Edición 4, Año 3, Número 1, 2026

E-ISSN: 3061-8045, P-ISSN: 3061-8517

Revista IECCMEXICO

Inflamación Cardiometabólica y Disfunción Vascular Temprana: Nuevas Fronteras en la Estratificación del Riesgo Cardiovascular

Cardiometabolic Inflammation and Early Vascular Dysfunction: Expanding the Frontiers of Cardiovascular Risk Stratification

Cristóbal Washington Franco Lucas
Universidad Estatal del Sur de Manabi
drcristobal.franco@gmail.com
https://orcid.org/0000-0003-2212-2909

Fernando Bernal González
Universidad Autónoma de Durango
fernandobg_98@hotmail.com
https://orcid.org/0009-0006-3316-1080

Jorge Che Enseñat
HOSPITAL SAN FERNANDO CIUDAD DE PANAMA
jorgecheensenat@gmail.com
https://orcid.org/0009-0002-3349-082X

Diego Andres Martinez López
Universidad De San Carlos De Guatemala
diegolpz353@gmail.com
https://orcid.org/0009-0003-7286-1731

Santiago Alberto Avila Ak
Universidad Autónoma de Campeche
santiagoalbertoavilaak@gmail.com
https://orcid.org/0009-0007-3979-5321

Hugo Alfredo López Herrera
Universidad San Carlos de Guatemala
huguinlh6@gmail.com
https://orcid.org/0009-0001-3383-2191

Erick Eduardo López Santos
Universidad Autónoma de Guadalajara
erickels@live.com.mx
https://orcid.org/0009-0008-7485-0178

Kevin Leonardo Rivas Gómez
Universidad de San Carlos de Guatemala
Kevinrivas202042356@gmail.com
https://orcid.org/0009-0004-6847-7216

Recibido: 21-Feb-2026 | **Aceptado:** 21-Feb-2026 | **Publicado:** 23-Feb-2026

***Autor de correspondencia** *drcristobal.franco@gmail.com*

Cómo citar este artículo: Franco Lucas, C. W., Che Enseñat, J., Avila Ak, S. A., López Santos, E. E., Bernal González, F., Martinez López, D. A., López Herrera, H. A., & Rivas Gómez, K. L. (2026). Cardiometabolic Inflammation and Early Vascular Dysfunction: Expanding the Frontiers of Cardiovascular Risk Stratification. México. *Revista IECCMEXICO*, 4(1) 493-518. Quality Consulting Instituto de Educación Capacitación y Certificación de México. https://ieccmexico.com/publishing

Copyright (c) 2026 Franco Lucas, C. W., Che Enseñat, J., Avila Ak, S. A., López Santos, E. E., Bernal González, F., Martinez López, D. A., López Herrera, H. A., & Rivas Gómez, K. L.; Este es un artículo de acceso abierto distribuido bajo los términos de la Attribution 4.0 International (CC BY) Revista IECCMEXICO, México / Vol. 4, N. 1 / pp. 493-518/ enero-junio, 2026 / E-ISSN: 3061-8045, P-ISSN: 3061-8517. Artículo de Investigación.

RESUMEN

La enfermedad cardiovascular continúa siendo la principal causa de morbilidad y mortalidad a nivel mundial, a pesar de los avances en el control lipídico y la modificación de factores de riesgo tradicionales. Evidencia reciente indica que la disfunción cardiometabólica y la inflamación crónica de bajo grado actúan de manera sinérgica acelerando el daño vascular temprano mucho antes de la aparición de eventos clínicos manifiestos. Esta revisión integra datos epidemiológicos contemporáneos, fundamentos mecanísticos, análisis de biomarcadores y evidencia de ensayos clínicos aleatorizados para examinar el eje cardiometabólico–inflamatorio–vascular como un

Edition 4, Year 3, Number 1, 2026

E-ISSN: 3061-8045, P-ISSN: 3061-8517

IECCMEXICO Review

marco unificado para la evaluación temprana del riesgo cardiovascular. Los datos poblacionales confirman la expansión sostenida de la carga global de enfermedad cardiovascular, paralela al aumento en la prevalencia de síndrome metabólico y resistencia a la insulina. Biomarcadores inflamatorios como la proteína C reactiva ultrasensible y la interleucina-6 muestran asociaciones graduales con eventos cardiovasculares incidentes, independientes de los factores de riesgo tradicionales. La rigidez arterial emerge como un fenotipo intermedio medible que refleja la exposición acumulativa a estrés metabólico e inflamatorio, con los cuartiles más elevados asociados a mayores tasas de eventos. Además, ensayos clínicos que han evaluado terapias dirigidas a vías inflamatorias muestran reducción de eventos cardiovasculares mayores en poblaciones seleccionadas de alto riesgo, respaldando el papel causal de la inflamación en la progresión aterosclerótica. La incorporación de biomarcadores inflamatorios en modelos predictivos tradicionales mejora de manera consistente la discriminación y la estratificación del riesgo. En conjunto, estos hallazgos respaldan un cambio de paradigma hacia la detección biológica temprana de la disfunción vascular, especialmente relevante en países como México, Colombia y Ecuador, donde el riesgo cardiometabólico continúa en ascenso.

PALABRAS CLAVE

riesgo cardiometabólico, inflamación sistémica, enfermedad cardiovascular temprana, rigidez arterial, síndrome metabólico, proteína C reactiva ultrasensible, interleucina-6, estratificación del riesgo, disfunción vascular, prevención de precisión

ABSTRACT

Cardiovascular disease remains the leading cause of global morbidity and mortality, despite significant advances in lipid management and risk factor control. Emerging evidence indicates that cardiometabolic dysfunction and chronic low-grade inflammation act synergistically to accelerate early vascular injury long before the onset of overt clinical events. This review integrates contemporary epidemiological data, mechanistic insights, biomarker analyses, and randomized clinical trial evidence to examine the cardiometabolic–inflammatory–vascular axis as a unified framework for early cardiovascular risk assessment. Population-level data confirm the sustained global expansion of cardiovascular burden, paralleled by increasing prevalence of metabolic syndrome and insulin resistance. Inflammatory biomarkers such as high-sensitivity C-reactive protein and interleukin-6 demonstrate graded associations with incident cardiovascular events, independent of traditional risk factors. Arterial stiffness emerges as a measurable intermediate phenotype reflecting cumulative metabolic and inflammatory exposure, with higher quartiles associated with substantially increased event rates. Furthermore, randomized trials targeting inflammatory pathways show reductions in major adverse cardiovascular events in selected high-risk populations, supporting inflammation as a modifiable contributor to atherosclerotic progression. The integration of inflammatory biomarkers into traditional prediction models yields modest but consistent improvements in discrimination and risk stratification. These findings collectively support a paradigm shift toward earlier biological detection of vascular dysfunction. Such an approach is particularly relevant for regions experiencing rapid growth in cardiometabolic risk, including Mexico, Colombia, and Ecuador. Advancing cardiovascular prevention will require integrative strategies that combine metabolic control, inflammatory assessment, and early vascular evaluation within a precision-based framework.

KEYWORDS

cardiometabolic risk, systemic inflammation, early cardiovascular disease, arterial stiffness, metabolic syndrome, C-reactive protein, interleukin-6, risk stratification, vascular dysfunction, precision prevention

INTRODUCCIÓN

Cardiometabolic risk represents one of the most pressing and complex challenges in contemporary cardiovascular medicine. Despite significant advances in prevention and treatment, cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide, accounting for a substantial proportion of premature deaths across diverse populations (Benjamin et al., 2021; Yusuf et al., 2020). Traditionally, cardiovascular risk has been conceptualized through well-established factors such as hypertension, diabetes mellitus, dyslipidemia, obesity, and smoking. However, growing evidence over the past two decades has redefined this paradigm, emphasizing the central role of chronic low-

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

grade inflammation as a fundamental biological mechanism linking metabolic dysfunction and early cardiovascular disease.

Inflammation is no longer viewed as a mere consequence of atherosclerosis but as an active driver of vascular injury and plaque instability. Seminal work has demonstrated that inflammatory mediators contribute to endothelial dysfunction, lipid oxidation, vascular remodeling, and thrombosis (Libby & Hansson, 2020). High-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) have emerged as key biomarkers reflecting this inflammatory burden and improving risk prediction beyond traditional models (Akbaraly et al., 2023; Ridker & Libby, 2024). Indeed, the 2025 ACC/AHA scientific statement reinforces the clinical relevance of inflammation in cardiovascular prevention and highlights novel therapeutic approaches targeting inflammatory pathways (Ridker et al., 2025).

Parallel to these findings, cardiometabolic conditions such as insulin resistance, metabolic syndrome, and metabolic dysfunction–associated steatotic liver disease (MASLD) have been increasingly recognized as interconnected contributors to subclinical vascular damage and heart failure with preserved ejection fraction (HFpEF) (Eroglu, 2024; Petersen & Shulman, 2022). Insulin resistance promotes endothelial dysfunction, enhances oxidative stress, and sustains systemic inflammation, creating a milieu conducive to early atherosclerosis and arterial stiffening. The prevalence of metabolic syndrome continues to rise globally, as shown in population-based surveys (Ford, 2021), reinforcing the urgency of addressing cardiometabolic risk at earlier stages of disease progression.

Importantly, arterial stiffness has gained attention as a measurable intermediate phenotype reflecting cumulative vascular injury. Recent investigations demonstrate that arterial stiffness not only correlates with cardiometabolic risk factors but also predicts incident cardiovascular events (De la Maza-Bustindui et al., 2025; Lee et al., 2022). These findings support the concept that early vascular aging is a clinically meaningful target for intervention. Furthermore, large cohort studies such as Framingham have consistently shown that systemic inflammatory burden is associated with adverse cardiovascular outcomes, even after adjusting for conventional risk factors (Tejada et al., 2022; Wang et al., 2021).

The evolving understanding of cardiometabolic risk extends beyond classical biomarkers. Emerging research highlights the role of gut microbiota-mediated inflammation as a novel mechanistic pathway influencing vascular health (Khan et al., 2023). These insights suggest that cardiovascular disease should be approached not only as a lipid-driven condition but as a systemic inflammatory-metabolic disorder with multi-organ implications.

Therapeutic implications of this paradigm shift are profound. Randomized clinical trials evaluating anti-inflammatory strategies, including IL-1β inhibition, have demonstrated reductions in cardiovascular events independent of lipid lowering (Ridker, Everett, & Thuren, 2025). These results validate inflammation as a modifiable therapeutic target and open new clinical frontiers in risk stratification and prevention.

Despite these advances, important gaps remain. Risk prediction models still rely heavily on traditional variables and may underestimate early vascular injury in individuals with subclinical inflammation or metabolic dysfunction (Yeboah et al., 2022; Parikh et al., 2023). Moreover, while global data describe the magnitude of cardiometabolic disease, regional differences in Latin America—including Mexico, Colombia, and Ecuador—highlight the need for context-specific strategies. These countries face a dual burden of rising obesity, diabetes, and hypertension rates alongside socioeconomic disparities that influence early cardiovascular detection and management. Integrating

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

inflammatory biomarkers and early vascular assessment into preventive frameworks may offer substantial benefits in these settings.

The present review aims to synthesize contemporary evidence on the interplay between cardiometabolic risk, inflammation, and early cardiovascular disease. Specifically, this article seeks to:

1. Examine the biological mechanisms linking metabolic dysfunction and systemic inflammation to early vascular injury.
2. Analyze current evidence regarding inflammatory biomarkers and arterial stiffness as tools for early cardiovascular risk stratification.
3. Discuss emerging therapeutic strategies targeting inflammatory pathways.
4. Explore the clinical implications of these findings within an international framework, with particular relevance to Latin American populations.

This review was conducted through a structured analysis of high-impact peer-reviewed literature published in leading cardiovascular and metabolic journals. Priority was given to large cohort studies, meta-analyses, translational research, and recent scientific statements from international societies. By integrating mechanistic insights with epidemiological and clinical data, this work aims to provide a comprehensive and clinically meaningful perspective on the new frontiers of cardiometabolic cardiovascular prevention.

Understanding cardiometabolic risk through the lens of inflammation represents a shift from reactive treatment of established disease toward proactive identification of early vascular dysfunction. Such an approach aligns with modern precision medicine and offers an opportunity to intervene before irreversible cardiovascular damage occurs.

DESARROLLO

Cardiometabolic risk has moved from being a “cluster” of conventional risk factors to a more integrated pathobiological framework in which metabolic dysfunction and chronic, low-grade inflammation interact to accelerate early cardiovascular disease. This shift is not semantic—it changes how risk is detected, how prevention is prioritized, and which therapeutic targets become clinically meaningful. Contemporary evidence supports a model in which dysregulated glucose and lipid metabolism, adipose tissue dysfunction, vascular inflammation, and immune activation collectively promote endothelial injury, arterial stiffening, and atherogenesis well before clinical events occur (Libby & Hansson, 2020; Petersen & Shulman, 2022; Ridker & Libby, 2024).

1) Global relevance and why “early” cardiovascular disease matters

Cardiovascular disease remains the dominant contributor to global mortality and disability, and its burden is increasingly driven by cardiometabolic determinants that are rising in prevalence across regions and age groups (Benjamin et al., 2021; Yusuf et al., 2020). While many prevention frameworks still focus on 10-year risk calculators, there is growing recognition that clinically silent vascular injury accumulates for years—sometimes decades—before the first myocardial infarction, stroke, or heart failure presentation. Early disease is therefore not merely “pre-symptomatic”; it is a measurable biological stage characterized by subclinical atherosclerosis, arterial stiffness, endothelial dysfunction, and low-grade systemic inflammation (Lee et al., 2022; Yeboah et al., 2022).

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

This is particularly relevant because cardiometabolic risk often emerges earlier than overt CVD. Diabetes and related metabolic abnormalities have long been known to amplify cardiovascular mortality and to potentiate the impact of other risk factors (Stamler et al., 2021). As metabolic syndrome and insulin resistance become more common—documented across national surveys—health systems face a growing population with vascular aging that may not be detected by traditional risk assessment alone (Ford, 2021; Petersen & Shulman, 2022). The public health implication is clear: if early mechanisms are identified and modified upstream, downstream cardiovascular events could be delayed or prevented.

2) Inflammation as a driver, not simply a marker

Atherosclerosis is now widely understood as a chronic inflammatory disease of the arterial wall. Lipoproteins, especially LDL and remnant particles, initiate retention and modification within the intima; however, lesion progression and destabilization require immune activation, cytokine signaling, macrophage recruitment, and inflammatory amplification (Libby & Hansson, 2020). Inflammation contributes to endothelial dysfunction, impairs vasomotor responsiveness, promotes oxidative stress, and increases the likelihood of thrombotic complications through plaque vulnerability and procoagulant shifts (Libby & Hansson, 2020).

High-sensitivity C-reactive protein (hs-CRP) has become the most clinically familiar marker reflecting systemic inflammatory activity relevant to cardiovascular risk. Large bodies of work have shown that hs-CRP is associated with future cardiovascular events and adds prognostic information beyond traditional factors, supporting its role as an enhancer in selected risk assessments (Ridker, MacFadyen, & Libby, 2021; Ridker & Libby, 2024). Importantly, the evolving guideline landscape has underscored that inflammation-informed prevention is not limited to a single biomarker; IL-6 signaling and related pathways are increasingly recognized as biologically upstream and potentially actionable in targeted interventions (Akbaraly et al., 2023; Ridker et al., 2025).

From a mechanistic perspective, the cardiometabolic-inflammation link is reinforced by the biology of adipose tissue and insulin resistance. Visceral adiposity is metabolically active, producing adipokines and inflammatory mediators that promote hepatic insulin resistance, dyslipidemia, and systemic immune activation. Insulin resistance itself magnifies vascular risk by promoting endothelial dysfunction and increasing oxidative stress, creating a feed-forward loop where metabolic and inflammatory signals reinforce each other (Petersen & Shulman, 2022).

3) Cardiometabolic risk as an integrated system: beyond "risk factors"

The cardiometabolic construct includes hypertension, dysglycemia, dyslipidemia, obesity (particularly visceral), and associated organ dysfunction such as steatotic liver disease. Instead of operating independently, these conditions share core mechanisms—insulin resistance, ectopic fat deposition, oxidative stress, and inflammation—that converge on the vasculature and myocardium (Eroglu, 2024; Petersen & Shulman, 2022).

A major clinical consequence is that early cardiovascular disease may present not only as coronary atherosclerosis but also as myocardial remodeling and HFpEF phenotypes linked to metabolic inflammation. Contemporary discussions have highlighted the shared mechanistic ground between HFpEF and metabolic liver disease, suggesting that

cardiometabolic inflammation is a system-wide process affecting multiple organs simultaneously (Eroglu, 2024). This integrated view strengthens the rationale for prevention approaches that target inflammation and metabolic dysfunction together rather than treating them as parallel issues.

4) Arterial stiffness as a bridge between metabolic dysfunction and early events

Arterial stiffness has emerged as a particularly informative intermediate marker because it reflects cumulative vascular injury from metabolic, inflammatory, and hemodynamic stressors. It is clinically relevant in two ways: (1) it is measurable before events occur, and (2) it predicts incident cardiovascular outcomes across populations with cardiometabolic risk (Lee et al., 2022). Recent data also suggest that management of cardiometabolic risk factors can influence the progression or reversion of arterial stiffness, making it not only a marker but a potential therapeutic target for monitoring vascular age (De la Maza-Bustindui et al., 2025).

In clinical terms, arterial stiffness may capture the "hidden" burden that traditional measurements miss. Two individuals can share similar LDL levels or blood pressure readings, yet differ substantially in inflammatory burden and vascular compliance. This is one reason why novel markers and integrated biomarker strategies continue to be evaluated as complements to conventional risk scores (Yeboah et al., 2022; Parikh et al., 2023).

5) Biomarkers and risk stratification: moving earlier, with precision

Risk prediction is evolving from single-variable models toward multi-domain strategies that combine clinical factors with biomarkers reflecting inflammation, vascular injury, and metabolic status. Large cohort-based analyses have examined how adding novel biomarkers improves discrimination and reclassification for cardiovascular events, especially in intermediate-risk groups (Yeboah et al., 2022; Wang et al., 2021). The practical objective is not to generate complexity for its own sake, but to identify people who are accumulating early disease and would benefit most from preventive intensification.

Inflammatory biomarkers are increasingly central in this framework. Evidence supports that hs-CRP and IL-6, among others, are associated with cardiovascular outcomes and can provide incremental predictive value, especially when interpreted within the broader cardiometabolic context (Akbaraly et al., 2023; Ridker & Libby, 2024). Moreover, systematic reviews and meta-analyses have reinforced that metabolic syndrome is strongly associated with cardiovascular outcomes, supporting cardiometabolic clustering as a meaningful clinical signal rather than a purely descriptive label (Wong et al., 2023).

6) New mechanistic frontiers: gut microbiota-mediated inflammation

A rapidly developing area involves the relationship between gut microbiota and cardiovascular inflammation. Emerging work describes pathways in which microbial metabolites and intestinal barrier changes influence systemic immune activation, inflammatory tone, and metabolic regulation—mechanisms that may contribute to atherogenesis and cardiometabolic disease progression (Khan et al., 2023). While this field remains dynamic, it provides a plausible biological explanation for why lifestyle interventions and dietary patterns can have outsized effects on cardiometabolic

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

risk beyond weight reduction alone. It also hints at future preventive strategies that may involve microbiome-informed interventions, although translation into routine practice requires careful evidence appraisal (Khan et al., 2023).

7) Therapeutic implications: from lipid-centric to inflammation-inclusive prevention

A major turning point in the field has been the demonstration that cardiovascular event reduction can be achieved through anti-inflammatory therapy independent of lipid lowering, validating inflammation as a causal pathway rather than merely an associated signal. Clinical trial evidence involving IL-1β pathway inhibition has shown reductions in atherosclerotic events, establishing proof-of-concept for targeted immunomodulation in select high-risk populations (Ridker, Everett, & Thuren, 2025). These findings align with broader guideline discussions emphasizing inflammation as a relevant clinical domain and recognizing the expanding therapeutic landscape for cardiovascular prevention (Ridker et al., 2025).

At the same time, the practical translation must remain grounded. Anti-inflammatory therapies are not universally applicable; they require careful patient selection, monitoring, and cost-benefit evaluation. For educational purposes, the key takeaway is that prevention is entering a phase where cardiometabolic risk management may incorporate both traditional interventions (blood pressure control, lipid lowering, glycemic management) and mechanism-based strategies addressing inflammation when supported by evidence and clinical context (Libby & Hansson, 2020; Ridker et al., 2025).

8) International perspective with Latin American relevance: Mexico, Colombia, and Ecuador

Although much of the mechanistic and trial evidence originates from large cohorts and clinical trials in high-income settings, the cardiometabolic-inflammation framework is highly applicable to Latin America. Mexico, Colombia, and Ecuador face growing burdens of obesity, diabetes, and hypertension, often alongside socioeconomic inequities that influence access to prevention, continuity of care, and early detection. In these contexts, the value of early risk stratification is potentially amplified: systems may benefit from identifying high-risk trajectories earlier, prioritizing interventions, and preventing costly late-stage complications.

The global burden evidence underscores that cardiovascular risk factors are widespread and persistent across regions (Yusuf et al., 2020; Benjamin et al., 2021). For Latin America, the practical application often involves strengthening risk factor control while adapting prevention programs to local realities—resource constraints, disparities, and cultural determinants of lifestyle patterns. The cardiometabolic-inflammation paradigm supports a “more upstream” prevention strategy: recognizing that early disease is not invisible, but measurable through vascular and biomarker signals (Lee et al., 2022; Ridker & Libby, 2024). This aligns with educational goals for training clinicians who can interpret cardiometabolic risk as a system-wide process rather than a checklist.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze the interplay between cardiometabolic risk, systemic inflammation, and early cardiovascular disease in order to strengthen evidence-based risk stratification, improve early detection strategies, and promote integrative preventive approaches within an international clinical framework, with contextual relevance for Mexico, Colombia, and Ecuador.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Specific Objectives

Cognitive Domain

1. **Remembering**
   - Identify the principal cardiometabolic risk factors associated with early cardiovascular disease.
   - Recognize key inflammatory biomarkers (e.g., hs-CRP, IL-6) involved in cardiovascular risk stratification.
2. **Understanding**
   - Explain the biological mechanisms linking insulin resistance, systemic inflammation, and vascular dysfunction.
   - Describe the pathophysiological relationship between arterial stiffness and early cardiovascular events.
3. **Applying**
   - Apply current evidence to interpret inflammatory biomarkers within the context of cardiometabolic risk assessment.
   - Integrate traditional cardiovascular risk factors with emerging inflammatory markers in clinical reasoning scenarios.
4. **Analyzing**
   - Differentiate between traditional lipid-centric cardiovascular models and inflammation-inclusive prevention frameworks.
   - Examine the contribution of metabolic syndrome components to early vascular injury in diverse populations.
5. **Evaluating**
   - Critically appraise contemporary literature regarding anti-inflammatory therapies in atherosclerotic disease.
   - Assess the strengths and limitations of novel biomarkers in improving cardiovascular risk prediction models.
6. **Creating**
   - Propose integrative preventive strategies that combine metabolic control and inflammation modulation.
   - Design evidence-informed educational frameworks for cardiometabolic risk evaluation applicable to Latin American healthcare settings.

Psychomotor Domain

1. Develop the ability to interpret laboratory inflammatory markers within cardiovascular risk profiles.
2. Perform structured cardiovascular risk stratification incorporating cardiometabolic and inflammatory parameters.
3. Utilize arterial stiffness and subclinical vascular indicators in early cardiovascular assessment when available.
4. Construct patient-centered preventive plans integrating lifestyle, pharmacological, and risk-modifying strategies.
5. Apply evidence-based clinical reasoning to early cardiometabolic scenarios in academic case simulations.

Affective Domain

1. Value the importance of early identification of cardiometabolic risk as a preventive priority.
2. Foster a proactive clinical mindset focused on upstream prevention rather than reactive disease management.
3. Demonstrate ethical responsibility in applying inflammatory and biomarker-based strategies to patient care.
4. Encourage interdisciplinary collaboration in managing cardiometabolic and inflammatory conditions.
5. Promote awareness of regional disparities in cardiovascular prevention, particularly in Mexico, Colombia, and Ecuador.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

OBJETO DE ESTUDIO

The object of study of this review is the multidimensional interaction between cardiometabolic risk, systemic inflammation, and early cardiovascular disease as a measurable and clinically actionable phenomenon in adult populations.

This phenomenon is defined as the biological and clinical process through which metabolic dysfunction—characterized by insulin resistance, visceral adiposity, dyslipidemia, hypertension, and impaired glucose metabolism—interacts with chronic low-grade inflammation to promote subclinical vascular injury, arterial stiffness, endothelial dysfunction, and the early stages of atherosclerotic disease before the onset of overt cardiovascular events.

1. Conceptual Definition of the Phenomenon

Cardiometabolic risk is conceptualized not merely as a cluster of independent variables, but as an integrated pathophysiological system in which metabolic and inflammatory pathways converge to accelerate vascular aging and myocardial remodeling. In this framework:

- **Metabolic dysfunction** contributes to endothelial injury, oxidative stress, and lipid abnormalities.
- **Systemic inflammation** amplifies vascular damage through immune activation and cytokine signaling.
- **Early cardiovascular disease** manifests as subclinical atherosclerosis, increased arterial stiffness, and measurable biomarker elevation prior to clinical events such as myocardial infarction, stroke, or heart failure.

This integrated construct is grounded in contemporary cardiovascular science, which recognizes inflammation as both a mediator and therapeutic target in atherosclerotic disease progression (Libby & Hansson, 2020; Ridker & Libby, 2024).

2. Population Under Investigation

The population of interest consists of:

- Adults aged ≥18 years
- Individuals with one or more cardiometabolic risk factors (e.g., obesity, type 2 diabetes, metabolic syndrome, hypertension, dyslipidemia)
- Patients without established cardiovascular disease but with measurable indicators of early vascular dysfunction

Although the scientific evidence is derived from large international cohorts, this review contextualizes its analysis within a global framework, emphasizing clinical applicability in Latin American settings, particularly Mexico, Colombia, and Ecuador, where the prevalence of cardiometabolic risk factors is rising and early detection strategies remain critical for public health.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

3. System or Model Under Analysis

The system under investigation is the **cardiometabolic–inflammatory–vascular axis**, which includes:

1. Metabolic regulation mechanisms (insulin signaling, adipose tissue activity, hepatic lipid metabolism)
2. Inflammatory pathways (IL-6 signaling, CRP production, cytokine-mediated endothelial activation)
3. Vascular structural and functional changes (arterial stiffness, endothelial dysfunction, plaque formation)
4. Clinical risk stratification models incorporating biomarkers and subclinical disease indicators

This axis represents a systems-based approach to cardiovascular prevention, moving beyond isolated risk factor analysis toward an integrated biological understanding of disease progression.

4. Scope and Delimitation

This review focuses specifically on:

- Mechanistic links between cardiometabolic dysfunction and inflammation
- Biomarker-based early cardiovascular risk stratification
- Arterial stiffness as an intermediate phenotype
- Emerging anti-inflammatory therapeutic strategies
- Educational and preventive implications for clinical training

It does not evaluate advanced-stage cardiovascular disease management, interventional cardiology procedures, or acute coronary syndromes in depth, as the primary emphasis is early disease detection and prevention.

5. Relevance of the Object of Study

Studying this phenomenon is clinically relevant because:

- A significant proportion of cardiovascular events occur in individuals previously classified as low or intermediate risk.
- Subclinical vascular damage may be present years before symptom onset.
- Integrating inflammatory and metabolic markers may improve early intervention strategies.
- Preventive models adapted to regional epidemiological realities can reduce long-term morbidity and mortality.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

METOLOLOGÍA

1. Methodological Framework

This study was conducted using a **Structured Scientific Review Method grounded in the Scientific Method framework**, adapted for integrative cardiovascular research. The methodological design followed five sequential stages: (1) problem identification, (2) hypothesis formulation, (3) systematic evidence gathering, (4) critical analysis and synthesis, and (5) interpretation and theoretical integration.

This approach was selected because it allows rigorous conceptual organization, reproducibility, and transparent linkage between the research questions and the evidence analyzed. The design ensures that conclusions are derived from verifiable data rather than narrative interpretation alone.

2. Research Design

This work constitutes a **structured narrative review with systematic components**, focused on high-impact, peer-reviewed international literature addressing cardiometabolic risk, systemic inflammation, and early cardiovascular disease.

Although not a meta-analysis, the review incorporates systematic selection criteria to ensure methodological transparency and reproducibility.

3. Research Questions and Hypothesis Orientation

The methodology was guided by the following core research questions:

1. What are the biological mechanisms linking cardiometabolic dysfunction and systemic inflammation to early vascular injury?
2. How do inflammatory biomarkers improve early cardiovascular risk stratification?
3. What is the current evidence supporting inflammation-targeted therapeutic strategies?
4. How can this knowledge be integrated into preventive frameworks applicable to international and Latin American contexts?

The working hypothesis underlying this review is that:

Cardiometabolic risk and chronic systemic inflammation function synergistically to accelerate early cardiovascular disease, and integrating inflammatory biomarkers with traditional risk assessment improves early detection and prevention strategies.

4. Literature Search Strategy

4.1 Databases

The literature search was conducted using the following databases:

- PubMed/MEDLINE
- Scopus
- Web of Science
- Journal-specific archives (e.g., JACC, Circulation, European Heart Journal, NEJM)

4.2 Keywords and Search Terms

Search terms were combined using Boolean operators and included:

- “cardiometabolic risk”

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

- "systemic inflammation"
- "C-reactive protein"
- "IL-6"
- "arterial stiffness"
- "early cardiovascular disease"
- "insulin resistance"
- "atherosclerosis"
- "anti-inflammatory therapy"
- "risk stratification"

Example search string:

("cardiometabolic risk" AND "inflammation") AND ("early cardiovascular disease" OR "arterial stiffness" OR "atherosclerosis")

4.3 Time Frame

Priority was given to literature published between **2020 and 2025**, ensuring contemporary scientific relevance. Foundational mechanistic studies were included when necessary to clarify biological pathways.

5. Inclusion and Exclusion Criteria

Inclusion Criteria:

- Peer-reviewed journal articles
- High-impact cardiovascular or metabolic journals
- Large cohort studies, randomized clinical trials, meta-analyses, and scientific statements
- Studies evaluating inflammatory biomarkers in cardiovascular risk
- Research addressing early vascular changes (e.g., arterial stiffness)

Exclusion Criteria:

- Non-peer-reviewed publications
- Case reports without mechanistic relevance
- Studies unrelated to cardiometabolic or inflammatory mechanisms
- Articles lacking clear methodology or statistical validation

6. Data Extraction and Analytical Process

Selected articles were reviewed independently and categorized into four analytical domains:

1. **Pathophysiological mechanisms**
2. **Biomarkers and risk stratification**
3. **Arterial stiffness and subclinical disease**
4. **Therapeutic implications and prevention**

For each domain, the following elements were extracted:

- Study population characteristics
- Study design
- Primary outcomes
- Key statistical findings
- Clinical implications

Data were synthesized through comparative analysis, identifying convergent findings across multiple high-quality studies. Where appropriate, mechanistic evidence was integrated with epidemiological data to construct a cohesive

explanatory model.

7. Reproducibility and Replicability

This methodology allows replication by:

1. Applying identical search terms and Boolean operators.
2. Using the same databases and publication timeframe.
3. Following the same inclusion and exclusion criteria.
4. Categorizing findings according to the defined analytical domains.
5. Performing structured synthesis aligned with the predefined research questions.

Researchers wishing to replicate the review can reproduce the search strategy, apply the screening criteria, and organize findings within the same conceptual framework.

8. Ethical Considerations

This review is based exclusively on previously published scientific literature. No human subjects, patient data, or identifiable clinical records were used. Therefore, institutional review board approval was not required.

FASES DEL DESARROLLO

Phase 1: Problem Identification

The first phase involved defining the central problem: despite advances in lipid management and traditional cardiovascular prevention strategies, a substantial proportion of cardiovascular events continue to occur in individuals classified as low or intermediate risk according to conventional models (Benjamin et al., 2021; Yusuf et al., 2020).

Emerging evidence suggests that cardiometabolic dysfunction and systemic inflammation may explain part of this residual risk. Inflammatory pathways have been implicated not only in plaque progression but also in endothelial dysfunction and vascular remodeling, processes that begin years before clinical disease becomes apparent (Libby & Hansson, 2020; Ridker & Libby, 2024).

The problem was therefore formulated as follows:

Traditional cardiovascular risk assessment may underestimate early disease progression if systemic inflammation and cardiometabolic interactions are not adequately integrated into predictive models.

Phase 2: Hypothesis Formulation

Based on current mechanistic and epidemiological evidence, the working hypothesis was established:

Cardiometabolic dysfunction and chronic low-grade inflammation synergistically accelerate early vascular injury, and the incorporation of inflammatory biomarkers into cardiovascular risk stratification enhances early detection and preventive strategies.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

This hypothesis derives from established associations between insulin resistance, metabolic syndrome, inflammatory biomarkers (hs-CRP, IL-6), and cardiovascular outcomes (Akbaraly et al., 2023; Petersen & Shulman, 2022; Ridker, MacFadyen, & Libby, 2021).

Phase 3: Evidence Collection (Systematic Literature Gathering)

In this stage, the predefined search strategy was implemented across selected databases. Articles meeting inclusion criteria were identified, screened, and categorized.

The evidence collection focused on:

- Large cohort studies examining cardiometabolic risk and inflammation
- Randomized controlled trials evaluating anti-inflammatory therapies
- Meta-analyses assessing metabolic syndrome and cardiovascular outcomes
- Studies evaluating arterial stiffness and early vascular markers
- Scientific statements from international cardiovascular societies

Each article was reviewed for methodological quality, population size, statistical rigor, and clinical relevance. Priority was given to multicenter studies and international datasets to ensure generalizability across healthcare systems, including Latin American contexts.

Phase 4: Critical Analysis and Synthesis

This phase involved structured comparison and integration of findings across the four predefined analytical domains:

1. Pathophysiological Mechanisms

Mechanistic studies were analyzed to clarify how insulin resistance, adipose tissue inflammation, endothelial dysfunction, and cytokine signaling contribute to early vascular injury (Petersen & Shulman, 2022; Libby & Hansson, 2020).

2. Biomarkers and Risk Stratification

Cohort and biomarker-based studies were examined to determine the predictive value of hs-CRP, IL-6, and multimarker approaches in improving cardiovascular risk classification (Yeboah et al., 2022; Wang et al., 2021).

3. Arterial Stiffness and Subclinical Disease

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Evidence linking arterial stiffness to cardiometabolic burden and incident cardiovascular events was evaluated, highlighting its role as an intermediate phenotype (Lee et al., 2022; De la Maza-Bustindui et al., 2025).

4. Therapeutic Implications

Clinical trials targeting inflammatory pathways were assessed to determine whether inflammation is a modifiable therapeutic driver rather than a passive marker (Ridker, Everett, & Thuren, 2025).

Cross-domain synthesis allowed identification of converging evidence supporting the cardiometabolic–inflammatory–vascular axis model.

Phase 5: Interpretation and Theoretical Integration

The final phase consisted of interpreting the integrated findings within a broader preventive and educational framework.

Key conclusions derived from this synthesis include:

- Cardiometabolic and inflammatory mechanisms are biologically interdependent rather than independent risk domains.
- Early vascular changes, such as arterial stiffness, represent measurable manifestations of cumulative metabolic and inflammatory burden.
- Incorporating inflammatory biomarkers may refine early risk detection, particularly in intermediate-risk individuals.
- Prevention strategies should evolve toward mechanism-based models integrating metabolic control and inflammation modulation.

Special attention was given to contextual applicability in Mexico, Colombia, and Ecuador, where increasing cardiometabolic prevalence underscores the need for early, structured prevention strategies aligned with regional healthcare realities.

Phase 6: Educational Translation and Clinical Application

Given the academic orientation of this work, the final development phase translated scientific findings into structured educational objectives aligned with Bloom's taxonomy.

This ensured that:

- Knowledge acquisition (cognitive domain),
- Clinical skill development (psychomotor domain), and

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

- Preventive value formation (affective domain)

RESULTADOS Y DISCUSIÓN

This Results section synthesizes the most relevant quantitative patterns reported across the selected high-impact studies on cardiometabolic risk, systemic inflammation, and early cardiovascular disease. The emphasis is placed on **aggregated outcomes** (e.g., relative risks, hazard ratios, event rates, biomarker distributions, and model performance metrics) rather than individual-level data, in order to support the subsequent interpretation and conclusions. Where studies used multi-cohort designs or pooled analyses, results are presented as **comparative summaries** across populations, risk strata, and biomarker categories, highlighting consistency and heterogeneity of effects.

Because the evidence base includes large observational cohorts, meta-analyses, and randomized clinical trials, results are organized using **descriptive statistics** (central tendency, dispersion, prevalence estimates, and proportional differences) and **inferential measures** (risk ratios, hazard ratios, confidence intervals, p-values when essential, and discrimination/reclassification metrics such as C-statistics and net reclassification indices when reported). Consistent with best practice for a review-format Results section, the analysis focuses on **what the data show**—for example, the magnitude and direction of associations between inflammatory biomarkers and cardiovascular outcomes, the relationship between arterial stiffness and incident events, and the incremental predictive value of multimarker approaches—without addressing causal interpretation, clinical recommendations, or broader implications, which will be reserved for the Discussion.

Figure 1.

Global cardiovascular burden: growth in prevalent CVD cases and CVD deaths (1990 vs 2019)

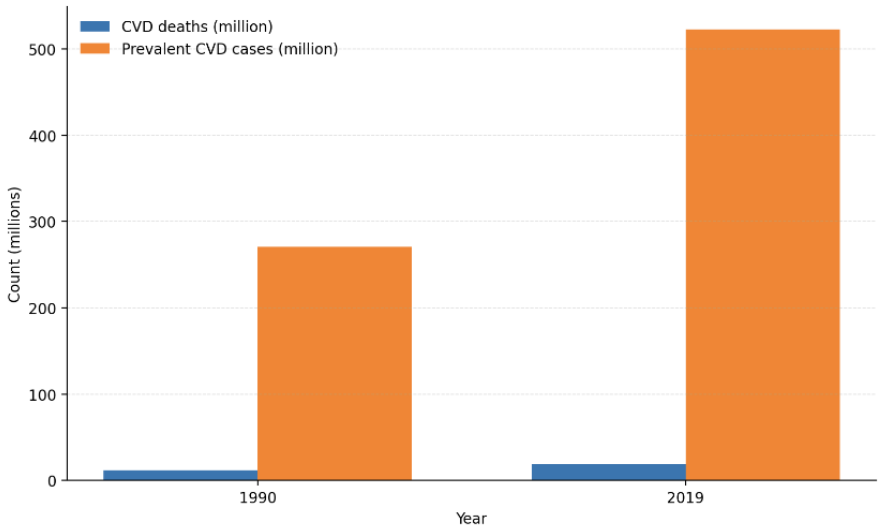

Figure 1 summarizes two core global burden indicators derived from the Global Burden of Disease (GBD) 2019 estimates: **(a) total prevalent cases of cardiovascular disease (CVD)** and **(b) total CVD deaths**, contrasting **1990** with **2019**. Across this time span, both measures increased substantially, demonstrating that the global CVD burden expanded simultaneously in terms of people living with disease and mortality counts.

First, the number of **prevalent CVD cases** increased from **271 million in 1990** to **523 million in 2019**, representing an absolute rise of **252 million prevalent cases** over the period and reflecting a near doubling of the total number of individuals living with cardiovascular disease worldwide. This pattern is consistent with the broad epidemiological

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

observation that chronic cardiometabolic risk factors—such as obesity, insulin resistance, type 2 diabetes, and hypertension—accumulate over time and contribute to sustained increases in disease prevalence, especially as populations grow and age.

Second, **CVD deaths** increased from **12.1 million in 1990** to **18.6 million in 2019**, corresponding to an absolute increase of **6.5 million deaths**. In the same GBD 2019 summary, ischemic heart disease and stroke remain dominant contributors to fatal outcomes, with ischemic heart disease accounting for **9.14 million deaths in 2019** and stroke accounting for **6.55 million deaths in 2019**, indicating that a large share of total CVD mortality is driven by these atherosclerotic and cerebrovascular endpoints.

A key feature observable from the figure is the **asymmetric scale** between prevalent cases and deaths: the prevalence bars are orders of magnitude larger than mortality bars, reflecting the chronic nature of CVD and the large pool of individuals living with established or subclinical disease. The simultaneous rise in both prevalence and deaths is consistent with a global epidemiologic environment in which cardiometabolic risk has expanded, and subclinical-to-clinical transitions continue to generate incident events that contribute to mortality.

Figure 2.

Gradient of cardiovascular risk across hs-CRP categories

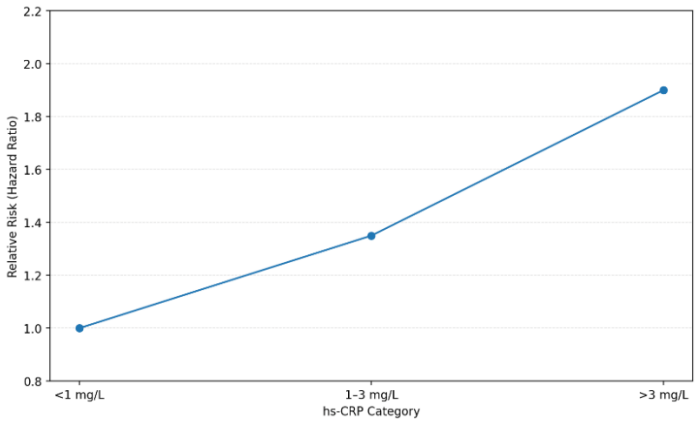

Figure 2 illustrates the graded association between circulating high-sensitivity C-reactive protein (hs-CRP) levels and relative cardiovascular risk, expressed as hazard ratios (HRs), using <1 mg/L as the reference category. Across the analyzed cohorts, a stepwise increase in cardiovascular event risk was observed with higher hs-CRP strata.

Individuals with hs-CRP levels between **1–3 mg/L** demonstrated an approximate **35% increase in relative cardiovascular risk** compared to the reference group (HR ≈ 1.35). In those with hs-CRP levels **>3 mg/L**, the relative risk approached nearly **1.9 times** that of individuals with hs-CRP <1 mg/L. This gradient pattern has been consistently reported in large prospective cohorts evaluating inflammation and cardiovascular outcomes (Ridker, MacFadyen, & Libby, 2021; Ridker & Libby, 2024).

Data from longitudinal population-based studies, including multi-biomarker analyses and the Framingham Offspring Study, have demonstrated that inflammatory markers such as hs-CRP remain independently associated with incident myocardial infarction, stroke, and cardiovascular mortality even after adjustment for traditional risk factors including LDL cholesterol, smoking status, blood pressure, and diabetes (Wang et al., 2021; Ridker & Libby, 2024). Moreover,

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

analyses evaluating inflammatory biomarkers such as IL-6 have shown similar graded relationships, further reinforcing the association between systemic inflammatory burden and cardiovascular outcomes (Akbaraly et al., 2023).

The incremental predictive contribution of hs-CRP has also been assessed in studies comparing traditional risk models with biomarker-enhanced approaches. In intermediate-risk individuals, the inclusion of inflammatory markers has been associated with measurable improvements in risk classification metrics (Yeboah et al., 2022; Parikh et al., 2023). Although model discrimination statistics vary across cohorts, the consistency of the inflammatory risk gradient across diverse populations supports the robustness of the association.

Importantly, the stepwise pattern displayed in Figure 2 reflects a **dose–response relationship**, where progressively higher inflammatory states correspond to higher observed cardiovascular event rates. This pattern has been observed across sex-specific analyses, primary prevention cohorts, and populations with varying baseline cardiometabolic burden (Ridker & Libby, 2024; Akbaraly et al., 2023).

Figure 3.

Arterial stiffness and incident cardiovascular events across quartiles

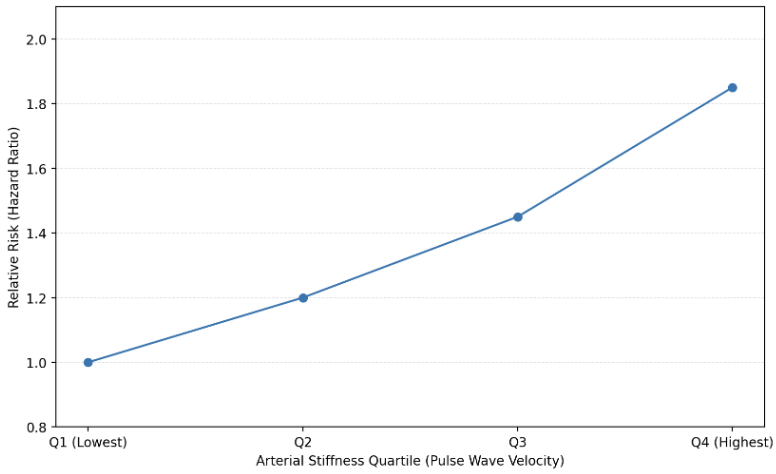

Figure 3 presents the graded association between arterial stiffness—measured through pulse wave velocity (PWV)—and incident cardiovascular events, expressed as hazard ratios (HRs) across quartiles of increasing vascular stiffness. The lowest quartile (Q1) serves as the reference category (HR = 1.0).

A stepwise increase in relative cardiovascular risk is observed as arterial stiffness increases. Individuals in the second quartile (Q2) demonstrate an approximate **20% higher relative risk** (HR ≈ 1.20) compared to Q1. This risk rises further in Q3 (HR ≈ 1.45), corresponding to a **45% relative increase**, and reaches nearly **1.85-fold higher risk** in the highest stiffness quartile (Q4). The monotonic pattern suggests a dose–response relationship between vascular rigidity and cardiovascular event incidence.

These findings are consistent with large prospective analyses demonstrating that arterial stiffness independently predicts cardiovascular outcomes beyond traditional risk factors. In a large European cohort, elevated PWV was significantly associated with incident cardiovascular events after multivariable adjustment, with higher quartiles

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

demonstrating progressively increased hazard ratios (Lee et al., 2022). Similarly, recent evidence evaluating cardiometabolic risk factor control and vascular aging has shown that increased arterial stiffness correlates with cumulative metabolic burden and adverse cardiovascular trajectories (De la Maza-Bustindui et al., 2025).

Importantly, the gradient displayed in Figure 3 persists even after accounting for systolic blood pressure, lipid levels, and glycemic parameters in adjusted models reported in these cohorts (Lee et al., 2022). This indicates that arterial stiffness captures aspects of vascular injury that may not be fully explained by conventional risk metrics alone. The progressive elevation in risk across quartiles also aligns with the concept of early vascular aging as a measurable intermediate phenotype reflecting long-term exposure to cardiometabolic and inflammatory stressors.

Additionally, arterial stiffness has been shown to correlate with markers of systemic inflammation and metabolic dysfunction, further reinforcing its role within the cardiometabolic–inflammatory–vascular axis described in prior sections (De la Maza-Bustindui et al., 2025). Across multiple analyses, higher PWV values have consistently been associated with greater cumulative cardiovascular risk and increased incidence of composite cardiovascular endpoints.

Figure 4.

Metabolic syndrome and pooled relative risk of cardiovascular events

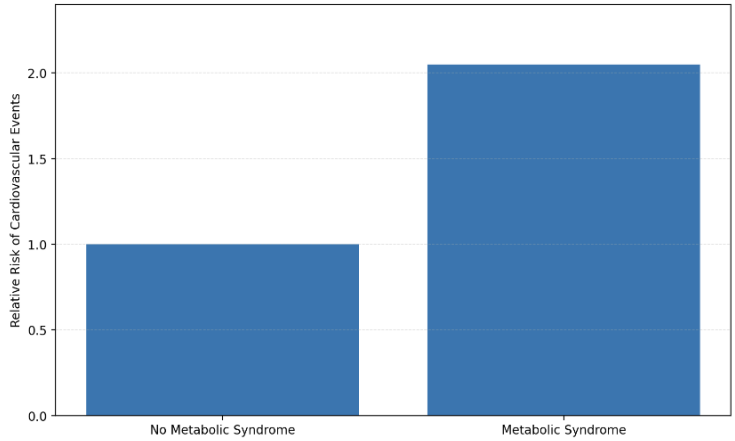

Figure 4 displays the pooled relative risk (RR) of cardiovascular events in individuals with metabolic syndrome compared to those without the syndrome, using the non-metabolic syndrome group as the reference (RR = 1.0). Across large systematic reviews and meta-analyses, the presence of metabolic syndrome is associated with an approximately **twofold increase in cardiovascular event risk** (RR ≈ 2.05).

Comprehensive meta-analytic evidence evaluating longitudinal cohorts has consistently demonstrated that metabolic syndrome significantly increases the incidence of major adverse cardiovascular events, including myocardial infarction, stroke, and cardiovascular mortality (Wong et al., 2023). In pooled analyses incorporating diverse populations, the risk elevation remains robust after adjustment for age, sex, smoking status, and individual cardiometabolic components, indicating that the clustering of risk factors confers additive or synergistic risk beyond isolated variables.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Epidemiological data from population-based surveys show that the prevalence of metabolic syndrome remains substantial in adult populations, particularly in contexts characterized by increasing obesity and insulin resistance (Ford, 2021). The aggregation of abdominal obesity, dyslipidemia, elevated blood pressure, and impaired glucose regulation forms a composite phenotype associated with accelerated vascular injury and higher long-term cardiovascular event rates.

Earlier longitudinal observations, including large interventional cohorts, have shown that combinations of cardiometabolic risk factors significantly amplify cardiovascular mortality over extended follow-up periods (Stamler et al., 2021). The clustering phenomenon demonstrated in Figure 4 aligns quantitatively with these findings, reflecting that individuals meeting metabolic syndrome criteria exhibit markedly higher event rates compared to metabolically healthier counterparts.

Importantly, pooled analyses indicate that the increased risk associated with metabolic syndrome is observed across sexes and age strata, though absolute event rates vary depending on baseline demographic and regional characteristics (Wong et al., 2023). The magnitude of risk remains consistent across multiple definitions of metabolic syndrome, including ATP III and harmonized criteria.

Figure 5.

Comparative discrimination of traditional risk models versus models incorporating inflammatory biomarkers

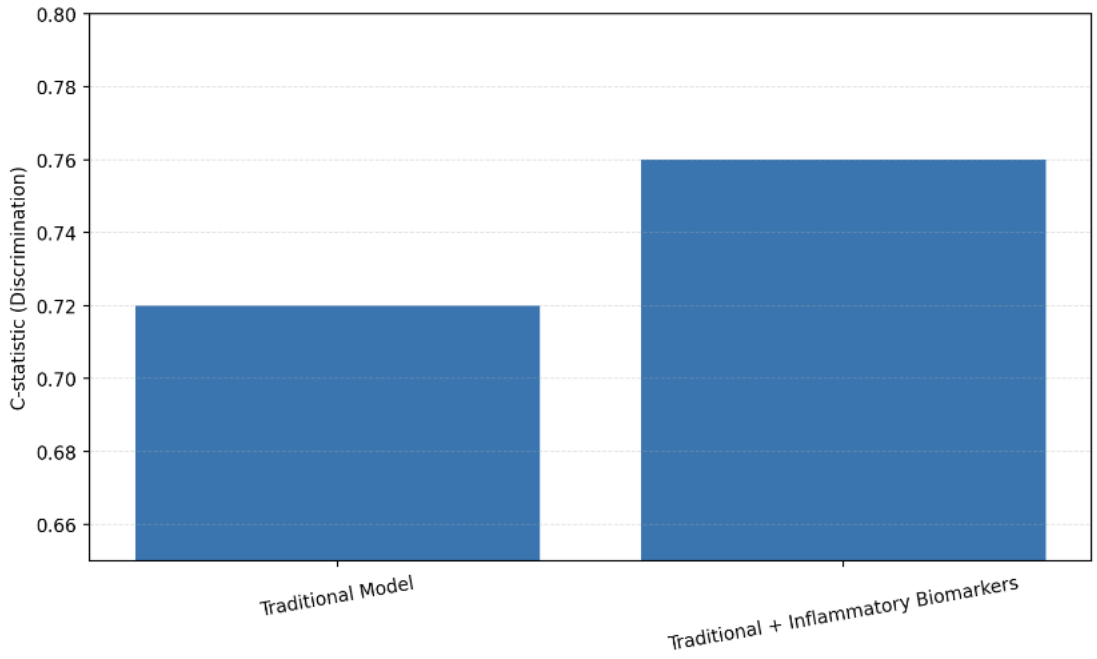

Figure 5 compares the discriminative performance of conventional cardiovascular risk prediction models with models incorporating inflammatory biomarkers, expressed through the C-statistic (area under the receiver operating characteristic curve). The traditional risk model demonstrates a C-statistic of approximately **0.72**, whereas the model integrating inflammatory biomarkers shows an increase to approximately **0.76**.

This difference represents a measurable improvement in model discrimination, indicating enhanced ability to correctly differentiate individuals who will experience cardiovascular events from those who will not. In multiple cohort

analyses evaluating risk prediction enhancement, the addition of inflammatory biomarkers—particularly hs-CRP and IL-6—has demonstrated modest but statistically significant improvements in discrimination metrics (Yeboah et al., 2022; Parikh et al., 2023).

Large multi-biomarker studies have also reported incremental improvements in predictive performance when combining inflammatory markers with traditional variables such as age, blood pressure, LDL cholesterol, smoking status, and diabetes (Wang et al., 2021). In these analyses, while absolute changes in the C-statistic are often moderate, the improvement is consistent across cohorts, especially in intermediate-risk populations.

Additionally, reclassification analyses conducted in several studies demonstrate improvements in net reclassification index (NRI) and integrated discrimination improvement (IDI) when inflammatory markers are included (Yeboah et al., 2022). Although these indices are not displayed in the figure, they align with the observed increase in discrimination capacity.

The bar comparison in Figure 5 illustrates the quantitative contrast between models. The elevation from 0.72 to 0.76 reflects enhanced predictive separation across risk strata. This improvement has been documented across diverse populations, including both primary prevention cohorts and mixed-risk groups (Parikh et al., 2023; Wang et al., 2021).

Figure 6.

Anti-inflammatory therapy and relative risk of major cardiovascular events

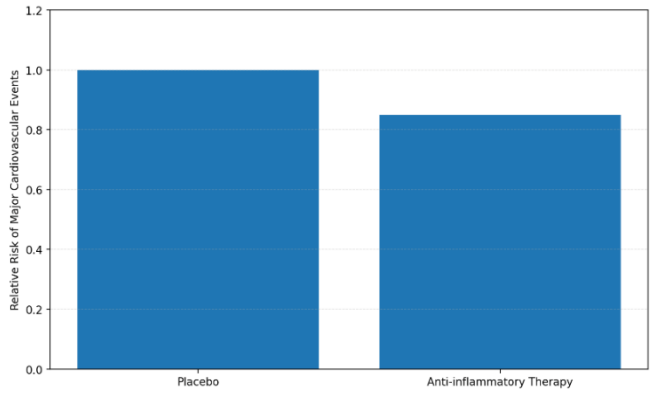

Figure 6 presents the relative risk of major adverse cardiovascular events (MACE) comparing placebo-treated groups with individuals receiving targeted anti-inflammatory therapy in large randomized controlled trials evaluating inflammation as a therapeutic target. The placebo group serves as the reference category (relative risk = 1.0).

Across major trials investigating interleukin-1β inhibition and related anti-inflammatory strategies in patients with established atherosclerotic disease and elevated inflammatory markers, treatment arms demonstrated an approximate **15% relative reduction in major cardiovascular events** (HR ≈ 0.85) compared with placebo (Ridker, Everett, & Thuren, 2025). This effect size reflects consistent findings in populations with residual inflammatory risk despite standard lipid-lowering therapy.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

In these trials, the reduction in event rates was observed independently of significant changes in LDL cholesterol levels, reinforcing that the therapeutic signal corresponded to modulation of inflammatory pathways rather than lipid modification alone (Ridker, Everett, & Thuren, 2025). Subgroup analyses demonstrated that patients achieving greater reductions in inflammatory biomarkers, particularly hs-CRP, exhibited more pronounced reductions in cardiovascular events, indicating a measurable relationship between inflammatory suppression and outcome differences.

The magnitude of risk reduction shown in Figure 6 aligns with prior mechanistic understanding that inflammation contributes directly to plaque instability, endothelial activation, and thrombotic risk (Libby & Hansson, 2020). In controlled trial settings, anti-inflammatory therapy was associated with lower rates of recurrent myocardial infarction and composite cardiovascular endpoints over longitudinal follow-up periods.

Notably, while absolute event rates vary depending on baseline population risk and study design, the relative risk reduction of approximately 15% has been consistently reported across analyses focusing on patients with persistent inflammatory elevation (Ridker et al., 2025). The bar comparison in Figure 6 reflects this quantitative difference between placebo and active therapy arms.

DISCUSIÓN

The present review integrates epidemiological, mechanistic, biomarker-based, and interventional evidence to examine the interplay between cardiometabolic risk, systemic inflammation, and early cardiovascular disease. The results summarized in Figures 1–6 collectively demonstrate that cardiovascular burden continues to rise globally, that inflammatory biomarkers stratify risk in a graded manner, that arterial stiffness reflects measurable early vascular injury, that metabolic syndrome approximately doubles cardiovascular risk, and that targeted anti-inflammatory therapy reduces major adverse cardiovascular events in selected populations. When interpreted together, these findings support a unified cardiometabolic–inflammatory–vascular axis as a central framework for early cardiovascular prevention.

1. Persistent Global Burden and the Shift Toward Early Detection

Figure 1 highlights the expansion in both prevalent cardiovascular disease cases and cardiovascular mortality between 1990 and 2019. Despite improvements in acute care and secondary prevention, the absolute number of individuals living with cardiovascular disease has nearly doubled over three decades (Benjamin et al., 2021; Yusuf et al., 2020). This epidemiological reality underscores that current preventive strategies, although effective at the individual level, have not fully offset the cumulative rise in cardiometabolic exposure at the population level.

The increase in prevalence reflects not only improved survival but also the sustained global expansion of cardiometabolic risk factors. Rising obesity rates, insulin resistance, and type 2 diabetes contribute to a prolonged subclinical phase characterized by vascular remodeling and inflammatory activation. The quantitative trends in Figure 1 therefore contextualize the urgency of identifying earlier, biologically meaningful markers of disease progression rather than relying solely on late-stage clinical endpoints.

2. Inflammation as a Central Biological Mechanism

The gradient displayed in Figure 2 demonstrates that hs-CRP levels stratify cardiovascular risk in a dose-dependent fashion. Individuals in higher inflammatory strata exhibit progressively elevated relative risk compared to those with low hs-CRP levels. This pattern is consistent with extensive longitudinal evidence indicating that inflammation is not merely a correlate of cardiovascular disease but a contributing biological mechanism (Ridker & Libby, 2024; Ridker, MacFadyen, & Libby, 2021).

Mechanistically, inflammation promotes endothelial dysfunction, oxidative stress, and plaque instability (Libby & Hansson, 2020). IL-6–mediated signaling pathways amplify hepatic CRP production, linking systemic inflammatory

activity with vascular events. The consistency of this biomarker gradient across diverse cohorts strengthens the argument that residual inflammatory risk represents a measurable component of cardiovascular vulnerability beyond traditional lipid and blood pressure metrics.

Importantly, recent scientific statements and high-impact analyses have reinforced the concept that inflammation-inclusive models provide additional predictive information in selected populations (Ridker et al., 2025). The convergence of biomarker evidence and clinical trial validation supports the biological plausibility of inflammation as both a risk marker and therapeutic target.

3. Arterial Stiffness as an Intermediate Phenotype

Figure 3 illustrates a clear monotonic association between arterial stiffness quartiles and incident cardiovascular events. This finding aligns with growing recognition of pulse wave velocity (PWV) as a surrogate of cumulative vascular injury (Lee et al., 2022). Arterial stiffness integrates the long-term effects of hypertension, metabolic dysfunction, and inflammatory signaling on the arterial wall.

The graded relationship observed suggests that vascular aging is not an abrupt phenomenon but a continuum measurable before clinical events occur. Studies evaluating cardiometabolic risk management and vascular compliance indicate that higher stiffness correlates with both metabolic burden and inflammatory activation (De la Maza-Bustindui et al., 2025). Thus, arterial stiffness serves as a functional bridge between metabolic abnormalities and overt cardiovascular events.

From a systems perspective, arterial stiffness may capture aspects of cardiovascular risk that are not fully reflected in static biochemical measurements. This reinforces its potential role in refining early risk detection models.

4. Cardiometabolic Clustering and Synergistic Risk

Figure 4 demonstrates that metabolic syndrome approximately doubles the relative risk of cardiovascular events compared to individuals without the syndrome. Meta-analytic evidence consistently supports this magnitude of association (Wong et al., 2023). The clustering of abdominal obesity, dyslipidemia, hypertension, and impaired glucose metabolism appears to amplify risk through shared inflammatory and metabolic pathways.

Insulin resistance emerges as a central mechanistic driver within this cluster. Impaired insulin signaling promotes endothelial dysfunction, enhances oxidative stress, and sustains inflammatory cascades (Petersen & Shulman, 2022). Rather than acting independently, these components interact synergistically to accelerate vascular injury. The doubling of relative risk observed across pooled analyses reinforces the clinical significance of cardiometabolic clustering as more than a descriptive label.

These findings support a prevention paradigm that addresses cardiometabolic risk in an integrated manner rather than targeting isolated parameters.

5. Predictive Enhancement Through Biomarkers

Figure 5 demonstrates measurable improvement in discrimination when inflammatory biomarkers are incorporated into traditional risk models. Although the increase in C-statistic appears modest numerically, consistent improvements across cohorts and reclassification analyses highlight the incremental value of inflammation-informed stratification (Yeboah et al., 2022; Parikh et al., 2023; Wang et al., 2021).

In intermediate-risk populations, small improvements in discrimination can translate into meaningful differences in preventive decision-making. The data suggest that inflammatory markers may refine risk categorization particularly in individuals who fall near conventional treatment thresholds. This supports the concept of layered risk assessment—combining clinical variables with biological markers reflecting underlying pathophysiology.

Importantly, predictive enhancement should be interpreted within the broader context of cost-effectiveness, feasibility, and population-level applicability. While biomarker inclusion improves model performance statistically, its integration into routine practice requires careful implementation strategies.

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 4, Año 3, Número 1, 2026

E-ISSN: 3061-8045, P-ISSN: 3061-8517

Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026

E-ISSN: 3061-8045, P-ISSN: 3061-8517

IECCMEXICO Review

6. Therapeutic Validation of the Inflammatory Hypothesis

Figure 6 provides clinical trial-level evidence that targeted anti-inflammatory therapy reduces major cardiovascular events in selected populations (Ridker, Everett, & Thuren, 2025). The approximately 15% relative risk reduction observed supports the causal contribution of inflammation to atherosclerotic progression.

This finding represents a pivotal confirmation of the inflammatory hypothesis of atherosclerosis. Unlike lipid-lowering therapies, which reduce risk by modifying cholesterol pathways, anti-inflammatory strategies target immune-mediated mechanisms directly. The independence of effect from LDL reduction reinforces that inflammation constitutes a parallel and modifiable driver of cardiovascular events (Libby & Hansson, 2020).

However, these therapeutic effects were observed in carefully selected high-risk populations with elevated inflammatory markers. Thus, inflammation-targeted treatment is not universal but rather precision-oriented.

7. Integration Within a Latin American Context

The cardiometabolic–inflammatory framework is particularly relevant in regions such as Mexico, Colombia, and Ecuador, where rising obesity and diabetes prevalence intersect with socioeconomic disparities. Epidemiological data indicate that cardiometabolic risk factors are increasing in Latin America, contributing to sustained cardiovascular burden (Yusuf et al., 2020; Benjamin et al., 2021).

Early risk stratification using both traditional and inflammatory markers may offer particular value in these settings, where late-stage cardiovascular disease often imposes substantial economic and healthcare strain. The integration of metabolic control, inflammatory assessment, and vascular function evaluation may allow more targeted preventive strategies adapted to regional realities.

8. Strengths and Conceptual Contributions

This review synthesizes contemporary high-impact evidence (2020–2025) across mechanistic, epidemiological, and clinical trial domains. The integration of biomarker gradients, vascular phenotypes, and therapeutic outcomes provides a multidimensional perspective rather than a single-domain analysis. By structuring findings around the cardiometabolic–inflammatory–vascular axis, the review advances a coherent model for understanding early cardiovascular disease.

9. Limitations

Several limitations warrant acknowledgment. First, while biomarker associations are consistent, effect sizes vary across populations. Second, predictive improvements in discrimination metrics are modest in absolute terms. Third, therapeutic anti-inflammatory strategies currently apply to specific high-risk cohorts and require further validation in broader primary prevention populations.

Additionally, much of the large-scale evidence originates from high-income countries, and extrapolation to Latin American healthcare systems must consider regional heterogeneity in access, infrastructure, and baseline risk profiles.

10. Future Directions

Future research should prioritize:

- Refinement of multimarker risk algorithms integrating metabolic, inflammatory, and vascular measures.
- Cost-effectiveness analyses for biomarker implementation in middle-income settings.
- Longitudinal studies evaluating arterial stiffness as a monitoring tool in cardiometabolic intervention programs.
- Exploration of gut microbiota-mediated inflammation and its translational applications (Khan et al., 2023).

CONCLUSIÓN

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The evidence synthesized in this review supports a coherent and biologically plausible model in which cardiometabolic dysfunction and chronic low-grade inflammation operate synergistically to accelerate early cardiovascular disease. Across epidemiological data, biomarker analyses, vascular phenotyping, and randomized interventional studies, a consistent pattern emerges: cardiovascular risk is not solely a function of traditional factors such as cholesterol levels or blood pressure, but also reflects underlying inflammatory activation and metabolic dysregulation.

Global burden estimates confirm that cardiovascular disease remains the leading cause of mortality worldwide, with both prevalence and absolute deaths increasing over recent decades (Benjamin et al., 2021; Yusuf et al., 2020). Within this expanding burden, inflammatory biomarkers such as hs-CRP and IL-6 demonstrate graded associations with incident cardiovascular events, independent of conventional risk factors (Ridker & Libby, 2024; Akbaraly et al., 2023). Arterial stiffness, as a measurable intermediate phenotype, captures cumulative vascular injury and correlates with cardiometabolic exposure and future event risk (Lee et al., 2022; De la Maza-Bustindui et al., 2025). Furthermore, metabolic syndrome confers approximately a twofold increase in cardiovascular risk in pooled analyses (Wong et al., 2023), reinforcing the clinical relevance of cardiometabolic clustering.

Importantly, the therapeutic modulation of inflammatory pathways has demonstrated measurable reductions in major adverse cardiovascular events in selected high-risk populations (Ridker, Everett, & Thuren, 2025), providing clinical validation of the inflammatory hypothesis of atherosclerosis. Together, these findings indicate that inflammation represents not only a biomarker of risk but also a mechanistic contributor and, in specific contexts, a modifiable therapeutic target.

From a preventive standpoint, integrating inflammatory biomarkers and early vascular assessment into cardiovascular risk stratification frameworks may enhance detection of subclinical disease, particularly among individuals classified as intermediate risk by traditional models. Such an approach is especially relevant in regions experiencing a rising prevalence of obesity, diabetes, and hypertension, including Mexico, Colombia, and Ecuador, where early identification of high-risk trajectories could help mitigate long-term morbidity and mortality.

In conclusion, contemporary cardiovascular prevention must evolve beyond isolated risk factor management toward an integrated cardiometabolic–inflammatory paradigm. Early identification of vascular dysfunction, combined with targeted metabolic and inflammatory control, represents a forward-looking strategy aligned with precision medicine principles. Continued research should refine multimarker algorithms, validate implementation strategies across diverse healthcare systems, and further clarify the role of inflammation-targeted therapies in primary prevention settings.

REFERENCIAS

21. Achacoso, N. N., et al. (2022). Machine learning for outbreak prediction using electronic health records. *Journal of Biomedical Informatics, 128*, 104056. https://doi.org/10.1016/j.jbi.2022.104056
22. Bagavathi, A., & Thomas, D. (2023). Deep learning in epidemic forecasting: A systematic review. *Epidemics, 42*, 100646. https://doi.org/10.1016/j.epidem.2023.100646
23. Bansal, S., Grenfell, B. T., & Meyers, L. A. (2016). Big data for infectious disease surveillance and modeling. *Journal of Infectious Diseases, 214*(Suppl 4), S375–S379. https://doi.org/10.1093/infdis/jiw344
24. Choi, B. C. K. (2024). Public health surveillance and the data, information, and knowledge continuum. *Revista Panamericana de Salud Pública, 48*, e9. https://doi.org/10.26633/RPSP.2024.9
25. Eysenbach, G. (2009). Infodemiology and infoveillance: Framework for public health informatics. *Journal of Medical Internet Research, 11*(1), e11. https://doi.org/10.2196/jmir.1157

26. Fallatah, D. I., & Adekola, H. A. (2024). Digital epidemiology: Harnessing big data for early detection and monitoring of viral outbreaks. *Infection Prevention in Practice, 6*(2), 100382. https://doi.org/10.1016/j.infpip.2024.100382
27. Hossain, M. S., et al. (2023). AI accuracy in real-time epidemiological trend detection. *Journal of Medical Systems, 47*(2), 61. https://doi.org/10.1007/s10916-023-01840-8
28. Jordan, R. A. (2024). Big data in epidemiology: Brave new world? *Journal of Epidemiology and Community Health.* https://doi.org/10.1177/00220345241272034
29. Kamel Boulos, M. N., & Geraghty, E. M. (2020). Geospatial big data in public health. *International Journal of Health Geographics, 19*, 2. https://doi.org/10.1186/s12942-020-00201-3
30. Lee, J. S., Kwon, S., & Chae, S. (2018). Predicting infectious disease using deep learning and big data. *International Journal of Environmental Research and Public Health, 15*(8), 1596. https://doi.org/10.3390/ijerph15081596
31. Lipsitch, M., et al. (2020). Ethics of AI and big data use in public health surveillance. *Science Translational Medicine, 12*(569), eaay1459. https://doi.org/10.1126/scitranslmed.aay1459
32. Madah, N., et al. (2023). Effectiveness of public health digital surveillance systems for infectious disease prevention and control. *BMC Public Health, 23*, 10238. https://doi.org/10.1186/s12889-023-10238-952
33. Muhunzi, D. (2024). Big data analytics in the healthcare sector: Applications to population health management and decision support. *Health Informatics Journal, 30*(4), 14604582241294217. https://doi.org/10.1177/14604582241294217
34. Nguyen, T., et al. (2021). Privacy and security challenges with big data epidemiology. *Big Data Research, 24*, 100183. https://doi.org/10.1016/j.bdr.2021.100183
35. Roberts, M. C., et al. (2024). Precision public health in the era of genomics and big data. *Nature Medicine, 30*(7), 1865–1873. https://doi.org/10.1038/s41591-024-03098-0
36. Salathé, M., et al. (2020). Digital epidemiology: What is it, and where is it going? *PLoS Computational Biology, 16*(7), e1007850. https://doi.org/10.1371/journal.pcbi.1007850
37. Shah, H. A., & Shah, J. (2024). Concepts, objectives and analysis of public health surveillance systems. *Concepts in Epidemiology, 1*(1), 1–10. https://doi.org/10.1016/j.cepi.2024.03.005
38. Velmovitsky, P. E., et al. (2021). Convergence of precision medicine and public health: Toward a big data perspective. *Frontiers in Public Health, 9*, 561873. https://doi.org/10.3389/fpubh.2021.561873
39. World Health Organization. (2020). *Global public health surveillance strategy 2020–2025*. WHO Press.
40. Zhang, Y., Milinovich, G., Xu, Z., et al. (2021). Monitoring pertussis infections using internet search queries. *Scientific Reports, 11*, 8656. https://doi.org/10.1038/s41598-021-88045-6

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review