

Endothelial Glycocalyx Degradation as a Central Mechanism in
Premature Atherosclerotic Cardiovascular Disease

Farozan Erdian Talab Radjamin^{1*} and Qian Qi²

¹ The University of Western Australia, Australia
^{1,2} National University Heart Centre, Singapore

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ARTICLE HISTORY	ABSTRACT
Received: 12 May 26 Final Revision: 28 September 26 Accepted: 28 September 26 Online Publication: 30 September 26	Premature atherosclerotic cardiovascular disease (ASCVD) poses a substantial clinical burden. Endothelial glycocalyx injury has been proposed as a contributor to vascular dysfunction and atherosclerotic processes, but its role in premature ASCVD remains uncertain. This narrative review examines evidence on glycocalyx structure and degradation, associated vascular mechanisms, candidate biomarkers, and potential therapeutic approaches. Literature published from 2010 to March 2026 was identified through PubMed, Scopus, Web of Science, and Google Scholar using terms related to the endothelial glycocalyx, atherosclerosis, endothelial dysfunction, and cardiovascular disease. Earlier foundational studies were also considered. Experimental and clinical literature links glycocalyx injury with altered vascular permeability, mechanotransduction, nitric oxide signaling, and inflammatory cell interactions. Oxidative stress, hyperglycemia, inflammation, and disturbed flow have been investigated as potential contributors to glycocalyx damage. Circulating glycocalyx components, including syndecan-1, are being studied as markers of endothelial injury, but their value for predicting premature ASCVD has not been established. Although glycocalyx preservation and restoration are potential therapeutic research directions, evidence that these approaches prevent premature cardiovascular events is lacking. Overall, glycocalyx injury is a biologically plausible contributor to atherosclerotic processes; prospective human studies are needed to establish its causal and predictive roles in premature ASCVD.
KEYWORDS	
Atherosclerotic Cardiovascular Disease, Endothelial Glycocalyx, Endothelial Dysfunction, Microvascular Dysfunction, Oxidative Stress	
CORRESPONDING AUTHOR	
arodjati@gmail.com	
DOI	
10.37034/medinftech.v4i3.143	

1. Introduction

Atherosclerotic cardiovascular disease has traditionally been conceptualized as a disorder primarily driven by lipid accumulation and vascular obstruction. However, modern cardiovascular research increasingly recognizes endothelial dysfunction as a critical initiating event preceding overt plaque formation [1], [2].

Among the most important regulators of endothelial physiology is the endothelial glycocalyx, a highly specialized gel-like extracellular matrix coating the luminal surface of vascular endothelial cells. The glycocalyx consists predominantly of proteoglycans, glycosaminoglycans, glycoproteins, plasma proteins,

and membrane-associated macromolecules that collectively maintain vascular homeostasis [1], [3].

Recent evidence suggests that glycocalyx degradation may represent one of the earliest detectable pathological changes in cardiovascular disease. Structural disruption of the glycocalyx contributes to endothelial inflammation, altered mechanotransduction, impaired nitric oxide bioavailability, vascular hyperpermeability, platelet activation, and atherogenesis. Importantly, glycocalyx injury may occur years before clinically detectable cardiovascular disease develops. Consequently, endothelial glycocalyx biology has emerged as a major focus of translational cardiovascular research.

Cardiovascular disease remains the leading cause of global mortality despite substantial advances in modern medicine [2], [4]. Contemporary cardiovascular research increasingly demonstrates that endothelial dysfunction precedes overt atherosclerotic plaque formation and contributes fundamentally to vascular inflammation, thrombosis, and microvascular injury.

Among the most important endothelial structures involved in vascular homeostasis is the endothelial glycocalyx. This highly specialized extracellular matrix regulates endothelial permeability, mechanotransduction, anticoagulant signaling, leukocyte adhesion, and nitric oxide bioavailability.

Recent evidence suggests that glycocalyx degradation may represent one of the earliest initiating events in premature atherosclerotic cardiovascular disease. Previous studies have demonstrated strong associations between endothelial glycocalyx injury and cardiovascular disorders including hypertension, diabetes mellitus, acute coronary syndrome, heart failure, and chronic inflammatory disease [5].

Research by Vink and Duling [6] demonstrated that the glycocalyx functions as an important vascular permeability barrier regulating interactions between circulating blood components and endothelial cells. Additional studies have shown that oxidative stress, inflammatory cytokines, disturbed shear stress, and hyperglycemia contribute substantially to glycocalyx degradation. Recent translational cardiovascular investigations additionally suggest that glycocalyx injury contributes to coronary microvascular dysfunction and plaque instability. Despite increasing recognition of endothelial glycocalyx biology, glycocalyx-centered mechanisms remain underrepresented in many conventional cardiovascular models. Most traditional cardiovascular frameworks primarily emphasize lipid accumulation and arterial obstruction while underestimating the importance of endothelial surface biology.

This study was therefore conducted to examine endothelial glycocalyx degradation as a central initiating mechanism underlying premature cardiovascular disease progression. The primary objective of this study is to analyze the molecular pathways, hemodynamic mechanisms, inflammatory signaling processes, and translational therapeutic implications associated with endothelial glycocalyx degradation in atherosclerotic cardiovascular disease.

Endothelial glycocalyx injury may contribute to early vascular dysfunction, but the interval between glycocalyx changes and clinical manifestations of premature ASCVD has not been established [7]. Exposure to cardiometabolic risk factors during early adulthood, including obesity, diabetes mellitus, smoking, dyslipidemia, chronic psychological stress, and hypertension, may accelerate glycocalyx

degradation and endothelial dysfunction. Consequently, individuals with early glycocalyx injury may experience accelerated vascular aging, enhanced lipid infiltration, and earlier development of atherosclerotic lesions, thereby increasing the risk of premature ASCVD. Understanding this relationship is essential for identifying novel preventive strategies aimed at interrupting the earliest stages of cardiovascular disease progression.

Premature atherosclerotic cardiovascular disease (ASCVD) is generally defined as the occurrence of atherosclerotic cardiovascular events before the age of 55 years in men and before the age of 65 years in women. Premature ASCVD is associated with significant morbidity, mortality, reduced quality of life, and long-term socioeconomic burden. Understanding the biological mechanisms responsible for early vascular injury is therefore essential for improving prevention and treatment strategies [8].

Although previous studies have extensively investigated endothelial dysfunction, inflammation, oxidative stress, and atherosclerosis as individual contributors to cardiovascular disease, relatively few reviews have comprehensively examined endothelial glycocalyx degradation as a central upstream mechanism linking these pathological processes in premature ASCVD. Furthermore, the role of glycocalyx injury in integrating hemodynamic disturbances, endothelial inflammation, microvascular dysfunction, and atherogenesis remains underrepresented in conventional cardiovascular models. This knowledge gap may limit the development of preventive strategies targeting the earliest stages of vascular injury.

Unlike previous reviews that primarily focus on endothelial dysfunction or lipid-driven atherosclerosis, this review specifically highlights endothelial glycocalyx degradation as a unifying upstream mechanism linking oxidative stress, inflammation, disturbed hemodynamics, and microvascular dysfunction in premature ASCVD. This integrative perspective may provide a foundation for future glycocalyx-targeted preventive and therapeutic strategies.

To facilitate understanding of the proposed pathophysiological concept, Figure 1 summarizes the sequential process of endothelial glycocalyx degradation from physiological homeostasis to premature atherosclerotic cardiovascular disease.

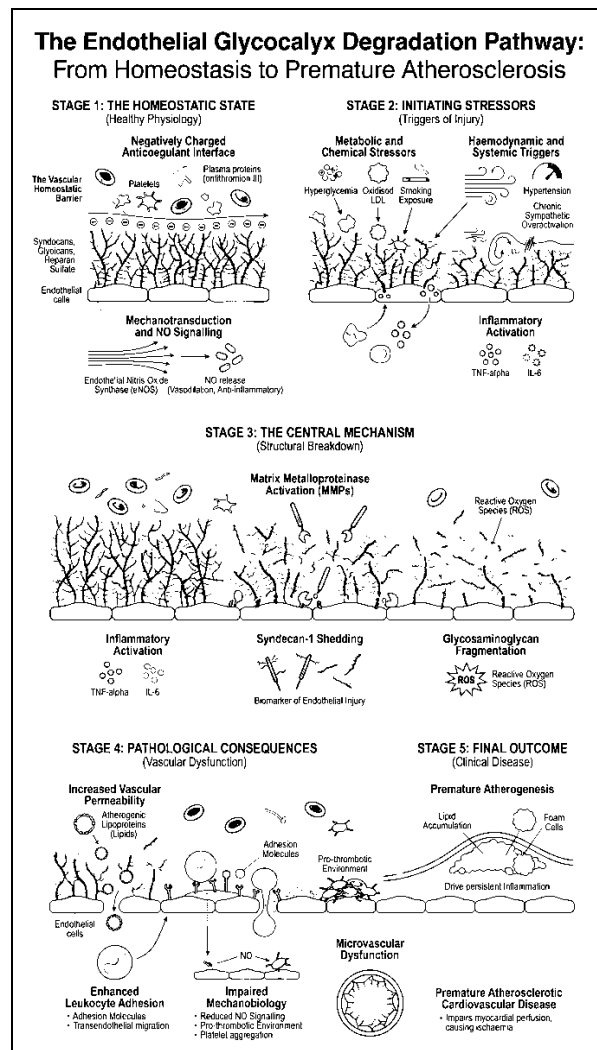


Figure 1. Endothelial Glycocalyx Degradation Pathway from Homeostasis to Premature Atherosclerosis

2. Research Method

2.1. Literature Search Strategy

This study employed a narrative literature review design to evaluate the role of endothelial glycocalyx degradation in the development and progression of premature atherosclerotic cardiovascular disease (ASCVD). A comprehensive literature search was conducted using multiple electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar. Publications from January 2010 to March 2026 were considered for the main narrative synthesis. Earlier foundational studies identified through reference screening were also included to explain glycocalyx structure, measurement, and mechanistic concepts. The search strategy incorporated combinations of the following keywords and Medical Subject Headings (MeSH) terms: “endothelial glycocalyx,” “glycocalyx degradation,” “atherosclerosis,” “premature cardiovascular disease,” “endothelial dysfunction,” “vascular inflammation,” “oxidative stress,” “microvascular dysfunction,” and

“cardiovascular risk.” Additional references were identified through manual screening of bibliographies from relevant articles to ensure comprehensive coverage of the available literature.

To enhance the validity and reliability of the evidence synthesized, priority was given to publications originating from high-impact peer-reviewed journals, internationally recognized cardiovascular guidelines, and studies demonstrating clear methodological rigor [9]. Evidence consistency was evaluated through comparison of findings across multiple studies, while particular attention was given to reproducibility of reported mechanisms and clinical observations. Publications lacking sufficient methodological transparency, duplicate reports, conference abstracts, editorials, and non-peer-reviewed sources were excluded from the analysis.

2.2. Inclusion and Exclusion Criteria

The selection of literature was guided by its relevance to the objectives of this review, particularly regarding the structure and function of the endothelial glycocalyx, mechanisms of glycocalyx degradation, endothelial dysfunction, and the pathogenesis of premature atherosclerotic cardiovascular disease. Eligible publications included original research articles, experimental investigations, observational studies, clinical studies, evidence-based guidelines, and review articles published in peer-reviewed journals. Studies examining vascular inflammation, oxidative stress, disturbed hemodynamics, microvascular dysfunction, endothelial injury, and therapeutic interventions associated with glycocalyx preservation were considered relevant for inclusion.

Publications were excluded when their primary focus was unrelated to cardiovascular or endothelial pathophysiology, when adequate methodological information was unavailable, or when the articles consisted solely of conference abstracts, editorials, commentaries, letters to the editor, or non-peer-reviewed reports. Duplicate publications and studies with limited relevance to endothelial glycocalyx biology and premature ASCVD were also excluded. The application of these criteria was intended to ensure the inclusion of scientifically rigorous and clinically relevant evidence supporting the objectives of the present review.

2.3. Conceptual Framework

The conceptual framework of this review proposes endothelial glycocalyx degradation as an upstream pathogenic event that contributes to the initiation and progression of premature atherosclerotic cardiovascular disease. Under physiological conditions, the endothelial glycocalyx functions as a critical regulator of vascular permeability, mechanotransduction, nitric oxide bioavailability, anticoagulant activity, and endothelial homeostasis. Disruption of glycocalyx

integrity by oxidative stress, chronic inflammation, hyperglycemia, dyslipidemia, disturbed shear stress, and sympathetic overactivation results in endothelial dysfunction and loss of vascular protective mechanisms.

Subsequent pathological alterations include increased endothelial permeability, enhanced leukocyte adhesion, platelet activation, inflammatory signaling, and lipid infiltration into the arterial wall. These processes collectively promote microvascular dysfunction, atherogenesis, plaque progression, and cardiovascular complications [10]. The framework further recognizes circulating glycocalyx degradation products and endothelial biomarkers as potential indicators of early vascular injury and future cardiovascular risk. Through this integrative model, glycocalyx degradation is positioned as a central mechanistic link connecting traditional cardiovascular risk factors with the development of premature ASCVD.

The conceptual framework presented in Figure 2 illustrates the relationship between endothelial glycocalyx degradation, downstream vascular pathophysiological processes, and potential therapeutic interventions. The framework proposes that glycocalyx injury functions as an upstream pathogenic event that promotes endothelial dysfunction, vascular inflammation, leukocyte adhesion, platelet activation, increased permeability, and microvascular impairment.

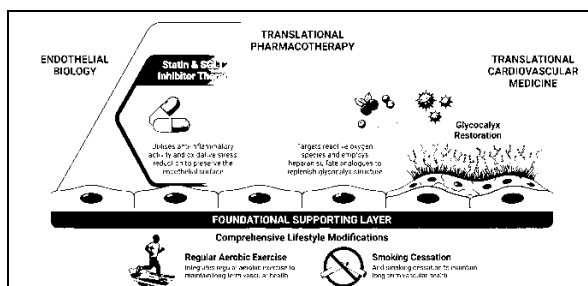


Figure 1. Implementing Glycocalyx-Targeted Therapeutic Strategies

2.4. Implementations

Implementation of the research framework involved integration of endothelial biology with translational cardiovascular medicine. The implementation phase additionally evaluated potential therapeutic interventions including statin therapy, sodium-glucose cotransporter-2 inhibitors, antioxidant therapy, and glycocalyx restoration approaches.

3. Result and Discussion

The reviewed literature describes several mechanisms through which endothelial glycocalyx injury may contribute to endothelial dysfunction, vascular inflammation, and atherosclerotic processes. However, evidence from prospective studies specifically evaluating glycocalyx-targeted interventions in premature ASCVD remains limited.

3.1. Structural Organization of the Endothelial Glycocalyx

The endothelial glycocalyx is a dynamic carbohydrate-rich meshwork extending from the apical endothelial membrane into the vascular lumen. The structure consists primarily of membrane-bound proteoglycans including syndecans and glypicans linked to glycosaminoglycan side chains such as heparan sulfate, chondroitin sulfate, dermatan sulfate, and hyaluronic acid [11].

Heparan sulfate constitutes the predominant glycosaminoglycan component and plays a critical role in anticoagulant regulation, endothelial permeability, and mechanotransduction. Glypicans anchored through glycosylphosphatidylinositol linkages additionally regulate nitric oxide signaling and vascular growth factor interactions [12].

The glycocalyx additionally incorporates adsorbed plasma proteins including albumin, antithrombin III, extracellular superoxide dismutase, and various coagulation regulators. This complex molecular arrangement produces a negatively charged vascular interface that repels circulating blood cells and limits inflammatory adhesion.

Reported glycocalyx dimensions vary according to vascular location and the measurement method used [13]. However, conventional histological preparation frequently collapses glycocalyx structure, contributing historically to underestimation of its biological significance.

3.2. Hemodynamic Mechanotransduction and Shear Stress Signaling

One of the most important functions of the endothelial glycocalyx involves mechanotransduction of laminar shear stress into intracellular biochemical signaling.

The endothelial glycocalyx participates in sensing fluid shear stress and transmitting mechanical signals to endothelial cells [14]. Nitric oxide subsequently promotes vasodilation, inhibits platelet aggregation, suppresses vascular inflammation, and limits smooth muscle proliferation.

Disturbed turbulent flow occurring at arterial bifurcations produces abnormal mechanical stress distribution across the glycocalyx. Chronic oscillatory shear stress disrupts glycocalyx organization and promotes endothelial inflammatory activation.

Regions exposed to disturbed flow demonstrate increased nuclear factor-kappa B activation, vascular cell adhesion molecule-1 expression, intercellular adhesion molecule-1 upregulation, and enhanced monocyte recruitment. These hemodynamic alterations contribute substantially to regional susceptibility for atherosclerotic plaque development.

The endothelial glycocalyx therefore functions not merely as a passive structural barrier but rather as a highly dynamic biomechanical sensor integrating vascular flow patterns with intracellular inflammatory and vasoactive signaling.

3.3. Molecular Mechanisms of Glycocalyx Degradation

Endothelial glycocalyx degradation results from the interaction of multiple molecular pathways involving oxidative stress, inflammatory mediators, matrix metalloproteinase activation, metabolic disturbances, dyslipidemia, and neurohumoral factors. These mechanisms interact synergistically to promote endothelial dysfunction and accelerate vascular injury. Figure 3 summarizes the principal molecular pathways involved in endothelial glycocalyx degradation and their downstream consequences leading to premature ASCVD.

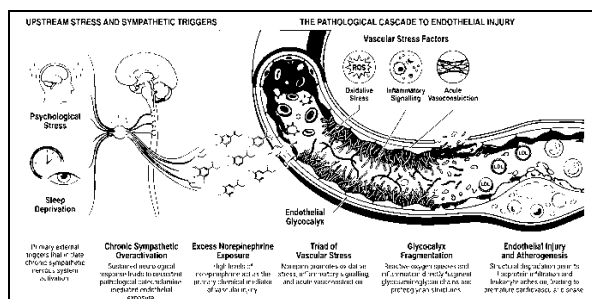


Figure 2. Endothelial Glycocalyx Degradation Pathophysiology

3.3.1. Oxidative Stress

Oxidative stress represents one of the principal mediators of glycocalyx degradation. Reactive oxygen species generated through smoking exposure, mitochondrial dysfunction, hyperglycemia, and chronic inflammation directly fragment glycosaminoglycan chains and proteoglycan structures. Superoxide radicals additionally reduce nitric oxide bioavailability through peroxynitrite formation, thereby worsening endothelial dysfunction [14].

3.3.2. Matrix Metalloproteinase Activation

Inflammatory cytokines including tumor necrosis factor- α and interleukin-6 stimulate activation of matrix metalloproteinases capable of cleaving glycocalyx-associated proteoglycans. Syndecan shedding represents a particularly important marker of endothelial injury. Elevated circulating syndecan-1 concentrations have been associated with acute coronary syndromes, septic shock, diabetes mellitus, and heart failure.

3.3.3. Hyperglycemia and Advanced Glycation End Products

Persistent hyperglycemia induces glycocalyx injury through nonenzymatic glycation, oxidative stress amplification, and inflammatory activation [15].

Advanced glycation end products interact with endothelial receptors for advanced glycation end products, triggering nuclear factor- κ B signaling and cytokine release. Diabetes-associated glycocalyx thinning significantly increases vascular permeability and microvascular dysfunction [13].

3.3.4. Dyslipidemia

Oxidized low-density lipoprotein particles directly damage endothelial glycocalyx integrity and promote inflammatory endothelial activation.

Lipoprotein infiltration into glycocalyx-deficient endothelium further accelerates intimal lipid accumulation and foam cell formation. Consequently, glycocalyx degradation and lipid deposition interact synergistically during early atherogenesis.

3.3.5. Sympathetic Overactivation

Chronic sympathetic nervous system activation associated with psychological stress and sleep deprivation increases catecholamine-mediated endothelial injury. Excess norepinephrine exposure promotes oxidative stress, inflammatory signaling, vasoconstriction, and glycocalyx fragmentation. This mechanism may partially explain increased cardiovascular risk among chronically stressed urban populations [16].

3.4. Glycocalyx Dysfunction and Atherosclerosis

Endothelial glycocalyx degradation fundamentally alters vascular biology in ways that strongly promote atherosclerotic disease progression.

Loss of glycocalyx thickness increases endothelial permeability and permits greater penetration of atherogenic lipoproteins into the arterial intima. Simultaneously, exposure of endothelial adhesion molecules enhances monocyte attachment and transendothelial migration.

Within the intima, recruited monocytes differentiate into macrophages that internalize oxidized lipoproteins and become foam cells. Persistent inflammatory signaling subsequently drives smooth muscle migration, extracellular matrix deposition, and necrotic core formation.

Importantly, glycocalyx degradation also contributes to plaque instability. Endothelial dysfunction impairs nitric oxide signaling and increases local thrombogenicity through platelet activation and reduced anticoagulant surface regulation.

Unstable plaques characterized by thin fibrous caps remain vulnerable to rupture, producing acute coronary syndromes and myocardial infarction.

3.5. Coronary Microvascular Dysfunction

Contemporary cardiovascular research increasingly recognizes coronary microvascular dysfunction as a

major contributor to ischemic heart disease independent of large epicardial coronary obstruction. The endothelial glycocalyx plays a central role in microvascular regulation through control of endothelial permeability, nitric oxide signaling, capillary hematocrit distribution, and leukocyte-endothelial interactions. Glycocalyx injury may affect microvascular function, but whether it directly reduces myocardial perfusion reserve in patients without obstructive epicardial coronary disease remains uncertain. Patients may experience ischemic symptoms despite the absence of obstructive coronary artery disease, as reflected in the diagnostic criteria for microvascular angina [17]. Microvascular dysfunction additionally contributes to heart failure with preserved ejection fraction through impaired myocardial relaxation, interstitial fibrosis, endothelial inflammation, and capillary rarefaction.

These mechanisms may be particularly important in the context of premature ASCVD. Persistent glycocalyx degradation occurring early in life may accelerate endothelial dysfunction, vascular inflammation, and atherogenic lipid retention long before clinically significant coronary obstruction develops [12]. Consequently, cumulative exposure to glycocalyx injury may contribute to earlier plaque initiation, faster plaque progression, and increased susceptibility to acute cardiovascular events at a younger age. This perspective supports the hypothesis that endothelial glycocalyx degradation represents an important biological link between traditional cardiovascular risk factors and premature ASCVD [18].

3.6. Glycocalyx Injury Biomarkers

Identification of circulating glycocalyx degradation products has become an important area of cardiovascular biomarker research. Syndecan-1, hyaluronic acid, heparan sulfate fragments, and soluble thrombomodulin have all been investigated as markers of endothelial injury [19]. In trauma patients, higher admission syndecan-1 levels were associated with inflammation and increased mortality [19]. Whether this marker predicts premature ASCVD requires separate validation. Emerging imaging technologies including sidestream dark field microscopy and intravital vascular imaging may additionally permit direct assessment of glycocalyx thickness and microvascular integrity.

3.7. Therapeutic Strategies Targeting the Glycocalyx

3.7.1. Statins

Beyond lipid reduction, statins demonstrate pleiotropic endothelial protective effects including anti-inflammatory activity, oxidative stress reduction, and glycocalyx preservation [20].

3.7.2. Sodium-Glucose Cotransporter-2 Inhibitors

Sodium-glucose cotransporter-2 inhibitors appear capable of improving endothelial function through reduction of oxidative stress, inflammation, and vascular stiffness. Recent studies additionally suggest possible glycocalyx-preserving effects independent of glucose lowering.

3.7.3. Antioxidant Therapy

Antioxidant approaches targeting mitochondrial reactive oxygen species generation remain under active investigation. Reduction of oxidative stress may attenuate glycocalyx fragmentation and endothelial dysfunction.

3.7.4. Heparan Sulfate Restoration

Experimental therapies involving heparan sulfate analogs and glycocalyx-replenishing biomaterials represent emerging translational research areas. Restoration of glycocalyx structure may theoretically improve endothelial barrier function, reduce vascular inflammation, and normalize mechanotransduction.

3.7.5. Lifestyle Modification

Exercise, smoking cessation, blood pressure control, glucose regulation, and adequate sleep duration all appear beneficial for endothelial glycocalyx preservation. Regular aerobic exercise particularly improves endothelial nitric oxide signaling and vascular function.

3.8. Artificial Intelligence and Glycocalyx Research

Artificial intelligence has shown potential in cardiovascular screening. For example, AI-enabled electrocardiography has been studied for identifying patients with atrial fibrillation during sinus rhythm and screening for cardiac contractile dysfunction [21] and for screening for cardiac contractile dysfunction [22]. Whether similar approaches can identify early endothelial glycocalyx dysfunction remains to be established. Deep learning applied to photoplethysmography has been investigated for cardiovascular risk prediction [23]. Its ability to identify endothelial glycocalyx dysfunction has not been established. Integration of endothelial biomarkers, genomic profiling, imaging data, and hemodynamic modeling may facilitate highly individualized cardiovascular risk prediction.

3.9. Discussion

The reviewed literature suggests that glycocalyx injury may contribute to endothelial dysfunction and atherosclerotic processes. Direct evidence establishing it as an initiating cause of premature ASCVD in humans remains limited. The analysis identified oxidative stress, inflammatory signaling, disturbed hemodynamic flow, hyperglycemia, and sympathetic

overactivation as major contributors to glycocalyx injury.

An important finding of the present review is the potential contribution of endothelial glycocalyx degradation to premature ASCVD. While conventional cardiovascular models primarily emphasize lipid accumulation and arterial stenosis, the evidence reviewed suggests that glycocalyx injury may represent an earlier pathogenic event occurring before detectable structural vascular disease develops. Individuals exposed to prolonged oxidative stress, metabolic abnormalities, smoking, or chronic inflammation may experience accelerated glycocalyx deterioration, thereby promoting earlier endothelial dysfunction and atherosclerotic progression. This mechanism may partially explain why certain individuals develop clinically significant cardiovascular disease at a relatively young age despite the absence of advanced traditional risk profiles.

Loss of glycocalyx integrity significantly altered endothelial permeability and promoted leukocyte-endothelial interaction, vascular inflammation, and lipid infiltration into the arterial wall. The reviewed literature proposes a possible relationship between glycocalyx dysfunction and coronary microvascular abnormalities; however, direct clinical evidence for this relationship remains limited.

This finding is particularly important because many younger cardiovascular patients may develop ischemic symptoms despite relatively limited obstructive coronary disease. The mechanotransduction analysis further demonstrated that disturbed shear stress patterns contribute significantly to endothelial inflammatory activation through nuclear factor-kappa B signaling pathways.

From a translational perspective, the study identified several therapeutic approaches potentially capable of preserving endothelial glycocalyx structure including statins, sodium-glucose cotransporter-2 inhibitors, antioxidant therapies, exercise intervention, and endothelial-targeted pharmacologic strategies. The integration of artificial intelligence into cardiovascular endothelial research may further improve early detection of glycocalyx dysfunction before irreversible structural vascular disease develops.

3.10. Critical Appraisal and Clinical Implications

The present review extends previous literature by emphasizing endothelial glycocalyx degradation as a central integrative mechanism linking oxidative stress, inflammation, disturbed hemodynamics, microvascular dysfunction, and premature ASCVD. While earlier reviews primarily focused on endothelial dysfunction or atherosclerosis as isolated processes, the current analysis highlights the glycocalyx as a potential upstream determinant of vascular injury.

However, several limitations within the existing evidence should be acknowledged. First, substantial heterogeneity exists regarding glycocalyx imaging techniques, biomarker assessment methods, and study populations, limiting direct comparisons across studies. Second, many mechanistic insights originate from experimental or observational investigations, and causal relationships in human populations remain incompletely established. Third, inconsistencies have been reported regarding the predictive value of certain glycocalyx biomarkers, reflecting differences in study design and methodological approaches.

Despite these limitations, preservation of glycocalyx integrity may have important clinical implications for the early prevention of premature ASCVD. Because glycocalyx injury frequently precedes overt endothelial dysfunction and plaque formation, early identification of glycocalyx abnormalities may facilitate risk stratification before irreversible vascular damage occurs. Consequently, glycocalyx-targeted prevention strategies may represent a promising future direction in precision cardiovascular medicine.

4. Conclusion

The endothelial glycocalyx has emerged as a critical regulator of vascular homeostasis and an important determinant of endothelial integrity. The evidence reviewed in this study suggests that glycocalyx degradation is closely associated with several pathophysiological processes involved in premature atherosclerotic cardiovascular disease (ASCVD), including oxidative stress, inflammatory signaling, impaired mechanotransduction, dyslipidemia-induced endothelial injury, and coronary microvascular dysfunction. Collectively, these mechanisms contribute to endothelial dysfunction, increased vascular permeability, leukocyte adhesion, platelet activation, and atherogenic lipid retention, thereby facilitating the development and progression of atherosclerotic disease.

The findings of this review further indicate that glycocalyx disruption may represent an early manifestation of vascular injury and may contribute to the transition from exposure to cardiovascular risk factors toward clinically apparent atherosclerosis. However, although experimental and observational studies increasingly support this concept, the available evidence remains insufficient to establish a definitive causal relationship, and further prospective investigations are warranted.

From a clinical perspective, preservation of glycocalyx integrity may provide a promising avenue for improving early cardiovascular risk assessment and preventive strategies. In addition, glycocalyx-associated biomarkers, including syndecan-1, hyaluronic acid, heparan sulfate fragments, and soluble thrombomodulin, may offer potential utility in

identifying subclinical endothelial injury prior to the development of overt cardiovascular disease. Nevertheless, challenges related to biomarker standardization, reproducibility, and clinical validation continue to limit their routine implementation in clinical practice.

Future research should focus on the development of standardized glycocalyx assessment methodologies, validation of circulating biomarkers in large prospective cohorts, and evaluation of glycocalyx-targeted therapeutic interventions through adequately powered clinical trials. Furthermore, integration of advanced vascular imaging, molecular profiling, and artificial intelligence-based analytical approaches may enhance the understanding of glycocalyx biology and facilitate the development of more precise strategies for the prevention and management of premature ASCVD.

In conclusion, the available evidence supports the growing recognition of endothelial glycocalyx integrity as an important component of vascular health and a potentially relevant factor in the pathogenesis of premature atherosclerotic cardiovascular disease.

Acknowledgements

The author would like to express sincere gratitude to the Department of Cardiac, Thoracic and Vascular Surgery, National University Heart Centre, Singapore, especially Dr. Li Yue, for the recommendation and opportunity to join and gain valuable exposure to cardiovascular research and clinical sciences. Also extends appreciation to Yong Loo Lin School of Medicine year 2024, for providing an inspiring academic environment that encouraged scientific curiosity and professional development in cardiovascular medicine.

The author would also like to express profound gratitude to his alma mater, The University of Western Australia, for shaping his academic foundation and professional perspective. Special appreciation is extended to lecturer Gavin Huangfu for his guidance, encouragement, and for inspiring the courage to return to Southeast Asia and begin the journey toward becoming a medical professional in the region. Express heartfelt gratitude to Alfred Yip from Melbourne for his guidance, encouragement, and support as a senior mentor. His advice, perspective, and academic motivation contributed significantly to the author's perseverance and growth throughout this research journey.

Special appreciation is dedicated to Co-ass Retina Ayu Zeta Adly Wirjopranoto for her unwavering trust, patience, and unconditional support throughout my journey as a junior resident. Her constant encouragement and enduring presence became a source of strength during the demanding academic, clinical, and professional challenges of this career path.

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