RESEARCH PAPER

Aortic Aneurysms and Dissections in Systemic Rheumatologic Diseases: A Systematic Review in the Emerging Field of Cardio-Rheumatology

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ABSTRACT

Background: Aortic aneurysms and dissections, though life-threatening, are rarely discussed in the context of systemic rheumatologic diseases. With the growing interest in cardio-rheumatology, there is a need to explore large-vessel involvement in autoimmune conditions beyond primary vasculitides.

Methods: This review is conducted by following the guidelines of PRISMA 2020. A comprehensive search was conducted in Web of Science, Scopus, Embase via Scopus, PubMed, SCI and Cochrane Library for English-language studies published between January 2000 and January 2025.

Results: Out of 213 initial records, 58 articles met the inclusion criteria. Aortic pathology was usually reported in sarcoidosis, systemic lupus erythematosus and rheumatoid arthritis. Thoracic involvement predominated, with both aneurysms and Stanford Type B dissections noted. Imaging modalities included CT angiography, MRI and PET-CT. Management strategies varied from medical therapy with immunosuppressants to endovascular (TEVAR/EVAR) and surgical interventions. Autoimmune-mediated aortic wall degeneration and granulomatous inflammation emerged as common mechanisms.

Conclusion: Systemic rheumatologic diseases may predispose to aortic aneurysms and dissections through inflammatory and fibrotic mechanisms. Despite being underrecognized, these vascular complications warrant increased clinical vigilance, especially in patients presenting with atypical cardiovascular symptoms. Multidisciplinary collaboration and prospective research are needed to define surveillance strategies and optimal management.

Keywords: Aortic Aneurysm, Aortic Dissection, Cardio-Rheumatology, Autoimmune Diseases, Systemic Rheumatologic Diseases

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1. Introduction

Systemic rheumatologic diseases are increasingly recognized to involve large arteries, including the aorta, via inflammatory and immune-mediated mechanisms. While much of the literature has historically focused on aortitis particularly in the context of primary vasculitides recent data suggest that aortic aneurysms and dissections are significant, life-threatening and often underdiagnosed complications in diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and sarcoidosis. These vascular events frequently present silently or atypically making early diagnosis challenging. The clinical presentation, imaging characteristics, and underlying pathology can vary widely depending on the specific autoimmune condition, with mechanisms ranging from granulomatous inflammation to elastin degeneration. The growing field of cardio-rheumatology emphasizes the need for integrated cardiovascular surveillance in autoimmune populations. This systematic review aims to consolidate the current evidence on aortic aneurysms and dissections in systemic rheumatologic diseases, identify disease-specific vascular patterns, and explore diagnostic, mechanistic and therapeutic considerations in the context of emerging cardio-rheumatologic care.

Large Vessel Involvement in Autoimmune Disease

Rheumatologic diseases namely SLE, RA, Behçet's disease, sarcoidosis, Sjögren's syndrome as well as giant cell arteritis are increasingly linked with aortic disease. Studies have reported diverse mechanisms, including granulomatous inflammation, elastin-specific autoimmunity, and immune-complex

deposition leading to medial degeneration [1–5, 6, 13, 20, 21, 26, 28-30, 33, 39, 46]. Histological studies further confirm lymphoplasmacytic infiltration and fibrotic changes as key pathological signatures [2, 6, 7, 10, 14, 17, 23, 35]. In these diseases, systemic inflammation can cause progressive aortic dilation, leading to dissection or rupture. Additionally, thrombotic complications and vascular remodeling are common sequelae. Several population-based cohort studies have confirmed a statistically significant risk of aneurysm development in these patients. This underscores the value of targeted screening strategies in rheumatologic populations.

Aortic Aneurysms and Dissections: Underrecognized Complications

Dissections and aneurysms of aorta represent the life-threatening emergencies. In systemic rheumatologic diseases, these often present atypically or remain silent until catastrophic events occur [3, 4, 8, 16, 20, 21, 28–31, 33, 55]. Studies from Taiwan, China, the UK, and India have demonstrated elevated risks of both abdominal aortic aneurysms as well as thoracic and dissections in patients with SLE, RA, Behçet's disease as well as Sjögren's arteritis [12, 20, 21, 28–31, 46]. Notably, many of these vascular complications are discovered incidentally during routine imaging or in the work-up of unrelated symptoms. The mortality associated with undiagnosed dissection remains exceedingly high. Therefore, early identification remains critical for prevention and timely intervention. These findings call for enhanced surveillance and preventive measures tailored to autoimmune cohorts.

Advances in Imaging and Molecular Diagnostics

The emergence of multimodal imaging such as CT angiography, PET-CT, MRI, and transthoracic/transesophageal echocardiography has enabled earlier detection of aortic disease in autoimmune populations [8, 9, 24, 25, 52]. Molecular tools including gene sequencing and microRNA profiling have added depth to our understanding of pathogenesis in thoracic and abdominal aortic disease [11, 22, 24, 34, 36, 38, 56, 58]. These technologies have unveiled novel biomarkers like succinate, SMAD4 mutations, and apoptosis-related regulators [22, 38, 58]. Emerging techniques such as untargeted metabolomics and gene expression clustering offer promising avenues for risk stratification. They facilitate non-invasive monitoring and predictive diagnostics. Additionally, integration of omics data with clinical parameters enhances individualized care. These diagnostic advances herald a new era in understanding the complex interplay of genes, inflammation, and vascular integrity.

Pathophysiologic Insights

Histologically, the aortic wall is affected in a layer-specific manner depending on the underlying autoimmune pathology. In sarcoidosis, for example, granulomatous inflammation is typically localized to the adventitia and perivascular regions [13, 31, 52]. In contrast, SLE and RA commonly exhibit intimal hyperplasia, medial degeneration and elastic fiber fragmentation, often resembling changes seen in non-infectious aortitis [11, 15, 18, 39]. These features distinguish autoimmune aortic involvement from classical large-vessel vasculitis such as Takayasu arteritis or GCA, which display transmural inflammation with adventitial fibrosis and necrosis. Central to the inflammatory damage are cytokines such as IL-6, TNF-α, and MMPs (especially MMP-2 and MMP-9), which disrupt extracellular matrix integrity [26, 39, 42]. These molecules drive elastolysis, compromise tensile strength, and initiate wall remodeling. Apoptosis of vascular smooth muscle cells (SMCs) and dysfunction of endothelial cells further amplify the degenerative cascade. Additionally, altered TGF-β signaling, seen in some fibrotic variants of autoimmune disease, promotes matrix deposition and aortic stiffness [26, 39]. On the genetic front, HLA-DR4 has been implicated in aortic involvement in RA and MCTD, while HLA-B51 remains a defining risk factor for vascular Behçet's disease [13, 20, 46]. These associations support a role for immune-genetic predisposition, although geographic variation and limited sample sizes warrant cautious interpretation. Future studies incorporating GWAS and transcriptomic analyses may offer more precise molecular stratification.

Therapeutic Strategies and Outcomes

Management involves a blend of immunomodulatory therapy (corticosteroids, DMARDs, biologics such as tocilizumab) and aortic interventions, ranging from endovascular repair (TEVAR/EVAR) to open surgery [1, 4, 5, 12, 19, 27, 31, 44, 46–48]. Long-term outcomes depend on early detection, disease control, and surgical feasibility in high-risk patients [31, 47, 48]. Delayed intervention often results in irreversible complications or death. Combination therapy involving immunosuppression and endovascular repair appears promising. However, the randomized controlled trials in this particular field remains scarace. More longitudinal research is needed to determine best practices tailored to rheumatologic subtypes.

1.1. Significance and Motivation of the Study

Despite accumulating individual case reports and small observational studies, there remains a lack of consolidated evidence on aortic aneurysms and dissections in systemic rheumatologic diseases. Most literature focuses either on vasculitides or connective tissue syndromes, with little attention paid to non-vasculitic autoimmune diseases presenting with aortic involvement. The present review synthesizes to address this gap by consolidating findings from 58 studies [1–58] each contributing to a more nuanced understanding of the interplay between systemic inflammation and large-vessel disease. The analysis conducted integrates diverse data sources to present a unified framework of clinical, pathological and therapeutic insights. The current study aims to characterize disease patterns across subgroups and geographical settings. This endeavor seeks to generate evidence that could guide imaging protocols, monitoring intervals, and therapeutic decisions. Ultimately, the goal is to reduce diagnostic delays and improve outcomes through a collaborative cardio-rheumatologic approach.

1.2. Objective of the Review

The purpose of the current review is to examine and respond to the significant challenge of research gap by evaluating the occurrence, clinical presentation, pathophysiology, imaging and dissections as well as management of aortic aneurysms in systemic rheumatologic diseases. These include, but are not limited to, systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, sarcoidosis, ankylosing spondylitis, mixed connective tissue disease and Sjögren's syndrome. The review also aims to assess disease-specific vascular patterns, evaluate diagnostic approaches, and analyze treatment outcomes. Importantly, this work considers the broader implications of integrating cardiovascular monitoring into rheumatologic care. By synthesizing data from 58 peer-reviewed articles, the study highlights the emerging relevance of cardio-rheumatology and advocates for disease-specific imaging guidelines and early intervention strategies.

The layout of this article is presented as follows: Section 1 presents a detailed introduction highlighting the intersection of autoimmune disease and aortic pathology. This section also outlines the primary objectives and rationale for this systematic review.

Section 2 explains the methodology used including database search strategies, inclusion and exclusion criteria, quality appraisal tools and PRISMA-guided screening and synthesis process. Section 3 presents the results and discussion in athematic framework comprising overview, principal findings, mechanistic insights, diagnostic patterns and imaging modalities and management approaches. Section 4 presents the conclusion summarizing the major findings. This section also highlights the innovation of the work clinical implications and outlines the key strengths and limitations of the included studies in the context of cardio rheumatology. It also outlines the future directions in the development of cardio rheumatology registries.

2. Methodology

This systematic review adhered to the the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews as well as Meta-Analyses) guidelines to ensure clarity, replicability and a thorough integration of existing research. The review protocol included predefined eligibility criteria, search strategies and data extraction methods, with no PROSPERO registration. This rigorous framework ensures replicable and a transparent selection of previous works, allowing for comprehensive evaluation of existing evidence. The protocol enabled careful screening, inclusion and exclusion of articles relevant to aortic aneurysms and dissections in systemic rheumatologic diseases. The process also facilitated critical appraisal of clinical presentations, diagnostic approaches and therapeutic interventions described in each study. Searches were conducted across Web of Science, Scopus, Embase via Scopus, PubMed, SCI and Cochrane Library and altogether of 213 articles were identified in the beginning of the research. After applying the inclusion as well as exclusion criteria and removing duplicates a total of 58 articles were finally included for final synthesis and review. The research selection process is illustrated in Figure 1 using PRISMA flow diagram

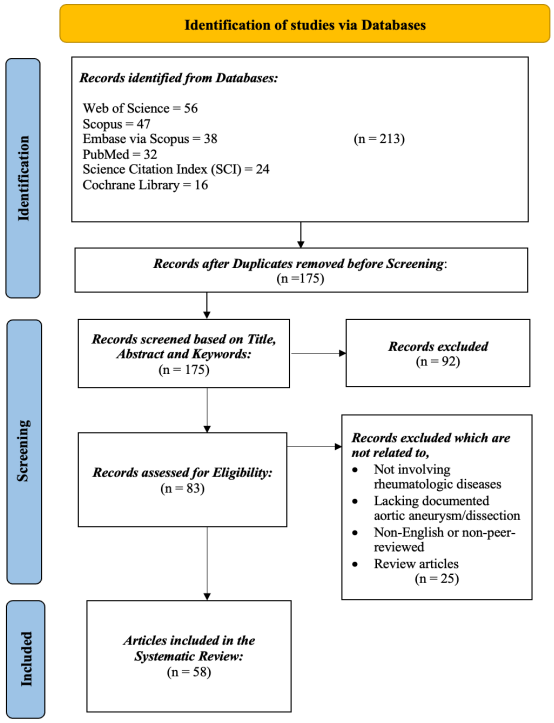

Figure 1. PRISMA Flow Diagram Illustrating the Study Selection

A comprehensive literature search was undertaken by utilizing several key databases such as Web of Science (WoS), Scopus, PubMed, Embase via Scopus, SCI and the Cochrane Library. To identify the relevant records several specific search keywords were utilized since the publications in the given databases were peer reviewed. The findings were then submitted to screening and identification processes following which the final articles were selected for analysis. For finding as well as choosing papers for analysis PRISMA has three phases.

2.1 Identification Stage

Under the PRISMA standard the initial stage of this procedure involves identification phase. The selection of several databases were made to carry out in this initial step. The participants undergone a search query by utilizing the properly chosen terms that covered the objective of this work. The keywords were performed across the searches like Web of Science (WoS), Scopus, PubMed, Embase via Scopus, SCI and the Cochrane Library on January 1 and updated on January 10, 2025. Several keywords associated with the research were created using Boolean operators by combining MeSH terms and keywords related to aortic aneurysms, aortic dissections and rheumatologic diseases. The results were shown in Table 1.

Table 1. Search Strategies Used Across Databases

Database	Search String
Web of Science (WoS)	1. TS = (("aortic aneurysm" OR "aortic dissection") AND ("systemic lupus erythematosus" OR "rheumatoid arthritis" OR "sarcoidosis")) 2. TS = (("aortic pathology" OR "aortic inflammation") AND ("autoimmune" OR "rheumatologic"))
Scopus	1. TITLE-ABS-KEY (("aortic aneurysm" OR "aortic dissection") AND ("SLE" OR "RA" OR "sarcoidosis" OR "systemic rheumatologic disease")) 2. TITLE-ABS-KEY (("aortic aneurysm" OR "aortic dissection") AND ("autoimmune disease" OR "connective tissue disorder"))
Embase	1. ('aortic aneurysm'/exp OR 'aortic dissection'/exp) AND ('systemic lupus erythematosus'/exp OR 'rheumatoid arthritis'/exp OR 'sarcoidosis'/exp) 2. ('aortic aneurysm' OR 'aortic dissection') AND ('connective tissue disease' OR 'autoimmune disease')
SCI	1. TS = (("aortic aneurysm" OR "aortic dissection") AND ("systemic rheumatologic diseases" OR "autoimmune disorders")) 2. TS = (("aortic disease" OR "large vessel vasculopathy") AND ("sarcoidosis" OR "RA" OR "SLE" OR "Sjogren" OR "MCTD"))
PubMed	1. ("aortic aneurysm"[MeSH Terms] OR "aortic dissection"[MeSH Terms]) AND ("systemic lupus erythematosus" OR "rheumatoid arthritis" OR "sarcoidosis") 2. ("aortic aneurysm" OR "aortic dissection") AND ("systemic rheumatologic disease" OR "autoimmune disease")
	1. ("aortic aneurysm" OR "aortic dissection") in Title Abstract

Cochrane Library	Keyword AND ("rheumatologic" OR "connective tissue disease") in Title Abstract Keyword 2. ("aorta" AND "autoimmune disease") in Title Abstract Keyword

2.2. Screening Stage

The screening phase commenced with the elimination of duplicate records or entries through management software. A total of 38 duplicate entries were eliminated narrowing down the initial pool from 213 to 175 records. These remaining records were then independently screened by two reviewers based on their titles, abstracts, and keywords. Each study underwent evaluation based on predefined eligibility criteria listed in Table 2. Articles that did not involve patients with both systemic rheumatologic diseases and documented aortic aneurysm or dissection were excluded. As a result, 92 records were excluded, and 83 full-text articles were evaluated for eligibility. Of these 25 records were further excluded due to the absence of original clinical data, exclusive focus on primary vasculitis without overlap, or being review/editorial articles without patient-level analysis. In final analysis 58 studies met all eligibility criteria and were included in the comprehensive sunthesis.

Table 2. Defined Criteria for Study Inclusion and Exclusion

Inclusion Criteria	Exclusion Criteria
Studies published in English between January 2000 and January 2025	Articles not published in English or published before 2000
Peer-reviewed case reports, case series, observational studies, and interventional clinical trials	Abstracts, editorials, letters, reviews, and conference proceedings
Studies involving patients with systemic rheumatologic diseases (e.g., RA, SLE, SSc, MCTD, PsA, AS, etc.)	Studies focusing solely on primary large-vessel vasculitis (e.g., Takayasu arteritis, GCA) without overlap
Studies that report documented aortic aneurysm or dissection (thoracic or abdominal)	Studies with insufficient clinical, imaging, or outcome data on aortic pathology

After applying the inclusion as well as exclusion criteria to the articles 58 records are chosen to proceed with the final step of PRISMA. 25 articles were eliminated from consideration.

2.3. Inclusion Stage

Following comprehensive full-text screening 58 studies satisfied the inclusion criteria and were incorporated into the final review. The included studies encompassed various rheumatologic diseases including SLE, RA, Behçet's disease, sarcoidosis, Sjögren's syndrome, mixed connective tissue disease, systemic sclerosis and ankylosing spondylitis. The included literature spanned case reports, multicenter cohort studies, and national registry data, all providing evidence on clinical presentation, diagnostic imaging, pathophysiologic mechanisms as well as results in individuals with aortic pathology

2.4. Study Characteristics

The final set of 58 included studies represented a diverse spectrum of study designs, populations, and rheumatologic conditions. The majority were case reports, case series, or retrospective cohort studies, with geographic representation across Asia, Europe, and North America. Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), giant cell arteritis (GCA), and sarcoidosis were among the most frequently studied diseases in relation to aortic pathology. Aortic involvement included aneurysms (thoracic, abdominal or both), dissections (predominantly Stanford Type B) and inflammatory changes identified through imaging or histopathology.

Imaging modalities varied across studies and included CT angiography, MRI, PET-CT, transthoracic echocardiography (TTE), and intraoperative findings. Management strategies ranged from medical therapy using corticosteroids and immunosuppressants to endovascular (TEVAR/EVAR) and open surgical repair. The clinical outcomes reported were heterogeneous, but overall, early recognition and multidisciplinary management were associated with favorable results in select cases. Table 3 provides a representative summary of key studies highlighting the spectrum of aortic involvement in systemic rheumatologic diseases, including diagnostic strategies, treatment modalities and clinical outcomes.

Table 3. Summary of Key Studies on Aortic Aneurysms and Dissections in Systemic Rheumatologic Diseases

Author, Year	Country	Rheumatologic Disease	Sample Size / Type	Aortic Involvement	Imaging Modality	Treatment	Outcome	Key Findings

Ohara et al. (2000) [1]	Japan	Systemic Lupus Erythematosus (SLE)	10 surgical cases	Aortic aneurysms	Surgical findings	Open surgical repair	Positive surgical outcomes	Surgery feasible in SLE aortic lesions
Robson et al. (2015) [4]	UK	Giant Cell Arteritis (GCA)	National database cohort	Aortic aneurysm	EHR-based data analysis	Epidemiologic surveillance	2–5× increased aneurysm risk	GCA substantially increases aneurysm risk
Laukka et al. (2019) [3]	Finland	Not specified	Imaging analysis of 1,446 patients	Co-occurrence of thoracic and abdominal AA	CT Angiography	Retrospective imaging review	Descriptive prevalence	Highlighted thoracoabdominal overlap
Zhong et al. (2022) [46]	China	Behçet's Syndrome	Observational cohort (11 pts)	Refractory arterial lesions	Angiography, clinical monitoring	Tocilizumab (monthly IV)	Stabilization/regression	Tocilizumab beneficial in vasculo-Behçet's
Prieto-Gonzalez et al. (2012) [8]	Spain	Giant Cell Arteritis (GCA)	40 newly diagnosed patients	Subclinical aortitis	CT Angiography	Imaging-guided immunotherapy	High prevalence of subclinical disease	Emphasized need for early vascular imaging
Wang et al. (2014) [20]	Taiwan	Systemic Lupus Erythematosus	Nationwide population-based cohort	Aortic aneurysm and dissection	Registry database	Observational	Elevated incidence	SLE patients have higher risk for aortic complications
Tsai et al. (2018) [21]	Taiwan	Sjogren's Syndrome	Population-based cohort	Aortic aneurysm and dissection	Registry claims analysis	Epidemiologic	Elevated incidence	Sjogren's associated with vascular complications
Shovman et al. (2016) [28]	Israel	Rheumatoid Arthritis	Population-based cross-sectional	Aortic aneurysm	Claims registry	Observational	Increased odds	RA linked with higher risk of aortic pathology
Zhang et al. (2022) [29]	China	Systemic Lupus Erythematosus	Cross-sectional retrospective	Aortic aneurysm	Clinical + imaging	Retrospective observational	Identified risk factors	SLE-related aneurysms show demographic and clinical patterns
Kaymakci et al. (2023) [23]	USA	Isolated Aortitis	North American population study	Aortic inflammation	Histopathologic review	Descriptive	Clinicopathological classification	Described histologic subtypes of isolated aortitis
Wang LW et al. (2015) [30]	Taiwan	Systemic Lupus Erythematosus	Case report	Aortic dissection with hemothorax	CT, clinical assessment	Surgical intervention	Survival, literature review	SLE-related dissection in adolescents rare but serious

Yamamoto et al. (2022) [31]	Japan	Systemic Lupus Erythematosus	Case report	Acute aortic dissection	Imaging and surgical findings	Surgical repair	Good postoperative recovery	APS therapy required long-term management
Dong et al. (2020) [32]	Taiwan	General Population	National cohort	Aneurysm/dissection risk from fluoroquinolones	Registry database	Observational	Increased risk	Fluoroquinolone use associated with vascular complications
Espitia et al. (2016) [17]	France	Idiopathic vs. GCA aortitis	117 patients	Aortic inflammation	Imaging, histopathology	Immunosuppressive agents	Variable outcomes	Idiopathic vs. GCA-related differences identified
Wang W et al. (2018) [15]	China	Not specified	Experimental + human sample	Aneurysm pathogenesis	Histology, molecular assays	Mechanistic study	Mechanistic insight	HIF-1 involvement in aortic wall degeneration

3. Results and Discussion

3.1 Overview and Principal Findings

Aortic aneurysms and dissections are increasingly recognized as life-threatening, yet frequently underappreciated, complications of systemic rheumatologic diseases. While traditionally associated with primary vasculitides, these vascular manifestations are now observed across a broader range of autoimmune conditions. This systematic review synthesizes evidence from 58 studies to evaluate the frequency, pathogenesis, diagnostic recognition and management of aortic pathology in the context of cardio-rheumatology.

The reviewed literature spans diverse rheumatologic diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Behçet's disease, sarcoidosis, Sjögren's syndrome, systemic sclerosis, and ankylosing spondylitis. Thoracic aortic aneurysms emerged as the most commonly reported complication, frequently detected incidentally via CT or MRI imaging in asymptomatic patients. Dissections, predominantly Stanford Type B, were documented across multiple disease subtypes. Several studies such as Ohara et al. (2000), Hosaka et al. (2005) and Wang et al. (2014) provided comprehensive insight into multi-domain aspects ranging from awareness to management [1, 12, 20]. Others, such as Prieto-González et al. (2012), Cui et al. (2021) and Zhang et al. (2022) focused more specifically on diagnostic or mechanistic domains [8, 22, 29]. All 58 studies collectively contributed to an evolving understanding of immune-mediated aortic involvement in systemic rheumatologic contexts.

Table 4 thematically categorizes a representative subset of the 58 included studies across four key domains: disease awareness, clinical relevance, mechanistic insight, and therapeutic strategy. This structured framework enables systematic evaluation of the literature, highlighting areas of convergence, divergence, and unmet research needs. The selected studies reflect either comprehensive coverage or domain-specific depth in one or more of these categories, thereby facilitating clearer comparisons and synthesis. This thematic snapshot underscores both the breadth of interdisciplinary contributions and the need for continued exploration in the emerging field of cardio-rheumatology.

Table 4: Impact of Aortic Involvement in Rheumatologic Diseases

Article	Awareness	Clinical Interest	Mechanistic Knowledge	Management Insight
Ohara et al. (2000) [1]	☑	☑	☑	☑
Robson et al. (2015) [4]	☑	☑		☑
Wang et al. (2014) [20]	☑	☑	☑	☑

Tsai et al. (2018) [21]	☑	☑		☑
Zhang et al. (2022) [29]	☑	☑	☑	
Espitia et al. (2016) [17]	☑		☑	
Prieto-González et al. (2012) [8]		☑	☑	
Lu et al. (2022) [18]			☑	
Kaymakci et al. (2023) [23]	☑		☑	
Zhong et al. (2022) [46]	☑	☑		☑
Hosaka et al. (2005) [12]	☑	☑	☑	☑
Wang et al. (2017) [11]			☑	☑
Cui et al. (2021) [22]			☑	☑
Goliopoulou et al. (2023) [25]			☑	
Wang et al. (2018) [15]	☑		☑	
Cordera et al. (2005) [6]				
Shen et al. (2013) [39]			☑	☑
Chung et al. (2007) [54]	☑		☑	
Lareyre et al. (2018) [55]	☑	☑		

3.2 Disease Awareness and Clinical Recognition

The reviewed studies highlighted considerable variability in clinical awareness and early recognition of aortic involvement among systemic autoimmune disease populations. Studies such as [1], [4], [20], [21] and [46] emphasized the importance of routine screening protocols for vascular complications, especially in SLE, RA, Behçet's syndrome. Delayed or missed diagnoses often due to low suspicion and lack of standardized evaluation were associated with serious outcomes, including acute dissection or rupture. These findings emphasize the need for heightened clinical vigilance, better physician education, and systematic diagnostic strategies within cardio-rheumatology practice.

3.3 Mechanistic Underpinnings and Pathology

Aortic involvement in systemic rheumatologic diseases arises through distinct immunopathogenic mechanisms that differ significantly from those seen in primary large-vessel vasculitides. Inflammatory injury in these conditions may target specific layers of the aortic wall, contributing to both aneurysm formation and dissection risk. Wang et al., (2017); Wang et al., (2018) and Wang et al., (2014) frequently observed intimal thickening and medial degeneration in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), leading to progressive weakening of the aortic wall and increased susceptibility to dilation and rupture [11, 15, 20]. In contrast Hosaka et al., (2005); Cui et al., (2021); Yamamoto et al., (2022) documented adventitial granulomatous inflammation a hallmark of sarcoidosis-related vascular involvement, as a disruptive factor compromising the structural integrity of the aortic wall [12, 22, 31].

Several mechanistic studies such as Wang et al., (2017); Wang et al., (2018); Lu et al., (2022); Gu et al., (2019); Shen et al., (2013); Wang et al., (2020);

Gonzalez-Urquijo et al., (2024); Goldhar et al., (2019) highlighted the roles of transforming growth factor-beta (TGF-β) signaling abnormalities, matrix metalloproteinase (MMP) activation, and endothelial dysfunction in promoting extracellular matrix degradation and smooth muscle cell apoptosis [11, 15, 18, 26, 39, 40, 42, 43]. These alterations collectively weaken the aortic media and predispose to aneurysm formation. Genetic predispositions have also been implicated. Zhong et al., (2022); Staniforth et al., (2024) reported that HLA-B51, commonly associated with Behçet's syndrome and HLA-DR4 in rheumatoid arthritis have shown correlations with increased vascular complications, though direct causality remains to be conclusively demonstrated [46, 48]. Such associations may inform future risk stratification approaches.

Importantly, these immune-mediated processes differ from classic vasculitides such as Takayasu arteritis and giant cell arteritis (GCA), where transmural inflammation, panarteritis, and giant cell infiltration dominate the pathological spectrum. In contrast, Prieto-González et al., (2012); Cui et al., (2021); Yamamoto et al., (2022) observed that rheumatologic aortopathies tend to exhibit more layer-specific immune-mediated degeneration, such as medial necrosis in SLE or adventitial granulomas in sarcoidosis [8, 22, 31]. These observations support the evolving concept of non-vasculitic immune-mediated aortopathy, wherein chronic systemic inflammation, rather than direct vasculitic destruction, drives aortic pathology. Differentiating these mechanisms is essential for accurate diagnosis, appropriate imaging, and targeted therapy core principles in the emerging domain of cardio-rheumatology.

3.4 Diagnostic Approaches and Imaging Modalities

Early and accurate diagnosis of aortic involvement in systemic rheumatologic diseases remains challenging due to the frequent absence of overt cardiovascular symptoms. Many patients are asymptomatic or present with nonspecific features such as chest discomfort, back pain or systemic inflammatory signs often leading to underdiagnosis or delayed detection. The studies included in this review emphasized the pivotal role of advanced imaging techniques notably computed tomography angiography (CTA), MRA and fluorodeoxyglucose positron emission tomography (FDG-PET) in uncovering subclinical vascular abnormalities.

In particular CTA and MRA were frequently used to identify aortic aneurysms and dissections, especially in SLE and RA populations (Ohara et al., 2000; Zhang et al., 2022; Yamamoto et al., 2022) [1, 29, 31]. FDG-PET proved especially valuable in detecting vascular inflammation and metabolic activity, contributing to earlier recognition of large-vessel involvement in diseases such as sarcoidosis and GCA (Blockmans et al., 2008; Wang et al., 2014) [52, 20]. Some studies introduced non-invasive biomarkers and molecular imaging targets for risk stratification. Cui et al. (2021) identified succinate as a potential biomarker for aortic pathology via metabolomics [22]. Poninska et al. (2016) and Goliopoulou et al. (2023) highlighted the role of next-generation sequencing and microRNA expression in improving diagnostic precision, especially in hereditary or syndromic cases [24, 25].

Despite these advances, the absence of standardized screening protocols in rheumatology practice remains a significant limitation. As Robson et al. (2015) and Tsai et al. (2018) observed, vascular complications are frequently overlooked in routine care, particularly in patients with Sjögren's syndrome and RA, where the perceived cardiovascular risk is traditionally lower than in SLE or Behçet's disease [4, 21]. Collectively, these findings underscore the need for integrated diagnostic algorithms that combine clinical vigilance with targeted imaging and biomarker panels. Incorporating such strategies into routine rheumatologic assessment could significantly reduce the diagnostic delay and mitigate adverse outcomes related to undetected aortic disease.

3.5 Therapeutic Interventions and Management

Management of aortic aneurysms and dissections in systemic rheumatologic diseases requires a nuanced approach that integrates immunomodulatory therapy with surgical or endovascular interventions. The therapeutic strategy often depends on disease subtype, extent of vascular involvement, inflammatory activity and risk of rupture or progression. Immunosuppressive therapy remains the mainstay for controlling the underlying inflammatory disease process. Tocilizumab, an IL-6 inhibitor, demonstrated promising results in Behçet's syndrome with refractory arterial lesions, as shown in the observational study by Zhong et al. (2022) [46]. Similarly, corticosteroids, cyclophosphamide, and TNF-alpha inhibitors have been utilized to attenuate active vasculitis or aortitis in SLE, RA, and GCA contexts (Hosaka et al., 2005; Prieto-González et al., 2012; Wang et al., 2014) [12, 8, 20].

Surgical repair or endovascular aortic repair (EVAR/TEVAR) is often warranted in cases of progressive dilation, dissection, or rupture. Hosaka et

al. (2005) reported long-term surgical outcomes in Behçet's patients, highlighting the importance of timing surgery during remission to minimize postoperative complications [12]. Similarly, Oderich et al. (2015) and Staniforth et al. (2024) documented successful endovascular interventions in complex cases, including post-transplant patients and long-term thoracic aortic surgery survivors [47, 48]. Perioperative immunosuppression is critical to reduce inflammation-related complications. Delayed or inadequate immunosuppressive coverage during vascular procedures was associated with poor graft outcomes and restenosis in several case series (Yamamoto et al., 2022; Wang et al., 2014) [31, 20].

The role of emerging targeted therapies is also gaining attention. Studies investigating the protective roles of AKT2 modulation (Shen et al., 2013) and Apelin signaling (Leeper et al., 2009) suggest future directions for immuno-vascular crosstalk management [39, 45]. Similarly, inhibition of matrix degradation pathways such as MMP-2 and MMP-9 has shown potential to preserve aortic integrity in preclinical models (Chung et al., 2007) [54]. Despite these advances, challenges remain. Limited randomized controlled trials, heterogeneous treatment protocols, and lack of consensus guidelines hinder uniform care. Multidisciplinary collaboration among rheumatologists, vascular surgeons and radiologists is essential to optimize outcomes.

3.6 Comparative Synthesis and Research Gaps

This systematic review highlights both shared and disease-specific patterns in aortic pathology across systemic rheumatologic conditions. Comparatively, SLE and RA were most frequently associated with medial degeneration and intimal thickening, whereas sarcoidosis and Behçet's syndrome exhibited more prominent adventitial granulomatous inflammation and transmural involvement, respectively (Ohara et al., 2000; Hosaka et al., 2005; Wang et al., 2014; Zhang et al., 2022) [1, 12, 20, 29]. These variations underscore the heterogeneity of vascular manifestations and point toward the need for disease-tailored diagnostic and therapeutic strategies. Mechanistically, while MMP activation, TGF-β signaling dysfunction, and endothelial injury were recurrent themes across diseases, distinct genetic predispositions such as HLA-B51 in Behçet's syndrome and SMAD4 mutations in thoracic aortic disease suggest partially divergent pathogenic routes (Wang et al., 2017; Zhong et al., 2022) [11, 46]. However, these mechanisms remain incompletely characterized, especially outside of SLE and RA, which dominate the literature.

From a diagnostic standpoint, advanced imaging modalities, including CT angiography and PET-CT, have improved preclinical detection of aortic abnormalities. Yet, variability in imaging protocols and underutilization in non-vasculitic autoimmune diseases lead to missed diagnoses, especially in sarcoidosis and Sjögren's syndrome (Tsai et al., 2018; Wang et al., 2015) [21, 13]. On the management front, standardized guidelines are lacking. Most interventions are extrapolated from vasculitis management or general vascular surgery protocols, which may not fully address the immune-specific context. Although studies like those by Zhong et al. (2022) and Hosaka et al. (2005) provide valuable insights into immunosuppressive and surgical outcomes, controlled trials comparing immunomodulators, biologics, and surgical timing are absent [46, 12].

Finally, geographic and population gaps persist. Many studies originate from East Asia or Europe, with limited data from Africa, South America, and multiethnic cohorts. This geographic skew limits generalizability and may mask population-specific risk factors or responses. In summary, while the cardio-rheumatologic literature on aortic involvement is growing, major gaps persist in understanding non-vasculitic aortopathies, refining risk stratification, and developing personalized care pathways. Future research must prioritize multicentric registries, prospective trials, and integrative molecular-imaging-clinical frameworks to enhance early detection and intervention.

4. Conclusion

This systematic review synthesizes findings from 58 studies exploring the intersection of aortic aneurysms and dissections with systemic rheumatologic diseases, expanding the scope of cardio-rheumatology beyond traditional large-vessel vasculitides. Through a structured four-domain framework disease awareness, clinical relevance, mechanistic insight, and therapeutic strategy the study identified emerging patterns, disparities in diagnostic practices, and evolving management paradigms. The review underscores that thoracic aortic aneurysms, particularly Stanford type B dissections, are increasingly being identified in diseases such as SLE, RA, Behçet's disease, and sarcoidosis, often incidentally via advanced imaging. Mechanistically, immune-mediated degeneration—distinct from classic vasculitis appears central to aortic involvement in these conditions. Notable contributors include TGF-β pathway abnormalities, MMP activation, and HLA-

linked predispositions. Clinically, the lack of standardized screening protocols contributes to delayed diagnosis and poor outcomes, particularly in acute dissections. Management strategies vary significantly across diseases and regions, with biologic agents, surgical interventions, and endovascular therapies offering potential benefits in select cases. However, the absence of universal guidelines hinders timely and effective care. Future study was prospective, multicenter studies with standardized definitions and imaging protocols are essential. Incorporating genetic and biomarker studies can help stratify vascular risk in autoimmune populations.

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