV morbidity.

There are a number of traditional and non-traditional risk factors associated with AT. Additionally, angiotensin II levels are high, smooth muscle hypertrophy is increased, peripheral resistance is increased, and low-density lipoprotein cholesterol (LDL) is oxidized along with plasma homocysteine levels and genetic changes occur [26]. Leukocyte adhesion and platelet permeability are increased by multiple types of injury, which result in an increase in vascular cell adhesion molecules (VCAM), intercellular adhesion molecules-1 (ICAM), selectins, and chemokines. A cascade of events occurs following macrophage differentiation, including the upregulation of toll-like receptors that activate macrophages and release vasoactive molecules including nitric oxide, reactive oxygen species, endothelin's, and protease enzymes. Each of these causes the plaque to destabilize and rupture more frequently. Besides T cells, T helper 1 lymphocytes (Th1) are also found in the subendothelial space. IL-4, -5, and -10 are anti-inflammatory mediators that dominate lymphocyte T helper 2 (Th2). This reaction is more pronounced in ADs producing high levels of TNF-α, IL-2, IL-6, IL-17, which enhances the activation of T cells even further and promotes the migration and proliferation of smooth muscle cells. As well as expressing human leukocyte antigen II, activated M cells present antigens to T lymphocytes. As well as OX-LDL and heat shock proteins 60/65, smooth muscle cells from lesions containing class II human leukocyte antigen molecules can also present these proteins to T cells. In addition to smooth muscles, endothelium, macrophages, and T cells, CD40 and its ligand CD40 are expressed [27]. Lesions of AT demonstrate immune activation by upregulating both proteins (Figure 2).

A group of autoantibodies against different autoantigens involved in CVD is called antioxidized low-density lipoprotein antibodies (anti-oxLDL). OxLDL's are macromolecules with many potential autoantigens. There is therefore a possibility that these autoantibodies will have a different clinical impact. Anti-oxLDL titers have been detected in patients with early-onset PVD, severe carotid artery disease, heart failure, CAD, and sudden death. Thus, these autoantibodies contribute to the progression of AT as a result of their proatherogenic properties [28].

Beta-2 glycoprotein-1 (β2GPI) serves as a key autoantigen in APS. Atherosclerotic plaques are commonly found in the subendothelial zone and the intima-media layer. In inflammatory conditions such as AT, elevated levels of IgM and IgG anti-β2GPI antibodies are frequently observed. Anticardiolipin antibodies (ACLAs), which often recognize β2GPI as an autoantigen, exhibit procoagulant properties, linking

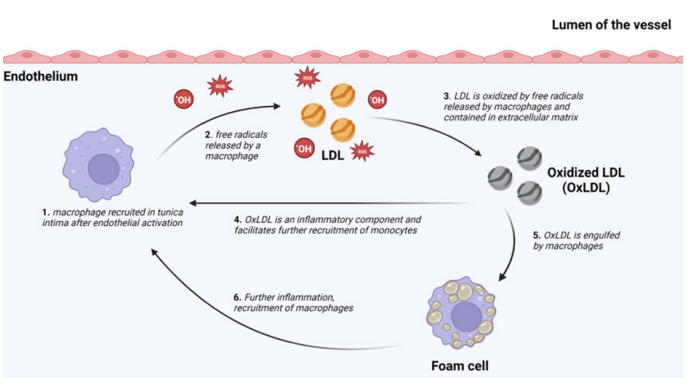

Figure 2: Circle of AT initiation.

autoimmunity to both AT and thrombosis.

ACLAs play a significant role in the progression of AT by enhancing monocyte adhesion to endothelial cells, which is facilitated by the presence of adhesion molecules like ICAM-1, VCAM-1, and E-selectin. As a result, ACLAs contribute to the exacerbation of AT beyond their traditional role as biomarkers for the condition. Furthermore, antibodies against heat shock protein 60 are commonly found in patients with CVD and are known to lyse endothelial cells under stress, further aggravating vascular damage and contributing to disease progression [29].

RA

It is not clear why patients with RA are at increased risk for heart disease compared to those without RA. Traditional CV risk factors do not fully explain this risk. Inflammatory conditions such as RA can be treated with therapies that suppress inflammation, which may also reduce the risk of heart disease developing. They can, however, increase heart disease risk by their other effects, such as steroids [30]. As well as diarthrodial joints, extraarticular manifestations of RA are also possible. Consequently, this group has a poor prognosis and a high mortality rate due to CVD. With the progression of RA, vascular damage accumulates prior to diagnosis. The endothelial dysfunction and subclinical AT in RA patients are higher than those in age-matched controls. Endothelial function, as assessed by flow-mediated vasodilation in the brachial artery, deteriorates as well with disease progression. The overall life expectancy of RA patients is shorter than that of the general population, and the CV mortality rate is higher. As compared with the general population, CVD occurs earlier and more frequently. The most common cause of death for RA patients around the world is CVD. IHD due to AT is the leading cause of death for patients with RA. The majority of mortality studies are conducted on European populations, and little is known about populations of other ethnicities. According to a meta-analysis of 24 RA mortality studies published between 1970 and 2005, the weighted combined all-cause mortality ratio (meta-SMR) for IHD was 1.59 and for CVA it was 1.52 [31]. A "silent" IHD with no symptoms is often followed by sudden cardiac death in patients with RA and CVD. Cardiac arrest is almost twice as common among RA patients as among the general population. According to the Rochester epidemiology project, RA patients had a higher MI risk than controls of the same age and gender. Recent systematic literature reviews examined CVD in Latin American populations by Sarmiento-Monroy et al. [2] This population has a prevalence of CVD ranging from 13.8% to 80.6%. Puerto Ricans had the highest prevalence (54.9%), followed by Brazilians (47.3%), Colombians (35.1%), and Argentines (30.5%). RA patients, however, have been the subject of relatively few studies on mortality. Cannarile et al. [32] found a mortality rate of 5.2% after six years of follow-up. Mortality rates from CVD were 44.7% and 22.2%, respectively. There are both traditional and nontraditional risk factors associated with CVD in RA patients. The paper summarizes those findings. Colombians are traditionally predisposed to CVD through male gender, hypercholesterolemia, and a high body mass index. In spite of these classical risk factors, CV events are more prevalent in RA than they are in other populations. A combination of traditional and nontraditional risk factors for CVD are associated with RA [32].

Inflammatory arthritis can be detected and managed using CV risk score calculators like Framingham scores and systematic coronary risk evaluation (SCORE), but these models have not been adequately evaluated to determine their accuracy in the context of inflammatory arthritis. Researchers found that SCORE underestimated RA patients' CV risk. A study found that people at moderate risk had more carotid plaques than those at high risk based on SCORE risk charts [33]. For classical risk factors to be controlled, healthy lifestyles must be developed. In RA patients, statins reduce CV-related and all-cause mortality when used for primary prevention of vascular events. The effects of ACE inhibitors and angiotensin II blockers on RA are similar [34]. A management system appropriate for the disease caused by novel risk factors is necessary in order to properly manage it. Managing disease activity and reducing CV burden should be the primary goals of treatment. A combination of conventional and biological drugs is used in treating RA. Nonconventional DMARDs, such as anti-TNF agents that improve endothelial function and lower C-reactive protein and IL-6 levels, are more effective at controlling disease than conventional DMARDs. HTN, obesity, and diabetes, all major CVD risk factors, may also be reduced by increased physical activity. RA patients treated with antimalarials (AMs) experience improved CV outcomes, improved glycemic control, improved lipid profiles, and a reduced chance of developing T2DM. As glucocorticoids (GC) affect metabolic parameters and blood pressure, they should be used carefully to minimize CV risks. Inflammatory arthritis patients treated with low doses of GC have no greater CV risk than those treated with high doses, as a result. Although this debate has not been resolved, GCs could be justified in short-term RA treatment, such as "bridging therapy" between DMARDs and response. Thus, the shortest possible period of treatment with the lowest dose was recommended. Studies have shown that anti-TNF reduces the risk of CV disease in young patients by improving lipid profiles, insulin resistance, endothelial function, and aortic compliance, as well as decreasing the progression rate of subclinical AT. A similar effect is also produced by other biological therapies. The treatment of RA patients with rituximab improved endothelial function after receiving anti-TNF-alpha drugs. Other biologics may also reduce CV risk, but conflicting and preliminary data exist, so randomized, controlled trials are needed [35].

SSc

A major feature of the disease is the involvement of the microvascular system and the macrovascular system. The most common form of vascular disease in SSc is microvascular occlusive disease, characterized by vasospasm and intimal proliferation (i.e., microvascular occlusive disease) [24]. It has been demonstrated that macrovascular disease occurs when the intimal layer fibrosis, thickens, and continues to multiply, with transmural lymphocytic infiltrates without evidence of atherosclerotic plaques by carotid ultrasonography, ankle brachial blood pressure indices, and peripheral angiography [36]. Currently, however, there is evidence that shows increased carotid CAC, subclinical CAD, and IMT. A major feature of the myocardium is patchy fibrosis within the subendocardium. Only 10% of patients with LVDD have symptoms of this fibrosis [37]. Infarctions due to coronary arteries may be caused by microvascular disease, although coronary AT is more common in patients with SSc. In SSc patients, coronary events are associated with low coronary flow reserves. In addition to ectasia, spasm, and coronary artery stenosis, other authors have reported similar findings [3, 38]. Arrhythmias as well as conduction disturbances are associated with SSc, in addition to hypertrophy and heart failure contractility. The evaluation of carotid arteries by ultrasound is also a reliable indicator of subclinical AT and a strong predictor of future strokes and MIs. SSc must also be treated for its vascular component once it has been diagnosed and confirmed. Research is being conducted to develop novel therapies to prevent further damage to arteries and promote vascular repair instead of vasodilators [39]. As well as prostacyclin analogs and endothelin antagonists, phosphodiesterase inhibitors, immunosuppressive therapy, and tyrosine kinase inhibitors,

there are other treatments available today.

SLE

Among young women with SLE of childbearing age, subclinical AT is the most common. SLE patients exhibit a bimodal mortality pattern, characterized by active disease, infections, and nephritis within 3 years of diagnosis and CVD for 20 years after diagnosis. Over the past 30 years, SLE patients have experienced improvements in overall mortality but remain at high risk for CVD (i.e., 3 - 25%). CVD is at least twice as common in SLE patients as in the general population. In over 65-year-olds with SLE, carotid plaque is found in over 100% of cases. Under 35, it affects 21% of patients. The prevalence of MI and angina in SLE patients has been confirmed in a number of population-based studies. It is found that the risk of CVA and MI among women with SLE aged 40 - 49 was 8 fold higher than in the general population. A number of research groups have reported prevalence rates for SLE cohorts. Eight PVD cases were detected in SLICC-RAS cohort of 1,249 patients after a two-year study. In lupus in minorities: nature versus nurture (LUMINA), 4.4 years were found to be the median follow-up. In several epidemiological studies, Schoenfeld et al. [40] found an elevated CVD risk in SLE patients. In previous epidemiological studies, there was variability regarding the relative importance of CVD risk factors among SLE patients due to different design methods and comparison groups. The Baltimore, Pittsburg, LUMINA, Toronto, and SLICC-RAS cohorts, as well as the LUMINA, Toronto, and SLICC-RAS cohorts, have tested independent predictive factors (from multivariate analysis) for CV events in patients with SLE. Various SLE cohorts have demonstrated advanced age, dyslipidemia, obesity, HTN, and hyperhomocysteinemia as classic CVD risk factors. In addition to traditional CVD risk factors, epidemiological data suggests SLE patients are more likely to develop CVD. 34.5% of SLE patients were found to have CVD by Hung et al. [41] in 310 consecutive cases. In addition to traditional risk factors, high coffee consumption in LA was found to contribute to this complication when combined with traditional risk factors (e.g., dyslipidemia and smoking). Despite the fact that traditional CVD risk factors do contribute to the increased CVD risk among SLE patients, these factors do not completely explain it [41]. After removing the influence of multiple risk factors, Matsuura et al. [42] found a high likelihood of developing CAD in two Canadian lupus cohorts using the Framingham multiple logistic regression model. The premature AT process characteristic of those patients is therefore closely related to SLE factors. It is therefore of increasing interest to identify novel risk factors that may explain accelerated AT development in these populations. There has been a proposal to manage SLE in the same way as T2DM by lowering lipid goals, using more aspirin, and potentially monitoring more aggressively [42].

The effectiveness of traditional treatment regimens in patients with SLE has been examined in studies. Many AMs have been shown to have beneficial effects on reducing CV risk for patients with SLE through new mechanisms of action. AM drugs taken with steroids reduce TC, elevate HDL, and reduce LDL. In addition, studies have shown that hydroxychloroquine (HCQ) reduces the formation of thrombi. HCQ use was associated with a 50 - 60% reduction in CVD risk [3, 43]. According to Petri et al. [44] in a randomized controlled study of 200 SLE patients over two years, atorvastatin did not slow subclinical AT progression. CD40-CD40 ligand interactions are interfered with by statins both in vivo and in vitro in SLE and AT. Inflammation associated with SLE is one of the treatment targets, so other immunosuppressants and biological therapies may also be considered, such as potential new antiatherogenic agents [44].

Conclusion

A variety of mechanisms are shared between AT and ADs. Classic risk factors alone do not adequately account for the elevated rates of CV events observed in patients with ADs. Instead, premature vascular damage is linked to several novel risk factors. The proatherogenic phenotype seen in this population arises from a complex interplay between traditional risk factors and disease-specific characteristics. In the absence of further research or disease-specific risk prediction tools, it is essential to adopt an aggressive approach in managing disease activity in patients with AD, while also carefully addressing modifiable traditional risk factors. By uncovering and understanding the complex interactions among predisposing factors such as genetics, environmental influences, and the diseases themselves, we can enhance our ability to describe and assess CV subphenotypes in individuals with AD.

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Conflict of Interest

None.

References

1. Ponnuswamy P, Van Vre EA, Mallat Z, Tedgui A (2012) Humoral and cellular immune responses in atherosclerosis: spotlight on B-and T-cells. Vascular Pharmacol 56: 193-203. https://doi.org/10.1016/j.vph.2012.01.009
2. Sarmiento-Monroy JC, Amaya-Amaya J, Espinosa-Serna JS, Herrera-Díaz C, Anaya JM, et al. (2012) Cardiovascular disease in rheumatoid arthritis: a systematic literature review in Latin America. Arthritis 2012: 1-17. https://doi.org/10.1155/2012/371909
3. Kaplan MJ (2006) Cardiovascular disease in rheumatoid arthritis. Curr Opin Rheumatol 18: 289-297. https://doi.org/10.1097/01.bor.0000218951.65601.bf
4. Balagopal PB, de Ferranti SD, Cook S, Daniels SR, Gidding SS, et al. (2011) Nontraditional risk factors and biomarkers for cardiovascular disease: mechanistic, research, and clinical considerations for youth: a scientific statement from the American Heart Association. Circulation 123: 2749-2769. https://doi.org/10.1161/cir.0b013e31821c7c64
5. Rho YH, Chung CP, Oeser A, Solus J, Asanuma Y, et al. (2009) Inflammatory mediators and premature coronary atherosclerosis in rheumatoid arthritis. Arthritis Rheum 61: 1580-1585. https://doi.org/10.1002/art.25009
6. Sandoo A, Hodson J, Douglas KM, Smith JP, Kitas GD (2013) The association between functional and morphological assessments of endothelial function in patients with rheumatoid arthritis: a cross-sectional study. Arthritis Res Ther 15: 1-9. https://doi.org/10.1186/ar4287
7. Gabriel SE (2008) Cardiovascular morbidity and mortality in rheumatoid arthritis. Am J Med 121: S9-14. https://doi.org/10.1016/j.amjmed.2008.06.011
8. Holmqvist M, Gransmark E, Mantel A, Alfredsson L, Jacobsson LTH, et al. (2013) Occurrence and relative risk of stroke in incident and prevalent contemporary rheumatoid arthritis. Ann Rheum Dis 72: 541-546. https://doi.org/10.1136/annrheumdis-2012-201387
9. Bateman M, Malins JM, Meynell MJ (1958) Rheumatoid arthritis and systemic lupus erythematosus. Ann Rheum Dis 17: 114. https://doi.org/10.1136/ard.17.1.114
10. Popa CD, Arts E, Fransen J, van Riel PLCM (2012) Atherogenic index and high-density lipoprotein cholesterol as cardiovascular risk determinants in rheumatoid arthritis: the impact of therapy with biologicals. Mediators Inflamm 2012: 1-9. https://doi.org/10.1155/2012/785946
11. Cohen MD, Keystone E (2015) Rituximab for rheumatoid arthritis. Rheumatol Ther 2: 99-111. https://doi.org/10.1007/s40744-015-0016-9
12. Akar S, Sarı İ, Çömlekci A, Birlik M, Önen F, et al. (2014) Body composition in patients with rheumatoid arthritis is not different than healthy subjects. Eur J Rheumatol 1: 106-110. https://doi.org/10.5152/eurjrheumatol.2014.035
13. Kiani AN, Vogel-Claussen J, Arbab-Zadeh A, Magder LS, Lima J, et al. (2012) Semiquantified noncalcified coronary plaque in systemic lupus erythematosus. J Rheumatol 39: 2286-2293. https://doi.org/10.3899/jrheum.120197

14. Haberka M, Skilton M, Biedroń M, Szóstak-Janiak K, Partyka M, et al. (2019) Obesity, visceral adiposity and carotid atherosclerosis. J Diabetes Complications 33: 302-306. https://doi.org/10.1016/j.jdiacomp.2019.01.002

15. Krzanowski M, Krzanowska K, Gajda M, Dumnicka P, Dziewierz A, et al. (2017) Pentraxin 3 as a new indicator of cardiovascular-related death in patients with advanced chronic kidney disease. Pol Arch Intern Med 127: 170-177. https://doi.org/10.20452/pamw.3944

16. Espinosa G, Bucciarelli S, Asherson RA, Cervera R (2008) Morbidity and mortality in the catastrophic antiphospholipid syndrome: pathophysiology, causes of death, and prognostic factors. Semin Thromb Hemost 34: 290-294. https://doi.org/10.1055/s-0028-1082274

17. Varghese TP (2024) Genetic biomarkers in cardiovascular disease. Curr Probl Cardiol 49:102588. https://doi.org/10.1016/j.cpcardiol.2024.102588

18. Kim SH, Lee CK, Lee EY, Park SY, Cho YS, et al. (2004) Serum oxidized low-density lipoproteins in rheumatoid arthritis. Rheumatol Int 24: 230-233. https://doi.org/10.1007/s00296-003-0358-4

19. Sitia S, Atzeni F, Sarzi-Puttini P, Di Bello V, Tomasoni L, et al. (2009) Cardiovascular involvement in systemic autoimmune diseases. Autoimmun Rev 8: 281-286. https://doi.org/10.1016/j.autrev.2008.08.004

20. Hassan GS, Yacoub D, Alaaeddine N, Nadiri A, Merhi Y, et al. (2013) CD154: the atherosclerotic risk factor in rheumatoid arthritis? Arthritis Res Ther 15: 1-9. https://doi.org/10.1186/ar4153

21. Horkko S, Olee T, Mo L, Branch DW, Woods JVL, et al. (2001) Anticardiolipin antibodies from patients with the antiphospholipid antibody syndrome recognize epitopes in both β2-glycoprotein 1 and oxidized low-density lipoprotein. Circulation 103: 941-946. https://doi.org/10.1161/01.cir.103.7.941

22. Ramos-Casals M, Brito-Zerón P, Sisó A, Vargas A, Ros E, et al. (2007) High prevalence of serum metabolic alterations in primary sjögren's syndrome: influence on clinical and immunological expression. J Rheumatol 34: 754-761.

23. Nowak B, Szmyrka-Kaczmarek M, Durazińska A, Płaksej R, Borysewiczet K, et al. (2012) Anti-Ox-LDL antibodies and anti-Ox-LDL-β2GPI antibodies in patients with systemic lupus erythematosus. Adv Clin Exp Med 21: 331-335.

24. Carbone F, Bonaventura A, Liberale L, Paolino S, Torre F, et al. (2020) Atherosclerosis in rheumatoid arthritis: promoters and opponents. Clin Rev Allergy Immunol 58: 1-14. https://doi.org/10.1007/s12016-018-8714-z

25. Font J, Loapez-Soto A, Cervera R, Balasch J, Pallarés L, et al. (1991) The 'primary' antiphospholipid syndrome: antiphospholipid antibody pattern and clinical features of a series of 23 patients. Autoimmunity 9: 69-75. https://doi.org/10.3109/08916939108997126

26. Kolitz T, Shiber S, Sharabi I, Winder A, Zandman-Goddard G (2019) Cardiac manifestations of antiphospholipid syndrome with focus on its primary form. Front Immunol 10: 1-11. https://doi.org/10.3389/fimmu.2019.00941

27. Haga H-J, Jacobsen EM, Peen E (2008) Incidence of thromboembolic events in patients with primary sjögren's syndrome. Scand J Rheumatol 37: 127-129. https://doi.org/10.1080/03009740701716843

28. Jobling K, Rajabally H, Ng WF (2018) Anti-Ro antibodies and complete heart block in adults with sjögren's syndrome. Eur J Rheumatol 5: 194-196. https://doi.org/10.5152/eurjrheum.2018.18019

29. Melissaropoulos K, Bogdanos D, Dimitroulas T, Sakkas LI, Kitas GD, et al. (2020) Primary sjögren's syndrome and cardiovascular disease. Curr Vasc Pharmacol 18: 447-454. https://doi.org/10.2174/1570161118666200129125320

30. Herrgott I, Riemekasten G, Hunzelmann N, Sunderkötter C (2008) Management of cutaneous vascular complications in systemic scleroderma: experience from the German network. Rheumatol int 28: 1023-1029. https://doi.org/10.1007/s00296-008-0556-1

31. Turiel M, Gianturco L, Ricci C, Sarzi-Puttini P, Tomasoni L, et al. (2013) Silent cardiovascular involvement in patients with diffuse systemic sclerosis: a controlled cross-sectional study. Arthritis Care Res 65: 274-280. https://doi.org/10.1002/acr.21819

32. Cannarile F, Valentini V, Mirabelli G, Alunno A, Terenzi R, et al. (2015) Cardiovascular disease in systemic sclerosis. Ann Trans Med 3: 1-11. https://doi.org/10.3978/j.issn.2305-5839.2014.12.12

33. Ungprasert P, Sanguankeo A, Upala S (2016) Risk of ischemic stroke in patients with systemic sclerosis: a systematic review and meta-analysis. Mod Rheumatol 26: 128-131. https://doi.org/10.3109/14397595.2015.1056931

34. Meiszterics Z, Tímár O, Gaszner B, Faludi R, Kehl D, et al. (2016) Early morphologic and functional changes of atherosclerosis in systemic sclerosis-a systematic review and meta-analysis. Rheumatology 55: 2119-2130. https://doi.org/10.1093/rheumatology/kew236

35. Derk CT, Jimenez SA (2007) Acute myocardial infarction in systemic sclerosis patients: a case series. Clin Rheumatol 26: 965-968. https://doi.org/10.1007/s10067-006-0211-8

36. Sidiropoulos PI, Karvounaris SA, Boumpas DT (2008) Metabolic syndrome in rheumatic diseases: epidemiology, pathophysiology, and clinical implications. Arthritis Res Ther 10: 1-9. https://doi.org/10.1186/ar2397

37. Roman MJ, Moeller E, Davis A, Paget SA, Crow MK, et al. (2006) Preclinical carotid atherosclerosis in patients with rheumatoid arthritis. Ann Intern Med 144: 249-256. https://doi.org/10.7326/0003-4819-144-4-200602210-00006

38. Massardo L, Aguirre V, Garcia ME, Cervilla V, Nicovani S, et al. (1995) Clinical expression of rheumatoid arthritis in Chilean patients. Semin Arthritis Rheum 25: 203-213. https://doi.org/10.1016/s0049-0172(95)80032-8

39. Lee KS, Kronbichler A, Eisenhut M, Lee KH, Shin JI (2018) Cardiovascular involvement in systemic rheumatic diseases: an integrated view for the treating physicians. Autoimmun Rev 17: 201-214. https://doi.org/10.1016/j.autrev.2017.12.001

40. Schoenfeld SR, Kasturi S, Costenbader KH (2013) The epidemiology of atherosclerotic cardiovascular disease among patients with SLE: a systematic review. Semin Arthritis Rheum 43: 77-95. https://doi.org/10.1016/j.semarthrit.2012.12.002

41. Hung G, Mercurio V, Hsu S, Mathai SC, Shah AA, et al. (2019) Progress in understanding, diagnosing, and managing cardiac complications of systemic sclerosis. Curr Rheumatol Rep 21: 68. https://doi.org/10.1007/s11926-019-0867-0

42. Matsuura E, Atzeni F, Sarzi-Puttini P, Turiel M, Lopez LR, et al. (2014) Is atherosclerosis an autoimmune disease? BMC Med 12: 1-5. https://doi.org/10.1186/1741-7015-12-47

43. Escárcega RO, Lipinski MJ, Garcia-Carrasco M, Mendoza-Pinto C, Galvez-Romero JL, et al. (2018) Inflammation and atherosclerosis: cardiovascular evaluation in patients with autoimmune diseases. Autoimmun Rev 17: 703-708. https://doi.org/10.1016/j.autrev.2018.01.021

44. Petri MA, Kiani AN, Post W, Christopher-Stine L, Magder LS (2011) Lupus atherosclerosis prevention study (LAPS). Ann Rheum Dis 70: 760-765. https://doi.org/10.1136/ard.2010.136762