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Evolution and frontiers of research on systemic lupus erythematosus and coronary atherosclerosis

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Abstract

Objective: The accelerated development of coronary atherosclerosis represents a major cause of morbidity and mortality in patients with systemic lupus erythematosus. While the clinical association is well-established, a comprehensive, data-driven analysis of the global research landscape, emerging trends, and their integration with pathobiological mechanisms are lacking.

Methods: We performed bibliometric analysis of publications from 2006 to 2025 in Web of Science, using VOSviewer, CiteSpace, Microsoft Excel, GraphPad Prism, and R for scientific mapping and network analysis.

Results: Analysis of 632 publications revealed the United States as the dominant contributor, leading in publications (207), citations (10,833), and international collaborations. A core author network established foundational knowledge, while the research focus evolved from initial epidemiological observations to mechanistic investigations of immune-inflammatory pathways and lipid dysfunction, and, more recently, to biomarker discovery and precision medicine approaches.

Conclusion: The field of systemic lupus erythematosus and coronary atherosclerosis has matured through distinct phases, with current research emphasizing molecular mechanisms and personalized risk assessment. These findings provide valuable insights for guiding future investigations and developing targeted cardiovascular protection strategies for SLE patients.

Introduction

Coronary Atherosclerosis (CAS), the primary pathological basis of coronary artery disease, is characterized by lipid deposition in the arterial intima, chronic inflammation, and the formation of fibrous plaques, ultimately leading to myocardial ischemia, myocardial infarction, or even sudden cardiac death. Atherosclerotic cardiovascular disease remains the leading cause of mortality and disability worldwide. Its incidence continues to rise globally, posing a major global health challenge [1]. In recent years, immune-mediated chronic inflammation contributes significantly to the onset and advancement of atherosclerotic disease.

Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disorder characterized by the sustained production of autoantibodies and immune complex deposition, leading to diverse and complex clinical manifestations [2]. With advancements in diagnostic and therapeutic strategies, the long-term survival rates of SLE patients have improved significantly. Consequently, cardiovascular events have emerged as a leading cause of mortality in this population [3]. SLE patients exhibit a substantially increased risk of premature coronary atherosclerosis compared to the general population, with a particularly pronounced risk among young, premenopausal women [4]. Traditional risk factors alone cannot fully explain this excessive risk, suggesting shared pathological underpinnings

such as immune dysregulation, chronic inflammation, oxidative stress, complement activation, and endothelial dysfunction.

Current research on the comorbidity of SLE and coronary atherosclerosis primarily focuses on elucidating pathophysiological mechanisms and improving clinical risk assessment. However, a comprehensive, systematic analysis of the scientific knowledge landscape, evolving research trends, core author groups, and collaborative networks within this field remains lacking. Therefore, this study employs bibliometric methods, utilizing VOSviewer and CiteSpace, to conduct a visual analysis of the scientific literature published between 2006 and 2025 concerning the relationship between SLE and coronary atherosclerosis. By integrating theoretical insights with the practical evidence base of this comorbidity, this study aims to offer a valuable reference and direction for future research endeavors.

Methods

Data sources and search strategy

The data for this bibliometric analysis were retrieved from the Web of Science Core Collection (WoSCC), a leading database recognized for its high-quality and multidisciplinary coverage of scientific literature. WoSCC supports the direct export of records in plain-text records that are fully compatible with commonly used visualization tools such as VOSviewer and CiteSpace. A systematic literature search was conducted to identify publications related to the association between SLE and CAS. The search encompassed articles published from 1 January 2006 to 31 October 2025. The following topic-based search strategy was applied in WoSCC: TS=((“systemic lupus erythematosus”) AND (“coronary arteriosclerosis” OR “coronary atherosclerosis” OR “coronary disease” OR “coronary artery disease” OR “coronary heart disease” OR “ischemic heart disease”)). To ensure reproducibility and minimize potential biases during literature retrieval, screening, and extraction of data, two investigators independently performed the search and evaluated the eligibility of the retrieved records. Any discrepancies in judgment were resolved through discussion or, when necessary, by consulting a third researcher. To maintain temporal consistency, all data were downloaded on the same day.

Inclusion and exclusion criteria

To ensure analytical relevance and quality, the selection of literature was conducted in accordance with predefined inclusion and exclusion criteria. A total of 1,008 records were initially retrieved. Of these, none were excluded for being outside the specified publication period. Non-research and review document types, including conference abstracts (n=6), editorials (n=3), and letters (n=2), as well as non-English language publications (n=2), were excluded. In addition, studies not related to SLE (n=122), not associated with CAS (n=106), or irrelevant to both conditions (n=135) were removed. Ultimately, 632 publications were included in the final analysis. These included original research articles and review papers published in English between 1 January 2006 and 31 October 2025 that specifically addressed the association between SLE and CAS (Figure 1). To maintain objectivity and consistency, all screening procedures were independently performed by two investigators.

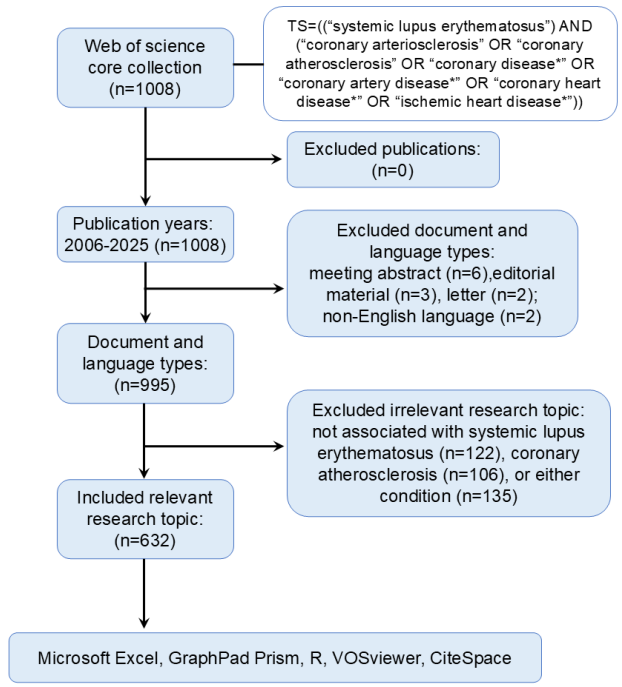

Figure 1: Flowchart of literature screening.

Data visual software and statistical analysis

After retrieval of records from the WoSCC, the dataset underwent a comprehensive data cleaning protocol. This process involved removing duplicate entries and standardizing terminology (e.g., author names, keyword spellings) to ensure consistency and integrity for subsequent computational analysis. Bibliometric analysis and visualization were conducted using several established software tools. Microsoft Excel (version 2021) was utilized for preliminary analyses, including the calculation of annual publication outputs and citation trends. GraphPad Prism (version 10.1.2) was used to generate the productivity of leading countries and institutions. Chord diagrams illustrating collaborations between countries and institutions were created using the *circlize package* in R. For more in-depth bibliometric mapping and analysis of countries/regions, institutions, keywords, and references, VOSviewer (version 1.6.20) and CiteSpace (version 6.2. R4) were utilized.

Results

Trends in the co-occurrence of SLE and CAS

Based on the WoSCC database and predefined screening criteria, a total of 632 eligible publications were included for bibliometric analysis (Figure 2). Overall, research productivity maintained a relatively strong momentum during 2006-2011, peaking around 2007–2009, followed by a gradual decline. After 2019, a marked decrease was observed, with the lowest publication numbers in 2023 and 2024. A slight rebound appeared in the most recent data, indicating that despite the overall downward trend, scholarly interest in the comorbidity between SLE and CAS persists.

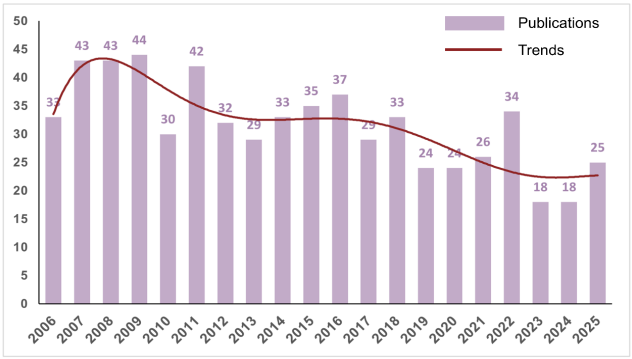

Figure 2: Trends in the co-occurrence of SLE and CAS.

Contributions of countries and institutions

A bibliometric analysis was conducted to evaluate the contributions and influence of various countries and institutions in the field of research on SLE and CAS. The United States of America (U.S.A.) led globally with 207 publications, and also ranked first in both total citations (10,833) and total link strength (123), reflecting its dominant role and central position in the global collaborative network in this field. The United Kingdom with 81 publications, along with high total citations (5,854) and link strength (109), forming together with the U.S.A., the core of the international collaboration network. Countries such as Canada, Italy, and Spain also exhibited substantial link strength (all above 60), indicating active international collaboration. In contrast, although China ranked fourth in publication output (46 articles), it recorded relatively low total citations (909) and link strength (6), suggesting that the international impact and integration of its research warrant further enhancement (Table 1, Figure 3A).

To visually represent collaborative relationships between countries, a chord diagram was generated based on the top 20 countries ranked by link strength (Figure 3B). In this diagram, each colored arc represents a country, with arc length proportional to its publication output. Ribbons connecting the arcs represent collaborative ties, with thickness corresponding to collaboration strength (i.e., the number of co-authored publications). The chord diagram reveals that the U.S.A. established collaborations with all countries listed, while the United Kingdom, Canada, and others maintained extensive connections with most nations. By comparison, China's collaborations were largely limited to the U.S.A. and Germany.

At the institutional level (Table 2, Figure 3C), the University of Toronto emerged as the most productive institution, with the highest number of publications (29) and the greatest total link strength (24), demonstrating high research output and extensive collaborative networks. Johns Hopkins University and the University of Manchester each produced 20 publications and achieved notably high citation counts (1,496 and 1,979, respectively). The institutional collaboration chord diagram (Figure 3D) further revealed that the University of Toronto formed a closely interconnected research cluster with Toronto Western Hospital, University Health Network, and other local institutions. This cluster engaged not only in intensive internal collaboration but also sustained partnerships with international institutions such as the University of Manchester and the University of Melbourne, facilitating knowledge exchange and collaborative output.

Table 1: Top 10 countries by publications, total citations, and total link strength.

Rank	Countries	Publications	Total citations	Total link strength
1	USA	207	10,833	123
2	UK	81	5,854	109
3	Canada	58	3,213	64
4	China	46	909	6
5	Spain	42	1,962	61
6	Italy	40	2,123	64
7	Greece	33	1,541	46
8	Sweden	31	1,683	48
9	Brazil	26	613	4
10	Mexico	23	564	40

Table 2: Top 10 institutions by publications, total citations, and total link strength.

Rank	Institutions	Publications	Total citations	Total link strength
1	University Toronto	29	1,228	24
2	Johns Hopkins University	20	1,496	12
3	University Manchester	20	1,979	10
4	Emory University	18	1,048	13
5	Vanderbilt University	15	728	11
6	Karolinska Inst	14	424	1
7	Onassis Cardiac Surg Center	12	281	9
8	Toronto Western Hospital	12	500	18
9	University Calif Los Angeles	11	748	4
10	Northwestern University	10	299	2

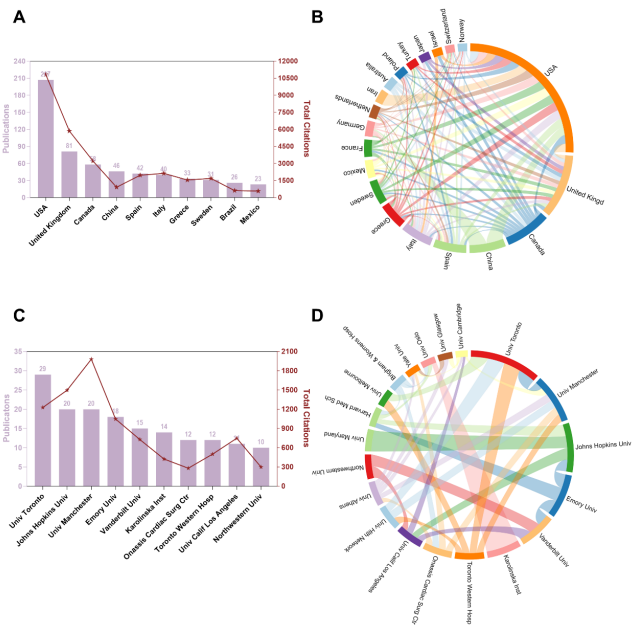

Figure 3: Profile of publications and citations across countries and institutions. **(A)** Top 10 countries by publications, total citations. **(B)** Chord diagram of cooperation among the top 20 countries for total link strength. **(C)** Top 10 institutions by publications, total citations. **(D)** Chord diagram of cooperation among the top 20 institutions for total link strength.

Contributions of authors and journals

In the research field of SLE and CAS, the author network is dominated by a core group of highly influential scholars. The top three most prolific authors were Gladman DD (18 publications), Urowitz MB (16 publications), and Petri MA (12 publications). These authors also ranked among the highest in total citations (996, 958, and 834, respectively), reflecting their sustained academic influence (Table 3). In the co-authorship network, Gladman DD (total link strength 39), Urowitz MB (37), and Ibanez D (25) show the strongest collaborative ties, forming the central cluster in this field. Co-citation analysis (Table 4) further identified that Petri MA (469 co-citations, link strength 7,036), Manzi S (430 co-citations, link strength 5,765), and Urowitz MB (361 co-citations, link strength 5,449) as the top three most co-cited authors, indicating that their work is widely recognized and frequently referenced. In the VOSviewer co-citation network map (Figure 4A), node size represents academic influence, connecting lines indicate collaborative co-citation strength, and colors distinguish thematic clusters. Petri MA and Manzi S anchor the red cluster, Ridker PM leads the green cluster, and McMahon M dominates is central to the blue cluster, collectively illustrating a research landscape shaped by a compact group of highly productive and highly cited experts.

Regarding journal distribution, publications in this field are concentrated primarily in rheumatology and immunology journals. *Lupus* (67), *Journal of Rheumatology* (32), and *Rheumatology* (26) were the most productive journals and also received the highest citation counts (1,842, 1,621, and 1,461, respectively), underscoring their authority and academic influence (Table 5). Additionally, *Journal of Rheumatology* (total link strength 260), *Lupus* (230), and *Rheumatology* (113) functioned as central hubs in the collaboration network, facilitating scholarly communication. Co-cited journal analysis (Table 6) revealed *Arthritis & Rheumatology* (3,171 co-citations, link strength 185,092), *Circulation* (2,074 citations, link strength 143,788), and *Journal of Rheumatology* (1,876 citations, link strength 121,326) as the three most influential co-cited journals, all of which are high-impact outlets in cardiovascular and rheumatology research. Visualization of co-cited journals (Figure 4B), further delineated three major clusters: the blue cluster encompasses core rheumatology journals (e.g., *Arthritis & Rheumatology*, *Annals of the Rheumatic Diseases*, *Lupus*); the green cluster focuses on cardiovascular and metabolic research (e.g., *Circulation*, *New England Journal of Medicine*, *Lancet*, *Arteriosclerosis*); and the red cluster highlights immunology and thrombosis-related journals (e.g., *Arteriosclerosis Thrombosis and Vascular Biology*, *Blood*, *Journal of Immunology*). Together, these patterns reflect a strong interdisciplinary integration between rheumatology/immunology and cardiovascular research.

Table 3: Top 10 authors by publications, total citations, and total link strength.

Rank	Authors	Publications	Total citations	Total link strength
1	Gladman DD	18	996	39
2	Urowitz MB	16	958	37
3	Petri MA	12	834	6
4	Rahman A	11	495	6
5	Bruce IN	9	236	6
6	Ibanez D	9	694	25
7	Su JD	7	218	14
8	Isenberg DA	6	256	5
9	Magder LS	6	258	6
10	Mavrogeni S	6	167	4

Table 4: Top 10 co-cited authors of co-citations and total link strength.

Rank	Authors	Co-citations	Total link strength
1	Petri MA	469	7,036
2	Manzi S	430	5,765
3	Urowitz MB	361	5,449
4	Bruce IN	329	5,012
5	Roman MJ	297	4,218
6	Esdaile JM	236	3,288
7	Ridker PM	222	2,344
8	Svenungsson E	193	3,083
9	Asanuma Y	192	2,859
10	Mcmahon M	174	2,975

Table 5: Top 10 journals by publications, total citations, and total link strength.

Rank	Journals	Publi-cations	Total citations	Total link strength	IF (JCR)
1	Lupus	67	1,842	230	1.9 (Q3)
2	Journal of Rheumatology	32	1,621	260	3.7 (Q2)
3	Rheumatology	26	1,461	113	4.7 (Q1)
4	Arthritis Research & Therapy	17	703	97	4.6 (Q1)
5	Clinical Rheumatology	17	231	38	2.8 (Q2)
6	Autoimmunity Reviews	14	1,022	62	8.3 (Q1)
7	Atherosclerosis	12	728	31	5.7 (Q1)
8	Rheumatology International	12	248	39	2.9 (Q2)
9	Arthritis Care & Research	10	670	79	3.3 (Q1)
10	Arthritis & Rheumatology	9	927	79	10.9 (Q1)

Table 6: Top 10 co-cited journals of total citations and link strength.

Rank	Journals	Co-citations	Total link strength	IF (JCR)
1	Arthritis & Rheumatology	3171	185,092	10.9 (Q1)
2	Circulation	2074	143,788	38.6 (Q1)
3	Journal of Rheumatology	1876	121,326	3.7 (Q2)
4	Lupus	1777	115,500	1.9 (Q3)
5	Annals of the Rheumatic Diseases	1729	127,407	20.6 (Q1)
6	New England Journal of Medicine	1331	95,602	78.5 (Q1)
7	Rheumatology	1238	92,214	4.7 (Q1)
8	Atherosclerosis	720	56,896	5.7 (Q1)
9	Arteriosclerosis Thrombosis and Vascular Biology	697	52,273	7.4 (Q1)
10	Journal of the American College of Cardiology	691	46,158	22.3 (Q1)

Note: During data processing in this study, we identified that the journal *Arthritis & Rheumatism* was renamed *Arthritis & Rheumatology* in 2013. To ensure consistency and accuracy in our statistical analysis, all articles published before the name change were uniformly categorized under *Arthritis & Rheumatism*.

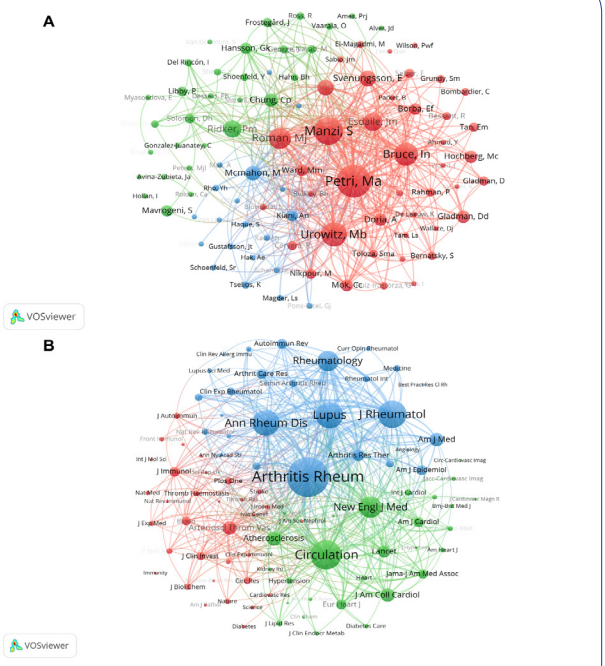

Figure 4: Visualization of author and journal co-citation networks. **(A)** Network of co-cited authors in the field of SLE and CAS. **(B)** Network of co-cited journals in the field of SLE and CAS.

Keywords co-occurrence, evolution, and burst analysis

Keywords analysis from the perspectives of co-occurrence distribution, temporal evolution, and burst detection provides a comprehensive overview of the knowledge structure and developmental trajectory of research on SLE and CAS. In the co-occurrence network generated by VOSviewer (Figure 5A), node size corresponds to keyword frequency, color indicates the temporal distribution of topics (2012–2018), and the density of connecting lines reflects the co-occurrence strength. Four major thematic clusters were identified. The first cluster centers on "risk factors" and "accelerated atherosclerosis," closely linked to terms such as "coronary artery disease" and "myocardial infarction," constituting a cluster focused on cardiovascular risk mechanisms. The second cluster emphasizes immune–metabolic regulation, featuring keywords like "inflammation," "metabolic syndrome," "c-reactive protein," and "low-density lipoprotein," highlighting metabolic–inflammatory crosstalk. The third cluster includes terms such as "prevalence," "mortality," and "intima-media thickness," representing clinical epidemiology and imaging assessment. The fourth cluster consists of "women," "lupus nephritis," and "systemic sclerosis," reflecting research on specific populations and disease subtypes. These clusters form a cohesive research framework through dense co-occurrence linkages.

The CiteSpace time-zone view (Figure 5B) displays keyword evolution from 2006 to 2025, with the horizontal axis representing time and the vertical axis representing cluster categories (#0–#10). Node size denotes frequency, and connecting lines indicate thematic inheritance and cross-domain relevance. From 2006 to 2010, research emphasized fundamental cardiovascular risk factors and assessment metrics, including "atherosclerosis," "low density lipoprotein," and "intima media thickness." Between 2011 and 2018, the focus expanded to metabolic mechanisms (e.g., "insulin resistance," "metabolic syndrome"), immune regulation (e.g., "inflammation," "autoimmune diseases"), and imaging techniques such as "echocardiography." From 2019 onward, the field experienced rapid innovation, characterized by molecular and omics-related keywords like "complement," "vascular biology," and "genome wide association," alongside emerging drug-related terms (e.g., "aspirin"), suggesting a shift toward clinical translation.

Keyword burst analysis (Figure 5C) highlights research frontiers based on burst strength and duration between 2006 and 2025. Red bars indicate active burst periods, and burst strength reflects the intensity of frequency surges. Early hotspots (2006–2015) included vascular pathology and immune markers, such as "vascular disease," "antibody," "endothelial function," and "c-reactive protein." The middle period (2011–2020) shifted toward risk identification and immune-inflammatory mechanisms, featuring keywords like "risk factor," "predictors," and "tumor necrosis factor alpha." Notably, "subclinical atherosclerosis" has sustained high burst strength since 2016, signifying growing emphasis on early detection. Recent hotspots (2020–2025) include "cardiovascular diseases," "systemic," "validation," "lupus erythematosus," and "cardiovascular risk," underscoring increased focus on clinical validation and preventive strategies for systemic cardiovascular involvement. Overall, the research evolution has progressed from mechanistic exploration to risk prediction, and from subclinical identification to clinical validation, demonstrating a clear trend toward precision prevention and targeted intervention.

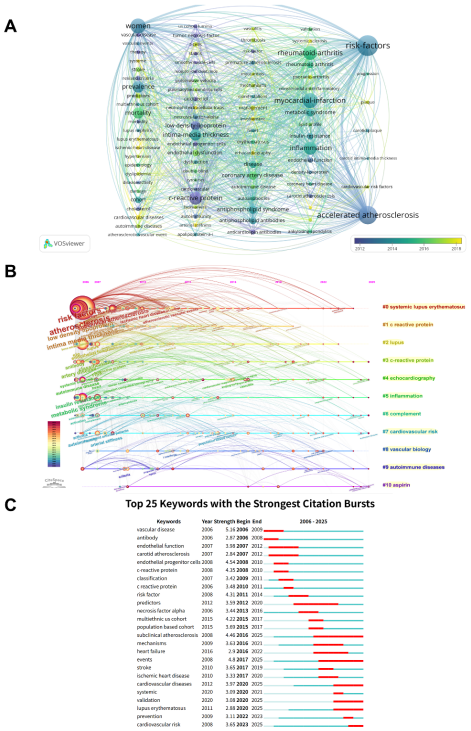

Figure 5: Keyword analysis of studies on SLE and CAS. **(A)** Keyword co-occurrence network. **(B)** Temporal evolution map of keywords. **(C)** Keyword burst analysis.

Highly cited publications and references analysis

Highly cited publications in this field reflect major research priorities and the evolution of scholarly understanding (Table 7). The study "Mean Platelet Volume: A Link Between Thrombosis and Inflammation?" by Gasparyan AY et al. ranks first with 1,013 citations. This work focuses on mean platelet volume as a marker of platelet activation and evaluates its role in assessing prothrombotic and inflammatory states. The authors highlight that platelet activation is closely associated with atherosclerotic

thrombosis, SLE, and other inflammatory disorders. Further insights are provided through co-citation analysis (Table 8). The study by Manzi S et al., published in the *American Journal of Epidemiology* (Q1), entitled "Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study," ranks first with 303 co-citations. This seminal work demonstrates that early-onset cardiovascular events—suggestive of accelerated atherosclerosis—are significantly more common in young premenopausal women with SLE than in the general population, providing essential epidemiological support for subsequent research.

The reference co-citation network (Figure 6A) identifies 16 thematic clusters, including mechanistic insight, literature review, metabolic syndrome, accelerated atherosclerosis, chronic inflammatory diseases, cardiovascular manifestation, and systemic sclerosis. The visualization encodes data visually: reference citation frequency by node size and co-citation strength by the density of the interconnecting lines. Clusters with denser connections show stronger thematic coherence and academic relevance. The author co-citation network (Figure 6B) further illustrates the distribution of influential authors and key publications. Color-coded nodes represent different clusters, and node size corresponds to citation frequency. High-impact authors and their pivotal works—such as Roman MJ (2003), Asanuma Y (2003), and Petri MA (2011)—are highlighted in red. These publications represent seminal contributions, with Roman MJ's 2003 study serving as a landmark in establishing the association between SLE and elevated cardiovascular risk.

An analysis of citation bursts among the top 25 references reveals distinct phases of intellectual development in this field (Figure 6C). During the early period (2003–2005), foundational studies by Roman MJ (2003) and Asanuma Y (2003) exhibited high burst strengths (24.31 and 13.63, respectively), addressing mechanisms and epidemiological evidence of accelerated atherosclerosis in SLE patients. In the middle period (2007–2012), studies by Urowitz MB (2007), Hak AE (2009), and others expanded the focus to cardiovascular risk management and biomarker discovery, with sustained burst durations. More recently (2019–2025), articles such as Petri MA (2019) continue to demonstrate strong citation bursts, emphasizing precision diagnosis and novel biomarkers in lupus-associated cardiovascular disease. These publications have been major drivers of current research hotspots.

Table 7: Top 10 cited publications.

Rank	Title	Journal	Author	JCR	Citations
1	Mean Platelet Volume: A Link Between Thrombosis and Inflammation?	Current Pharmaceutical Design	Gasparyan, Ay	Q2	1,013
2	Interplay Between Inflammation and Thrombosis in Cardiovascular Pathology	Nature Reviews Cardiology	Stark, K	Q1	615
3	Systemic Lupus Erythematosus: Diagnosis and Clinical Management	Journal of Autoimmunity	Fava, A	Q1	467
4	Neutrophil Extracellular Traps in Atherosclerosis and Atherothrombosis	Circulation Research	Döring, Y	Q1	396
5	Endothelial Dysfunction in Chronic Inflammatory Diseases	International Journal of Molecular Sciences	Steyers, Cm	Q1	369
6	Proinflammatory High-Density Lipoprotein as a Biomarker for Atherosclerosis in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis	Arthritis & Rheumatology	Mcmahon, M	Q1	336
7	Cardiovascular Disease in Patients with Chronic Inflammation: Mechanisms Underlying Premature Cardiovascular Events in Rheumatologic Conditions	European Heart Journal	Mason, Jc	Q1	308
8	Epidemiology of CVD in Rheumatic Disease, With a Focus on Ra and Sle	Nature Reviews Rheumatology	Symmons, Dpm	Q1	306
9	Mechanisms of Disease: Atherosclerosis in Autoimmune Diseases	Nature Clinical Practice Rheumatology	Sherer, Y	Q1	293
10	Cardiovascular Risk Reduction in High-Risk Pediatric Patients a Scientific Statement from the American Heart Association	Circulation	De Ferranti, Sd	Q1	284

Table 8: Top 10 co-cited references.

Rank	Title	Journal	Author	JCR	Citations
1	Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study	American Journal of Epidemiology	Manzi S	Q1	303
2	Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus	Arthritis & Rheumatology	Esdaile JM	Q1	231
3	Prevalence and correlates of accelerated atherosclerosis in systemic lupus erythematosus	New England Journal of Medicine	Roman MJ	Q1	208
4	Premature coronary-artery atherosclerosis in systemic lupus erythematosus	New England Journal of Medicine	Asanuma Y	Q1	154
5	Risk factors for coronary artery disease in patients with systemic lupus erythematosus	The American Journal of Medicine	Petri MA	Q1	137
6	Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus	Arthritis & Rheumatology	Hochberg MC	Q1	130
7	The bimodal mortality pattern of systemic lupus erythematosus	The American Journal of Medicine	Urowitz MB	Q1	129
8	Risk factors for coronary heart disease in women with systemic lupus erythematosus: the Toronto Risk Factor Study	Arthritis & Rheumatology	Bruce IN	Q1	112
9	Prevalence and risk factors of carotid plaque in women with systemic lupus erythematosus	Arthritis & Rheumatology	Manzi S	Q1	104
10	Risk factors for cardiovascular disease in systemic lupus erythematosus	Circulation	Svenungsson E	Q1	102

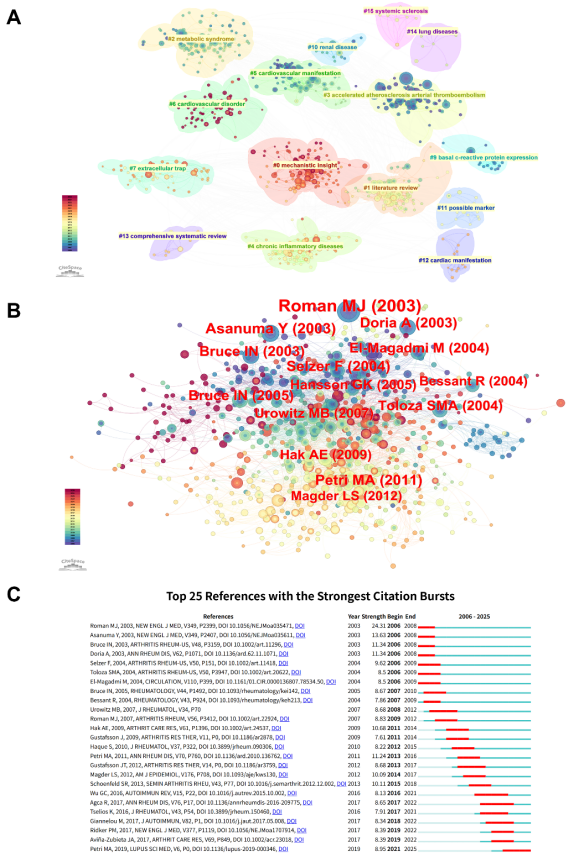

Figure 6: Visualization of reference in the field of SLE and CAS. **(A)** Research topic clustering based on reference. **(B)** High-impact author literature network map. **(C)** Top 25 references with the strongest citation bursts.

Discussion

This bibliometric study examines the breadth of worldwide research activity regarding the association between SLE and CAS from 2006 to 2025. By integrating quantitative visualization with mechanistic evidence, our study traces the evolution of scientific focus, highlights major contributors, and identifies translational research priorities. The findings demonstrate that research in this field has evolved from initial epidemiological observations to sophisticated mechanistic investigations, culminating in current efforts toward precision risk stratification and targeted interventions.

Research landscape and collaborative networks

A key finding of this study is the dominant academic influence of Western countries, particularly the United States, the United Kingdom, and Canada, which form the core of international collaboration networks (Table 1). These countries contribute not only the highest volume of publications but also sustain the highest citation impact and collaborative connectivity, indicating their leadership in shaping the conceptual and clinical understanding of SLE-associated atherosclerosis. In contrast, although China ranks among the top countries in terms of publication output, its lower citation count and limited link strength suggest relatively limited international integration and global visibility. Enhancing multinational collaboration and methodological rigor may help elevate the global impact of research from emerging regions.

At the institutional level (Table 2), the University of Toronto emerges as a hub of research productivity and collaboration, maintaining both local research clusters and extensive international ties. The high citation counts of institutions like Johns Hopkins University and the University of Manchester—despite moderate publication numbers—highlight that research quality and impact are not merely functions of output volume. These patterns underscore the importance of established collaborative networks in amplifying the reach and impact of scientific output in this interdisciplinary field.

Intellectual structure and knowledge evolution

Author contribution analysis reveals a concentrated research landscape in the study of SLE and CAS. A limited number of influential investigators—notably Gladman DD, Urowitz MB, and Petri MA—account for a substantial proportion of both publication output and citation impact, forming a tightly interconnected collaborative core (Table 3). Their sustained academic leadership is further reflected in their prominent roles in co-citation analysis, where they serve as foundational references for methodological and conceptual guidance. Co-citation clusters visualization demonstrates how these key investigators anchor distinct themes domains (Figure 4A): Petri MA and Manzi S are central to lupus-related mechanistic studies, Ridker PM leads cardiovascular risk research, and McMahon M anchors immunology-focused inquiry, collectively shaping the intellectual architecture of this interdisciplinary field.

Journal distribution patterns underscore the convergence of rheumatology and cardiovascular research. While specialty journals such as *Lupus* and *Journal of Rheumatology* account for the highest number of publications (Table 5), co-citation analysis identifies *Arthritis & Rheumatology*, *Circulation*, and *Journal of Rheumatology* as the most frequently cited sources (Table 6). The clear clustering observed in journal co-citation networks—distinguishing core rheumatology journals, cardiovascular/metabolic, and immunology/thrombosis journals—reflects the multidisciplinary foundations of this research area. This integration suggests that progress in elucidating the mechanisms link SLE and CAS relies on synergistic input from traditionally distinct scientific disciplines, with high-impact journals acting as crucial conduits for cross-disciplinary knowledge dissemination.

Evolution of research themes: From epidemiology to precision medicine

Keyword and citation analyses reveal three distinct evolutionary phases in the development of this research field. The initial phase (2006-2010) was characterized by foundational epidemiological studies that established the increased burden and premature onset of cardiovascular disease in SLE patients. Landmark publications from this period, including those by Roman MJ [5] and Manzi S [6], delineated the epidemiological basis of accelerated atherosclerosis in SLE, while the Framingham comparison by Manzi S et al. provided crucial age-stratified risk evidence that redefined cardiovascular risk assessment in young women with autoimmune conditions. The subsequent phase (2011-2018) witnessed a shift toward mechanistic investigations, with an emerging focus on immune-metabolic interactions, vascular dysfunction, and novel imaging modalities. This period saw increased attention to HDL dysfunction, oxidative stress, and endothelial activation as central pathogenic mechanisms. The recent phase (2019-2025) has been marked by a growing emphasis on molecular pathways and targeted interventions, including IFN-I signaling, NETs, T and B cell dysregulation, and autoantibody-mediated effects. This progression reflects an evolution from establishing

clinical associations to elucidating biological mechanisms and advancing toward precision medicine approaches.

Integration of mechanistic evidence: Pathobiological insights

The bibliometric clustering of high-frequency keywords—particularly "inflammation," "low-density lipoprotein," "risk factor," "subclinical atherosclerosis," and "tumor necrosis factor alpha"—highlights immune–metabolic crosstalk as the core pathogenic axis in SLE-associated coronary atherosclerosis. Mechanistically, sustained activation of IFN-I, a hallmark of SLE, promotes endothelial dysfunction by downregulating eNOS and reducing nitric oxide bioavailability, thereby impairing vasodilation and vascular repair [7]. IFN-I further activates the JAK–STAT pathway, suppresses endothelial progenitor cell survival, and enhances expression of adhesion molecules such as VCAM-1 and ICAM-1, facilitating leukocyte recruitment and vascular inflammation [8,9]. In parallel, excessive formation and defective clearance of neutrophil extracellular traps amplify TLR- and STING-dependent signaling, augment oxidative stress, and induce inflammasome activation, reinforcing a feed-forward inflammatory loop [10-13]. These mechanisms correspond closely to the persistent keyword bursts related to "endothelial function," "antibody," and "tumor necrosis factor alpha," underscoring chronic immune activation as a sustained research frontier.

Concurrently, the co-occurrence of "low-density lipoprotein," "metabolic syndrome," and "c-reactive protein" reflects the importance of lipid dysfunction and systemic inflammation. In SLE, HDL undergoes structural and functional remodeling, characterized by reduced ApoA1 content, diminished PON1 activity, and increased oxidation, resulting in a shift toward a pro-inflammatory phenotype that weakens reverse cholesterol transport [14-16]. Simultaneously, heightened susceptibility to LDL oxidation leads to elevated circulating ox-LDL, which enhances endothelial adhesion molecule expression, promotes macrophage lipid uptake and foam-cell formation, and accelerates necrotic core expansion [17]. PCSK9 upregulation further exacerbates LDL receptor degradation and vascular inflammation [18,19]. Pathogenic autoantibodies—including antiphospholipid antibodies and anti-dsDNA antibodies—synergize with dyslipidemia by activating complement, inducing endothelial injury, and forming pro-inflammatory immune complexes with ox-LDL and β2GPI, thereby intensifying plaque progression [20-22]. Collectively, these interwoven immune-inflammatory and lipid-metabolic disturbances create a pro-oxidative, pro-atherogenic vascular microenvironment, providing mechanistic substantiation for the bibliometric transition from mechanistic exploration to early detection and cardiovascular risk validation.

Clinical implications and future directions

Recognition of the heightened burden of coronary atherosclerosis in patients with SLE carries critical consequences for clinical practice. First, cardiovascular risk assessment in SLE should go beyond conventional risk factors to incorporate immune-mediated determinants such as disease activity, autoantibody profile, cumulative glucocorticoid exposure, and markers of vascular inflammation [23]. Second, early and sustained control of systemic inflammation—while minimizing glucocorticoid-related metabolic toxicity—represents a key strategy for preventing vascular injury [24]. Third, integrating advanced imaging modalities, including carotid ultrasonography and coronary computed tomography angiography, may facilitate earlier identification of subclinical atherosclerosis in high-risk individuals. Finally, multidisciplinary collaboration among rheumatologists, cardiologists, and vascular specialists is essential to develop individualized preventive strategies, optimize immunosuppressive regimens, and reduce long-term cardiovascular morbidity and mortality in this population.

The convergence of bibliometric trends and mechanistic evidence points to several promising research directions. Multi-omics approaches may refine the pinpointing of biomarkers and therapeutic targets toward personalized risk stratification. Targeted clinical trials focusing on specific inflammatory pathways—such as IFN-I signaling, IL-17–mediated responses, and NET-driven vascular injury—may yield novel cardioprotective therapies for SLE. In addition, elucidating the effects of conventional immunosuppressive agents on cardiovascular outcomes will be essential for optimizing treatment selection and while balancing disease control vascular safety.

Research limitations

Several limitations should be acknowledged. First, bibliometric analyses rely on database-indexed literature and may overlook relevant studies not captured in major databases, potentially introducing selection bias. Second, citation metrics do not directly reflect scientific quality and can be influenced by publication time, disciplinary norms, and geographic disparities. Third, heterogeneity in study designs, methods, and outcome definitions across included publications limits direct comparison of findings and precludes causal inferences regarding immune mechanisms in atherosclerosis. Finally, although keyword and co-citation analyses reveal research hotspots, they may not fully capture emerging themes reported in very recent or less-cited literature. Future studies integrating machine-learning–based topic modeling and full-text analysis may provide deeper mechanistic insights.

Conclusion

This comprehensive analysis demonstrates that research in SLE-associated atherosclerosis has evolved through distinct phases, from initial epidemiological observations to current mechanistic and translational investigations. Immune dysregulation, lipid oxidation, complement activation, and endothelial injury have emerged as central drivers of accelerated atherosclerosis in SLE, extending beyond traditional cardiovascular risk paradigms. Despite meaningful advances, significant gaps remain in elucidating underlying causal mechanisms and assessing the cardiovascular impact of contemporary targeted immunotherapies. Strengthening interdisciplinary collaboration, standardizing outcome measures, and conducting longitudinal and mechanism-driven translational studies will be crucial to improve cardiovascular risk prediction and prevention in this vulnerable population. These findings offer a structured roadmap for future research and reinforce the urgency of integrating cardiovascular prevention strategies into the standard management of SLE.

Declarations

Data availability statement: Data underlying this study are available from first author and corresponding author, upon reasonable request.

Author contributions: Dexiu Li: manuscript drafting, scientific illustration; Ziyi Qiu: literature retrieval; Yinuo Zhang and Liying

Zheng: data curation; Lin Zhao: methodology support; Mei Xue: supervision, funding acquisition, manuscript editing. All authors have reviewed and endorsed the final version of the manuscript.

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References

1. Boudoulas KD, Triposciadis F, Geleris P, Boudoulas H. Coronary Atherosclerosis: Pathophysiologic Basis for Diagnosis and Management. Prog Cardiovasc Dis. 2016; 58: 676-692.

2. Dörner T, Furie R. Novel paradigms in systemic lupus erythematosus. Lancet. 2019; 393: 2344-2358.

3. Barber MRW, Drenkard C, Falasinnu T, et al. Global epidemiology of systemic lupus erythematosus. Nat Rev Rheumatol. 2021; 17: 515-532.

4. Kiani AN, Magder LS, Post WS, et al. Coronary calcification in SLE: comparison with the Multi-Ethnic Study of Atherosclerosis. Rheumatology (Oxford). 2015; 54: 1976-1981.

5. Roman MJ, Shanker B, Davis A, et al. Prevalence and correlates of accelerated atherosclerosis in systemic lupus erythematosus. N Engl J Med. 2003; 349: 2399-2406.

6. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997; 145: 408-415.

7. Oliveira CB, Kaplan MJ. Cardiovascular disease risk and pathogenesis in systemic lupus erythematosus. Semin Immunopathol. 2022; 44: 309-324.

8. Sirobhushanam S, Lazar S, Kahlenberg JM. Interferons in Systemic Lupus Erythematosus. Rheum Dis Clin North Am. 2021; 47: 297-315.

9. Liu YD, Yu X, Zhang WD, Zhang X, Wang M, Ji FS. Mechanistic insight into premature atherosclerosis and cardiovascular complications in systemic lupus erythematosus. J Autoimmun. 2022; 132: 102863.

10. Reshetnyak T, Nurbaeva K. The Role of Neutrophil Extracellular Traps (NETs) in the Pathogenesis of Systemic Lupus Erythematosus and Antiphospholipid Syndrome. Int J Mol Sci. 2023; 24.

11. Wang H, Kim SJ, Lei Y, et al. Neutrophil extracellular traps in homeostasis and disease. Signal Transduct Target Ther. 2024; 9: 235.

12. Kahlenberg JM, Carmona-Rivera C, Smith CK, Kaplan MJ. Neutrophil extracellular trap-associated protein activation of the NLRP3 inflammasome is enhanced in lupus macrophages. J Immunol. 2012; 190: 1217-1226.

13. Smith CK, Vivekanandan-Giri A, Tang C, et al. Neutrophil extracellular trap-derived enzymes oxidize high-density lipoprotein: an additional proatherogenic mechanism in systemic lupus erythematosus. Arthritis Rheumatol. 2014; 66: 2532-2544.

14. Kim SY, Yu M, Morin EE, Kang J, Kaplan MJ, Schwendeman A. High-Density Lipoprotein in Lupus: Disease Biomarkers and Potential Therapeutic Strategy. Arthritis Rheumatol. 2019; 72: 20-30.

15. Mak A, Chan JKY. Endothelial function and endothelial progenitor cells in systemic lupus erythematosus. Nat Rev Rheumatol. 2022; 18: 286-300.

16. Pérez-Ocampo J, Taborda NA, Yassin LM, Higuita-Gutiérrez LF, Hernandez JC. Exploring the Association Between Systemic Lupus Erythematosus and High-Density Lipoproteins: A Systematic Review and Meta-Analysis. ACR Open Rheumatol. 2024; 6: 648-661.

17. Zeng X, Qiu R, Peng W. The protective effects of annexin A1 against oxidized-LDL-induced monocytes adhesion to endothelial cells: implication in atherosclerosis. J Thromb Thrombolysis. 2024; 58: 267-275.

18. Hummelgaard S, Vilstrup JP, Gustafsen C, Glerup S, Weyer K. Targeting PCSK9 to tackle cardiovascular disease. Pharmacol Ther. 2023; 249: 108480.

19. Mok CC, Ho LY, Chan KL, Tse SM, To CH. Circulating Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) is Associated with Disease Activity and Risk of Incident Cardiovascular Disease in Patients with Systemic Lupus Erythematosus. Inflammation. 2023; 46: 1458-1470.

20. Polytarchou K, Varvarousis D, Manolis AS. Cardiovascular Disease in Antiphospholipid Syndrome. Curr Vasc Pharmacol. 2020; 18: 538-548.

21. Kostopoulou M, Nikolopoulos D, Parodis I, Bertsias G. Cardiovascular Disease in Systemic Lupus Erythematosus: Recent Data on Epidemiology, Risk Factors and Prevention. Curr Vasc Pharmacol. 2020; 18: 549-565.

22. Patiño-Trives AM, Pérez-Sánchez C, Pérez-Sánchez L, et al. Anti-dsDNA Antibodies Increase the Cardiovascular Risk in Systemic Lupus Erythematosus Promoting a Distinctive Immune and Vascular Activation. Arterioscler Thromb Vasc Biol. 2021; 41: 2417-2430.

23. Atzeni F, Rodríguez-Pintó I, Cervera R. Cardiovascular disease risk in systemic lupus erythematous: Certainties and controversies. Autoimmun Rev. 2024; 23: 103646.

24. Fedorchenko Y, Suigenbayev D, Sagtaganov Z, Imanbayeva N, Mahmudzoda K. Myocardial infarction in rheumatic diseases. Rheumatol Int. 2025; 45: 270.