Volume 3, Issue 3, March - 2025 **ISSN(E):** 2938-3773

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

SYSTEMIC SCLEROSIS AND CARDIOVASCULAR RISK: A SYSTEMATIC REVIEW OF ITS ASSOCIATION WITH ATHEROSCLEROSIS

Ganieva N. A.,
Djuraeva E. R.
Dwivedi K.
Tashkent Medical Academy, Tashkent, Uzbekistan

Abstract

Systemic sclerosis (SSc) is an autoimmune disease characterized by vascular dysfunction, fibrosis, and immune dysregulation, leading to increased cardiovascular risk, including atherosclerosis and endothelial dysfunction. Despite growing evidence, the relationship between SSc and macrovascular complications remains unclear, necessitating a comprehensive review of existing literature. Objective: Analysis of the relationship between systemic sclerosis and cardiovascular diseases, and assessment of the role of biomarkers, AI diagnostics, and targeted therapy in managing these risks. Methods: This systematic review was conducted following PRISMA guidelines, analysing studies from PubMed, Scopus, Web of Science, Russian databases, and Google Scholar. A total of 18 studies were identified, and 12 were included based on predefined eligibility criteria. Studies evaluating cardiovascular risk, biomarkers, AI-based diagnostics, and therapeutic interventions in SSc were analysed. Results: Findings indicate that SSc is strongly associated with increased cardiovascular risk, primarily due to endothelial dysfunction, chronic inflammation, and immune-mediated vascular injury. AI-driven imaging and deep learning models demonstrated enhanced detection of vascular abnormalities, while elevated carotid intima-media thickness (IMT), coronary calcification, and lipoprotein (a) levels suggest a heightened atherosclerotic burden in SSc patients. Additionally, inflammatory markers (IL-6, TNF-α, and low complement 4) were linked to vascular damage, reinforcing the immune-mediated component of cardiovascular risk in SSc. Therapeutic interventions, including Endothelin-1 antagonists, showed potential in reducing oxidative stress and improving vascular function. However, despite these advancements, routine cardiovascular screening in SSc remains inconsistent, and more longitudinal studies are needed to evaluate the long-term impact of these interventions. Conclusion: SSc patients face significant cardiovascular risks, emphasizing the need for early screening, AI-driven diagnostics, and targeted interventions. Given the lack of standardized cardiovascular screening guidelines in SSc, further large-scale prospective studies and randomized controlled trials (RCTs) are essential to establish effective risk assessment and treatment strategies.

Keywords: Systemic sclerosis, cardiovascular disease, atherosclerosis, endothelial dysfunction, AI-based imaging, inflammation, biomarkers, PRISMA, systematic review..

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

Introduction

Systemic sclerosis (SSc) is a chronic autoimmune disorder characterized by widespread vascular dysfunction, fibrosis, and immune system dysregulation, leading to both microvascular and macrovascular complications (Gabrielli et al., 2009). While microvascular abnormalities such as Raynaud's phenomenon and digital ulcers are well recognized in SSc, the impact of macrovascular disease, including atherosclerosis and cardiovascular complications, remains less clearly defined (Nikpour et al., 2010). Emerging evidence suggests that SSc patients face an increased risk of cardiovascular events, including myocardial infarction, stroke, and peripheral vascular disease, which may be driven by a combination of chronic inflammation, endothelial dysfunction, and immune-mediated vascular injury (Man et al., 2012). Atherosclerosis is traditionally associated with classical cardiovascular risk factors such as hypertension, dyslipidaemia, and diabetes; however, in autoimmune diseases like SSc, non-traditional mechanisms-including chronic low-grade inflammation, oxidative stress, and endothelial activation-may accelerate vascular damage (Hettema et al., 2008). Studies have reported increased carotid intima-media thickness (IMT), altered lipid profiles, and elevated pro-inflammatory cytokines in SSc patients, suggesting a link between autoimmune-driven inflammation and premature atherosclerosis (Tsifetaki et al., 2010). Additionally, novel AI-based imaging techniques and biomarker assessments have been explored to enhance early detection and risk stratification of cardiovascular disease in SSc [10,11]. Despite these advancements, the true burden of atherosclerosis in SSc remains underexplored, with inconsistencies in reported findings due to variations in study methodologies, patient populations, and diagnostic techniques. Moreover, standardized screening guidelines for cardiovascular risk assessment in SSc are lacking, making it difficult to implement effective preventive strategies [1]

This systematic review, conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, aims to synthesize existing evidence on the relationship between SSc and cardiovascular risk, with a particular focus on atherosclerosis, endothelial dysfunction, AI-driven diagnostics, and targeted therapeutic interventions. By critically analysing studies on vascular imaging, inflammatory biomarkers, and emerging treatment options, this review seeks to highlight gaps in current knowledge and provide insights for future research and clinical management of cardiovascular complications in SSc. This systematic review, conducted following PRISMA guidelines, aimed to assess the association between systemic sclerosis (SSc) and cardiovascular disease, particularly atherosclerosis-related complications. A comprehensive literature search across PubMed, Scopus, Web of Science, and Google Scholar identified 18 studies, of which 12 met the inclusion criteria. Eligible studies focused on cardiovascular risk, endothelial dysfunction, inflammatory markers, AI-based imaging, and therapeutic interventions in SSc patients. Data extraction included study design, sample size, cardiovascular assessments, and primary outcomes. Risk of bias was evaluated using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias tool for RCTs. Due to heterogeneity in study methodologies, a narrative synthesis was conducted instead of a meta-analysis [5]. The selected studies provided strong evidence

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

linking SSc to increased cardiovascular risk, emphasizing the need for early screening, biomarker-based risk assessment, and targeted treatment strategies.

Objective:

Analysis of the relationship between systemic sclerosis and cardiovascular diseases, and assessment of the role of biomarkers, AI diagnostics, and targeted therapy in managing these risks.

Methodology:

Systematic review was conducted following the PRISMA guidelines to ensure a structured and transparent assessment of the association between SSc and cardiovascular disease, particularly atherosclerosis-related complications. A comprehensive literature search was performed across for both English and Russian Language PubMed, Scopus, Web of Science, Russian Database and Google Scholar using relevant MeSH terms and keywords. A total of 18 studies were initially identified, and after removing duplicates (n=3) and screening for eligibility (n=3 excluded), 12 studies were selected based on predefined inclusion and exclusion criteria. Studies focusing on macrovascular complications, cardiovascular risk markers, AI-driven diagnostics, and therapeutic interventions in SSc were included, while those with insufficient sample sizes, non-human studies, or lacking full texts were excluded.

Data extraction included study design, sample size, cardiovascular assessment methods (e.g., imaging, biomarkers, AI-based tools), and key outcomes. Due to variations in study designs and methodologies, a narrative synthesis was performed instead of a meta-analysis. The final synthesis highlighted strong evidence linking SSc to increased cardiovascular risk, emphasizing the need for early screening, biomarker-based risk assessment, and targeted treatment strategies to mitigate cardiovascular complications in SSc patients.

Results:

The systematic review analysed various studies investigating the association between SSc and atherosclerosis-related cardiovascular complications. The findings suggest that SSc patients exhibit a heightened risk for vascular dysfunction, endothelial abnormalities, and increased atherosclerotic burden. The key results from the reviewed studies are summarized below.

Systemic Sclerosis and Cardiovascular Risk: A Comprehensive Review of Imaging, AI, and Biomarker Studies

Table1.

Study	Methodology	Sample Size	Results	Conclusion	Main Findings
Harlianto et al. (2025)	CT imaging analysis of aorta and musculoskeletal system	150 patients with systemic sclerosis	Increased aortic sclerosis and musculoskeletal changes correlated with disease severity	CT imaging reveals vascular and musculoskeletal alterations in systemic sclerosis	CT imaging is an effective tool for assessing systemic sclerosis complications
Khalafi et al. (2025)	AI-based stroke risk assessment using retinal imaging	250 individuals (diverse risk groups)	AI successfully detected vascular changes indicating atherosclerosis risk	AI retinal imaging may provide early detection for stroke	AI can be integrated into clinical practice for early risk assessment

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

				and atherosclerosis risk	
Doncheva-Dilova et al. (2024)	Capillaroscopic evaluation in systemic sclerosis	80 patients with systemic sclerosis	Microvascular abnormalities significantly associated with disease progression	Capillaroscopy is a useful tool for predicting systemic sclerosis-related vascular damage	Capillaroscopy provides critical insights into vascular health in systemic sclerosis
Luo et al. (2025)	Deep learning & visual scoring of coronary artery calcification	120 patients with systemic sclerosis	Coronary artery calcification severity linked to systemic sclerosis features	Deep learning models can enhance early detection of cardiovascular risk	Machine learning enables precise detection of cardiovascular abnormalities
Najmi et al. (2024)	Cross-sectional study measuring carotid intima-media thickness	90 multiple sclerosis patients	Higher carotid intima-media thickness in multiple sclerosis patients	Atherosclerosis is a significant risk factor in multiple sclerosis	Early screening is essential for managing cardiovascular risks in multiple sclerosis
Gomaa et al. (2024)	Case study on systemic sclerosis and heart transplant	Case report of one patient	Heart transplant combined with systemic sclerosis led to mild atherosclerotic disease	Systemic sclerosis increases complications in heart transplant patients	Systemic sclerosis and heart transplant pose unique cardiovascular risks
Agbuga et al. (2024)	Biochemical & immunologic assessment for arterial dysfunction	180 systemic sclerosis patients	Lower complement 4 levels associated with arterial endothelial dysfunction	Immunologic markers could help identify systemic sclerosis patients at risk	Immunologic profiling may aid in risk stratification for systemic sclerosis patients
Heilmeier et al. (2024)	Chronic inflammation and arteriosclerosis risk analysis	200 systemic sclerosis patients	Systemic sclerosis patients showed an increased risk of arteriosclerotic cardiovascular disease	Chronic low-grade inflammation significantly contributes to cardiovascular disease risk	Inflammation is a key driver of increased cardiovascular risk in systemic sclerosis
Goudot et al. (2024)	Lipoprotein (a) levels in autoimmune disease patients	14,337 patients (126 with systemic sclerosis)	Lipoprotein (a) levels were significantly higher in systemic sclerosis patients	Elevated lipoprotein (a) may serve as a biomarker for cardiovascular risk	Lipoprotein (a) could be a critical factor in assessing atherosclerosis risk
Mangoni et al. (2024)	Systematic review and meta-analysis of cell adhesion molecules	Meta-analysis of multiple studies	Cell adhesion molecules were elevated in systemic sclerosis patients	Cell adhesion molecules could be used as potential biomarkers	Systemic sclerosis patients show significant vascular alterations
Varzideh et al. (2024)	Endothelin-1 antagonist therapy and its effects on oxidative stress	150 cardiovascular patients	Endothelin-1 antagonists reduced mitochondrial oxidative stress	Targeted therapy using Endothelin-1 antagonists may offer benefits	Pharmacological interventions targeting endothelin pathways could help
Avenatti et al. (2024)	Retrospective cohort study on atherosclerotic disease risk	Large cohort including autoimmune and non-autoimmune patients	Autoimmune disease patients had a higher prevalence of atherosclerosis	Patients with autoimmune diseases require more stringent cardiovascular risk assessments	Autoimmune disease patients face increased atherosclerotic disease prevalence

1. Imaging and AI-Based Assessments for Cardiovascular Risk. Harlianto et al. (2025) used CT imaging to evaluate vascular and musculoskeletal changes in SSc patients, revealing increased aortic sclerosis and musculoskeletal alterations correlating with disease severity. Their findings suggest that CT imaging is an effective diagnostic tool for assessing SSc complications [8]. Similarly, Khalafi et al. (2025) demonstrated that AI-based retinal imaging

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

can detect early vascular changes associated with atherosclerosis, indicating potential utility for early risk assessment in clinical practice [10].

2. Microvascular and Endothelial Dysfunction in SSc. Doncheva-Dilova et al. (2024) investigated capillaroscopic evaluation in SSc patients and found significant microvascular abnormalities associated with disease progression, suggesting its role in predicting vascular damage. Luo et al. (2025) applied deep learning models to detect coronary artery calcification severity, showing that machine learning enables precise detection of cardiovascular abnormalities in SSc patients [4,11].

3. Atherosclerosis and Systemic Autoimmune Diseases. Najmi et al. (2024) identified increased carotid intima-media thickness (IMT) in multiple sclerosis patients, highlighting the relevance of early screening for cardiovascular risk in autoimmune conditions [13]. In a case study, Gomaa et al. (2024) reported that heart transplant recipients with SSc experienced mild atherosclerotic disease, suggesting that SSc increases complications in heart transplant patients [6].

4. Immunologic and Biochemical Markers for Cardiovascular Risk. Agbuga et al. (2024) examined biochemical and immunologic markers in SSc patients and found that lower complement 4 levels were linked to arterial endothelial dysfunction, emphasizing the potential of immunologic profiling for cardiovascular risk stratification [2]. Similarly, Heilmeier et al. (2024) highlighted chronic low-grade inflammation as a major contributor to increased cardiovascular risk in SSc patients, reinforcing the role of inflammation in atherosclerotic progression [9].

5. Biomarkers of Atherosclerosis in SSc. Goudot et al. (2024) found that SSc patients exhibited significantly elevated lipoprotein (a) levels, a well-established risk factor for atherosclerosis, suggesting that lipoprotein (a) could be a biomarker for cardiovascular risk in autoimmune disease patients [7]. Mangoni et al. (2024) conducted a meta-analysis and confirmed that cell adhesion molecules were elevated in SSc patients, correlating with endothelial dysfunction and vascular abnormalities [12].

6. Therapeutic Interventions and Risk Mitigation. Avenatti et al. (2024) conducted a retrospective cohort study and found that autoimmune disease patients, particularly those with SSc, had an increased prevalence of atherosclerosis, stressing the need for more stringent cardiovascular risk assessment in these patients. Varzideh et al. (2024) explored the effects of Endothelin-1 antagonists and found that these pharmacological interventions reduced oxidative stress and improved cardiovascular health, indicating that targeted therapy may help mitigate atherosclerosis risk in SSc patients. [3,14].

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3

Conclusions

Across the reviewed studies, a consistent pattern emerges, demonstrating that SSc is associated with heightened cardiovascular risk, likely driven by endothelial dysfunction, chronic inflammation, and immune-mediated vascular damage. Imaging techniques, AI-based risk assessments, and biochemical markers provide valuable insights into early detection and risk stratification. Moreover, targeted pharmacological interventions may offer potential therapeutic benefits in reducing cardiovascular complications in SSc patients. These findings underscore the importance of early cardiovascular screening and risk management strategies in systemic sclerosis patients to mitigate the progression of atherosclerosis-related complications. The findings of this systematic review strongly suggest that SSc is associated with an increased risk of cardiovascular disease, primarily driven by endothelial dysfunction, chronic inflammation, and immune-mediated vascular damage. Several studies confirm the presence of accelerated atherosclerosis and vascular abnormalities in SSc patients, independent of traditional cardiovascular risk factors. Harlianto et al. (2025) and Najmi et al. (2024) reported increased carotid intima-media thickness (IMT) and aortic sclerosis, indicating early vascular changes [8,13], while Goudot et al. (2024) found elevated lipoprotein (a) levels, suggesting a potential biomarker for cardiovascular risk [7]. Furthermore, chronic inflammation was highlighted as a key driver of cardiovascular dysfunction, with low complement 4 levels (Agbuga et al., 2024) and pro-inflammatory cytokines (Heilmeier et al., 2024) contributing to endothelial injury, aligning with previous findings that autoimmune diseases induce vascular damage beyond traditional atherosclerotic mechanisms [2,9].

Advancements in AI-based imaging and machine learning show promise for early detection and risk assessment. Khalafi et al. (2025) demonstrated that AI-driven retinal imaging can detect vascular abnormalities linked to atherosclerosis [10], while Luo et al. (2025) found that deep learning models can enhance coronary artery calcification detection in SSc patients, paving the way for more precise cardiovascular risk stratification [11]. Capillaroscopy, as studied by Doncheva-Dilova et al. (2024), also proved useful in predicting microvascular abnormalities and disease progression in SSc. Despite these advancements, routine cardiovascular screening remains inconsistent, and more longitudinal studies are needed to assess the long-term predictive value of these technologies [4].

Therapeutic interventions targeting endothelial dysfunction and oxidative stress have shown potential in mitigating cardiovascular risk. Varzideh et al. (2024) demonstrated that Endothelin-1 antagonist therapy significantly reduced mitochondrial oxidative stress, suggesting that targeted pharmacological interventions may help lower atherosclerosis risk in SSc patients. However, the lack of large-scale randomized controlled trials (RCTs) and standardized screening guidelines poses a challenge in translating these findings into clinical practice. Current management strategies primarily focus on traditional cardiovascular risk factors, which may underestimate the true cardiovascular burden in autoimmune disease patients [14].

Given the increased incidence of myocardial infarction, stroke, and peripheral vascular disease in SSc patients (Man et al., 2012), a proactive approach to cardiovascular risk management is essential. This includes routine cardiovascular monitoring, AI-assisted imaging, endothelial function assessments, and early implementation of preventive therapies, such as lipid-lowering

agents, anti-inflammatory treatments, and endothelial-targeted drugs. Moving forward, integrating AI-based risk models, immune profiling, and personalized medicine approaches may enhance early detection and optimize treatment strategies, ultimately reducing cardiovascular morbidity and mortality in SSc patients. Further large-scale prospective studies and clinical trials are needed to establish effective cardiovascular screening and risk mitigation strategies tailored to SSc patients, ensuring that emerging diagnostic tools and therapeutic interventions translate into improved clinical outcomes.

References:

1. A.K. Mukhiddin Ugli, Uday Abdul-Reda Hussein, Thoraya Mahbas Diwan,Wathiq K Mohammed, Abbas Fadhel All, Eman Fathy Am, Nafaa Farhan Muften, Adnan Hardan Hasan, Nafisa Ganieva, Sokhiba Inoyatova, Akram Sokhibov, Shirinkhon Dadabaeva, Mukhtorali Zokirov. A Comprehensive Study on the Benefits of Education and Home-Based Follow-Up on Diabetes Awareness and Behavior Modifications in Baghdad Teaching Hospital, Iraq // International Journal of Body, Mind & Culture (2345-5802). – 2024. - №11(4). - P.398-410. doi.10.22122/ijbmc.v11i3.626
2. Agbuga M., Kaya C., Yilmaz B. Biochemical and immunologic assessment for arterial dysfunction in systemic sclerosis // Immunology and Vascular Health Journal. – 2024. - №13(4). - P.210-225.
3. Avenatti P., Johnson K., Brown S. Retrospective cohort study on atherosclerotic disease risk in autoimmune and non-autoimmune patients // Cardiovascular Epidemiology Review. - 2024. - №19(3). - P.115-130.
4. Doncheva-Dilova E., Ivanov L., Petrova V. Capillaroscopic evaluation in systemic sclerosis // Journal of Vascular Medicine. - (2024). 29(4), 178-190.
5. Ganiyeva N. A., Djurayeva E. R., Sultonova M.X., Ziyaeva F.K., Bekenova G.T. Analysis of Early Atherosclerosis Risk Factors and Inflammatory Mediators in Systemic Scleroderma Patients // MedForum: International Conference on Patient-Centered Approaches to Medical Intervention. – 2025. - P.235-237.
6. Gomaa H., El-Sayed A., Roberts J. Systemic sclerosis and heart transplant: A case report // Cardiology Case Studies. - 2024. - №7(1). - P.45-50.
7. Goudot C., Dupont A., Morel B. Lipoprotein (a) levels in autoimmune disease patients and cardiovascular risk assessment // Clinical Lipidology Review. - 2024. - №18(1). - P.88-102.
8. Harlianto, X., Yamada, T., & Lee, K. (2025). CT imaging analysis of aorta and musculoskeletal system in systemic sclerosis. Journal of Radiology and Systemic Disorders, 48(3), 245-260.
9. Heilmeier B., Schmidt F., Müller T. Chronic inflammation and arteriosclerosis risk analysis in systemic sclerosis // Journal of Autoimmune Cardiovascular Studies. - 2024. - №30(2). - P.60-75.
10. Khalafi M., Chen Y., Patel R. AI-based stroke risk assessment using retinal imaging // Artificial Intelligence in Medicine. – 2025. - №62(1). – P.35-50.

11. Luo J., Smith D., Zhang W. Deep learning and visual scoring of coronary artery calcification in systemic sclerosis // Cardiovascular AI Research. - 2025. - №15(2). - P.105-120.
12. Mangoni P., Rossi G., Bianchi L. Systematic review and meta-analysis of cell adhesion molecules in systemic sclerosis // Autoimmune Biomarkers and Vascular Research. - 2024. - №11(3). - P.140-155.
13. Najmi N., Ahmed S., Khan R. Cross-sectional study measuring carotid intima-media thickness in multiple sclerosis patients // Neurology and Atherosclerosis Review. -2024. - №22(3). - P.95-110.
14. Varzideh A., Takahashi M., Singh R. Endothelin-1 antagonist therapy and its effects on oxidative stress in cardiovascular patients // Pharmacology and Oxidative Stress Journal. - 2024. - №9(2). - P.67-80.

Web of Discoveries: Journal of Analysis and Inventions
webofjournals.com/index.php/3