THE EXPANDING ROLE OF LABORATORY BIOMARKERS IN CARDIOVASCULAR DISEASES: CLINICAL AND EMERGING PERSPECTIVES

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Abstract
The major cause of morbidity and mortality in the world is cardiovascular diseases (CVDs), with over 20 million deaths annually being attributed to CVDs. Even with the great achievements in diagnostics and treatments, early diagnosis and personalized treatment an essential clinical issues. Laboratory biomarkers have gained importance to enhance the accuracy of diagnosis, risk estimation, and monitoring of therapy for cardiovascular disorders. The accepted biomarkers that are still used to make clinical decisions include cardiac troponins, the B-type natriuretic peptides (BNP/NT-proBNP), and C-reactive protein (CRP). However, there have been findings like microRNAs, long non-coding RNAs, growth differentiation factor-15 (GDF-15), soluble suppression of tumorigenicity-2 (sST2), galectin-3, and extracellular vesicle-derived molecules, which are adding value to cardiovascular diagnostics. Together with artificial intelligence (AI), digital health applications, and multi-omics platforms (including genomics, proteomics, metabolomics, and transcriptomics), these new markers are collectively enabling cardiology to become more precise. This paper will discuss conventional and emerging biomarkers, their clinical utility, mechanism, and how these biomarkers can modify medical treatment. It also covers the concerns that include the lack of standards, inadequate translational data, and exorbitant prices, and future opportunities, possibly including AI-based analytics, biosensor-

based monitoring, and biomarker-directed medicines. Biomarker-based strategies could improve heart health by combining molecular research with clinical application. This would allow clinicians to detect problems earlier, better estimate risk, and personalize treatment to each patient's needs.

INTRODUCTION

Globally, cardiovascular disease (CVD) is the primary cause of death and disability. Despite the availability of reasonably priced treatments to alleviate the burden of CVD, global adoption has been too sluggish. Controlling CVD and its risk factors requires both high-risk and population approaches, both of which are advantageous. For a few very high-risk individuals, relying on expensive medications and tertiary care measures might be helpful, but it won't solve the global issue (Mendis et al., 2022; Ashraf et al., 2025). In the past thirty years, the prevalence of CVD has dramatically increased worldwide. While annual mortality has increased from 12.1 million to over 20 million, the prevalence of cases has nearly doubled from 271 million in 1990 to 523 million in 2019 and is expected to reach over 600 million by 2021 (Roth et al., 2020; Li et al., 2023). Advances in prevention and care have led to a worldwide reduction in age-standardized incidence and mortality rates, but as the population ages and grows, the absolute burden keeps rising. 35.6 million cardiovascular deaths are predicted to occur in 2050 as a result of an estimated 90.0% increase in cardiovascular prevalence, 73.4% increase in crude mortality, and 54.7% increase in crude health-adjusted life loss between 2025 and 2050 (up from 20.5 million in 2025) (Chong et al., 2024).

Area and socioeconomic status have a substantial impact on the burden of CVD. The highest rates are found in Central and Eastern Europe, Central Asia, and parts of Asia and Africa; over 80% of deaths from CVD occur in low- and middle-income countries (Roth et al., 2020; Hu et al., 2024). Age-standardized mortality has decreased more quickly in high-income nations, but other areas are preserving or even undoing earlier gains (Amini et al., 2021). Socioeconomic circumstances exacerbate the variations in CVD outcomes, insufficient access to healthcare, and underreporting.

Because CVDs are the major basis of morbidity and mortality in the world, there has been an urgent need for more specific and personalized diagnostics, prognostics, and treatment strategies. New biomarkers such as microRNAs, long non-coding RNAs, and Trimethylamine N-oxide (TMAO) have been incorporated into the already existing biomarkers, such as cardiac troponins, B-type Natriuretic Peptide (BNP), N-terminal pro-B-type Natriuretic Peptide (NT-proBNP), and C-reactive Protein (CRP). However, it requires additional research (Omran et al., 2022; Qiu et al., 2021). Although extracellular vesicles and cell-free DNA have potential in acting as non-invasive biomarkers, imaging and artificial intelligence are leading to more accurate diagnosis, especially when combined with the data of biomarkers. (Sun et al., 2023; Jafari et al., 2023). Targeted therapies and theranostics are being made possible by RNA-based techniques, nanotechnology, and aptamer-based nanosystems; new pathways such as Tumor Necrosis Factor-related apoptosis-inducing ligand (TRAIL) signaling and epitranscriptomic changes are opening up new avenues for diagnosis and treatment (Bocancia-Mateescu et al., 2023; Lu et al., 2019).

Because they enable early detection, risk assessment, prognosis, and customized treatment, laboratory biomarkers are essential for enhancing clinical decision-making in CVDs. Natriuretic peptides (BNP, NT-proBNP) are essential for the diagnosis and management of CVDs, while cardiac troponins remain the gold standard for detecting myocardial infarction (Netala et al., 2025; van Genuchten et al., 2025). While new biomarkers like microRNAs, long non-coding RNAs, and transcriptome signatures hold promise for earlier and more accurate detection, inflammatory and fibrotic markers like CRP, Interleukin-6 (IL-6), growth differentiation factor-15 (GDF-15), and galectin-3 enhance risk prediction (Netala et al., 2025; Castiglione et al., 2022; Wu et al., 2025). Digital biomarkers from wearables, multi-marker approaches, and artificial intelligence integration enhance prognostic accuracy and enable tailored treatment, making biomarkers essential in contemporary CVD care (Wong et al., 2021).

The review presents a critical analysis of the growing role of laboratory biomarkers in CVDs, especially in regard to the application in prognosis, risk, diagnosis, and personalized treatment. We touch upon the emergent and established biomarkers, how they may interact with the latest technology, including digital health and artificial intelligence, and how they may change clinical judgment. The most topical issues, translational gaps, and opportunities of cardiovascular treatment with biomarkers are also discussed in the paper.

Overview of Laboratory Biomarkers in Cardiovascular Diseases:

Laboratory biomarkers are visible biological pointers of healthy and unhealthy processes, in addition to responses to treatment procedures. Biomarkers in CVDs are very useful in clinical decision-making, which provides crucial information on disease pathogenesis. The four broad categories in which they are typically divided are diagnostic, prognostic, predictive, and therapeutic monitoring biomarkers (Netala et al., 2025). Diagnostic biomarkers are highly specific and sensitive to detect disease, e.g., natriuretic peptides in heart failure and cardiac troponins in acute myocardial infarction (DeGroat et al., 2024). The prognosis biomarkers include CRP, GDF-15, and certain microRNAs that may be utilized to predict the outcomes of patients and determine the probability of future cardiovascular events (Antonopoulos et al., 2022). The field of cardiovascular medicine is still developing predictive biomarkers that assess a person's likelihood of responding to a particular treatment; transcriptome and genetic indicators are being researched for their potential utility in guiding customized treatment options (DeGroat et al., 2024). To gauge the course of the disease and the efficacy of treatment, therapeutic monitoring biomarkers are used, such as variations in BNP or NT-proBNP levels during heart failure medication (Pamies et al., 2025).

Very few biomarkers have become staples of clinical practice because of their high diagnostic and prognostic value, particularly cardiac troponins and natriuretic peptides (Netala et al., 2025). Nevertheless, some of the new markers, such as transcriptome, microRNAs, and proteins such as GDF-15, are yet to be accessible in research laboratories (Pamies et al., 2025; Lyngbakken et al., 2019). Problems such as a lack of standardization, limited evidence of added value to other available biomarkers, and a lack of efficiency have hampered the clinical adoption of these new biomarkers, although they can help to improve precision medicine by initial identification and individualized risk assessment.

The ideal cardiovascular biomarker must be sensitive and specific, constant in biological media, readily quantifiable, reproducible, and least affectable by external factors like comorbidities or variations in the body metabolism (Esteve-Pastor et al., 2019). Beyond the analytical performance, clinically relevant information, that is, information that generates action, is essential in diagnosis, treatment, or prognosis. It must also be economical to work with, user-friendly, and quick to turn around to achieve acceptance as a common practice. Before biomarkers can be extensively applied, they have to go through rigorous validation in a diverse population and demonstrate superior statistical reliability, such as discrimination, calibration, and reclassification ability (Lippi et al., 2025).

Established Biomarkers in Clinical Practice:

Cardiac Injury Biomarkers

With the assistance of cardiac disease biomarkers, CVD can be identified, anticipated, and treated, particularly acute myocardial infarction (MI) and HF. Heart troponins (cTnI and cTnT) are the most commonly used and accurate biomarkers of myocardial injury and are considered the gold standard due to their excellent sensitivity and specificity to detect even a small amount of heart damage (Beumer Prieto et al., 2025; Qin et al., 2020). High-sensitivity cardiac troponin tests (hs-cTn) have significantly improved early identification and classification of risk. However, in non-ischemic or non-cardiac cases, they tend to be more sensitive, and thus interpretation may prove difficult (Lyngbakken et al., 2019). Myoglobin, heart-type fatty acid-binding protein (H-FABP), and creatine kinase-MB (CK-MB) are additional significant biomarkers that might be useful in the early diagnosis and monitoring of reinfarction or the extension of infarction (Netala et al., 2025; Castiglione et al., 2022). Since they indicate myocardial stress and remodeling, BNP and NT-proBNP of the heart have become important in diagnosing and managing heart failure (Dong et al., 2024). Vascular inflammation is possible to be indicated by such inflammatory factors as TNF-α, IL-6, and CRP, and increases the likelihood of major cardiovascular events (Antonopoulos et al., 2022). GDF-15, microRNAs, ST2, galectin-3, and other new and emerging biomarkers have been researched to be used in expanding cardiovascular care by improving early detection, danger detection, and tailored therapy (Ammar et al., 2025).

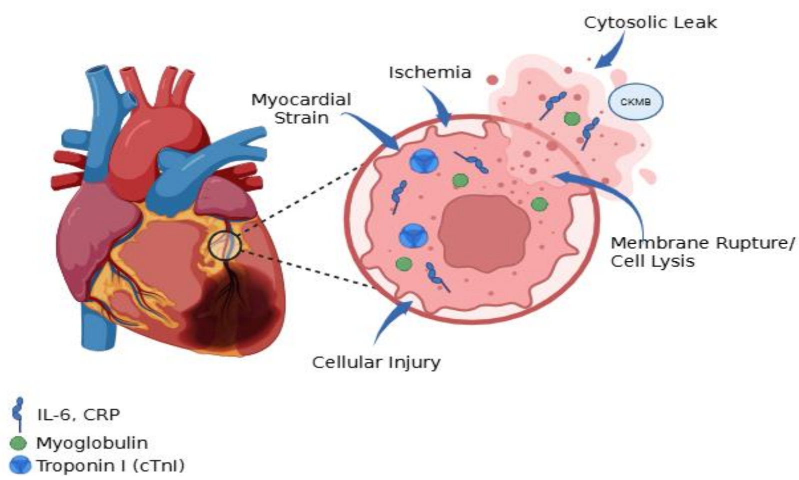

Figure 1: The figure presents the progression of myocardial ischemia by membrane breakdown and cellular injury. Myocardial strain occurs in cardiomyocytes during stressful conditions or ischemia and leads to cytosolic leakage and cardiac biomarkers being released to the bloodstream. Inflammatory markers like CRP and IL-6, myoglobin, and troponin I (cTnI) are found to leak out of injured heart cells. These biomarkers are useful in the diagnosis of myocardial infarction and other cardiovascular diseases.

Heart Failure Biomarkers:

Biomarkers of HF are vital in diagnosis, prognosis, risk, and treatment. The most common and widely studied natriuretic peptides are BNP, NT-proBNP, which are the gold standard for diagnosing and determining the severity of heart failure (HF) because they are highly sensitive and specific (Bastos et al., 2025; Berezin et al., 2023). The cardiac myocytes, which are activated by hypertrophy, volume overload, and stress on the ventricle walls, release these peptides into the circulation. High concentrations of BNP and NT-proBNP are closely associated with HF, whereas low concentrations are effective to exclude it (Pena-Duran et al., 2025).

Besides the natriuretic peptides, increasing numbers of new biomarkers can help to understand the complicated pathophysiology of HF. The markers such as soluble inhibition of tumorigenicity-2 (sST2) and galectin-3 indicate myocardial stress, fibrosis, and remodeling; the GDF-15 and mid-regional pro-adrenomedullin (MR-proADM) indicate systemic stress and vascular homeostasis; and cystatin-C, CRP, and IL-

6 indicate kidney failure and inflammation (Ammar et al., 2025; Berezin et al Such new biomarkers are fibrosis, inflammation, multi-organ, and hemodynamic stress.

Inflammatory and Metabolic Biomarkers:
Many metabolic and cardiovascular diseases are closely associated with the development and the evolution of inflammatory and metabolic indicators. CRP, IL-6, TNF-α, and cell adhesion molecules are associated with increased levels in metabolic syndrome, coronary artery disease, and non-alcoholic fatty liver disease (Liu et al., 2024; Antic et al., 2023; Gorog et al., 2022). Such metabolic indicators as the apolipoprotein B/A1 (APOB/A1) ratio, insulin, and triglyceride-glucose index (TYG) are linked independently to the risk of disease and the disease outcome and can also be predictive (Antic et al., 2023; Gorog et al., 2022). Gut microbiota are one of the factors that determine the interaction between inflammation and metabolism, and can modulate inflammatory markers associated with chronic diseases (including type 2 diabetes and obesity) (Liu et al., 2024). Improved risk prediction by metabolic profile (including glycerophospholipid and arginine metabolism) and systemic immune-inflammatory markers (including neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio) could be used to improve the personalized treatment (Antic et al., 2023). The exosomes and its building blocks are also under research as potential noninvasive markers of metabolic and inflammatory diseases.

Coagulation and Thrombosis Biomarkers:
Coagulation and thrombosis biomarkers are critical for detecting, diagnosing, and treating thrombotic abnormalities in cancer, sepsis, CVDs, and COVID-19. Traditional markers, including fibrinogen, antithrombin, and D-dimer, are still widely employed. Despite its poor specificity, D-dimer can assist in diagnosing disseminated intravascular coagulation (DIC) and rule out venous thromboembolism (VTE). Although complexes such as thrombin-antithrombin (TAT), plasminogen activator inhibitor-1 (PAI-1), and protein C can aid in the diagnosis of severe coagulopathy, low fibrinogen and antithrombin levels are associated with poor outcomes in sepsis and DIC (Hisada et al., 2024; Li et al., 2023; Ghantous et al., 2020). Beyond standard testing, new biomarkers provide clinical insight. While D-dimer, fibrinogen, vWF, and P-selectin combinations are associated with thrombotic load and death in COVID-19, tissue factor (TF), extracellular vesicle-derived TF, and thrombin generation assays (TG) predict thrombosis risk in cancer (Netala et al., 2025; Li et al., 2023). Markers such as PAI-1, EV-TF, vWF, and factor VIII have prognostic value in acute leukemia and stroke. Although they must be validated, emerging approaches such as impedance spectroscopy, nanopore sensing, synthetic urine biomarkers, and microRNA profiling provide real-time or noninvasive coagulation evaluation. The need for greater translational research is underlined by ongoing challenges such as poor selectivity, illness variability, inconsistent tests, and insufficient integration into clinical procedures.

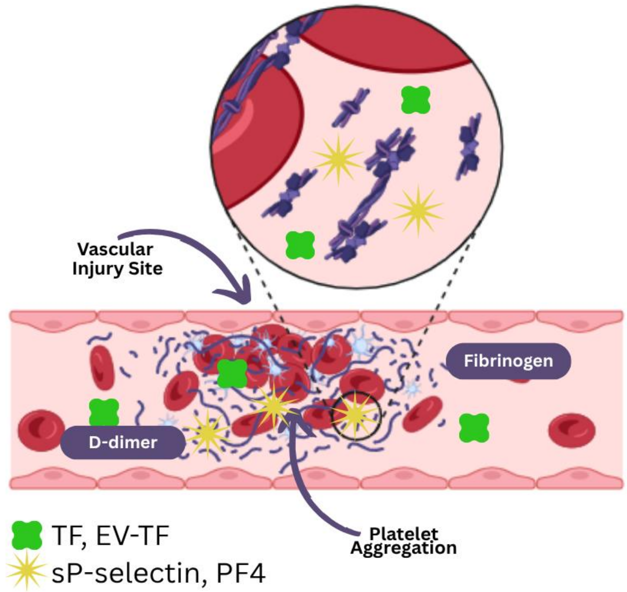

Figure 2: An illustration showing how vascular damage occurs and the biomarkers for coagulation and thrombosis that follow. The extrinsic coagulation cascade is initiated by the exposure of tissue factor (TF) and extracellular vesicle-derived TF (EV-TF) caused by endothelial rupture. Following platelet aggregation at the site of injury, soluble P-selectin (sP-selectin) and platelet factor-4 (PF4), markers of platelet activation, are produced. D-dimer denotes fibrin breakdown and ongoing thrombus turnover, while fibrinogen is converted into fibrin strands that stabilize the clot. In order to highlight how these biomarkers work together to provide diagnostic and prognostic information for thrombotic illnesses like cardiovascular diseases, the diagram shows the spatial relationship between endothelial injury, platelet activation, and fibrin network formation.

Emerging and Novel Biomarkers:

The biomarker landscape in CVDs is quickly expanding as molecular, cellular, immunological, and genetic markers emerge, providing essential tools for early detection, risk stratification, and tailored care. Several novel candidates are being developed, even though established biomarkers such as cardiac troponins for myocardial infarction, natriuretic peptides (BNP, NT-proBNP) for HF, and CRP for inflammation remain important in clinical practice (Sipos et al., 2021). While protein and peptide markers such as GDF-15, soluble suppression of tumorigenicity 2 (sST2), galectin-3, heart-type fatty acid-binding protein (H-FABP), and soluble urokinase-type plasminogen activator receptor (suPAR) provide important insights into inflammation, fibrosis, and cardiac remodeling, high-sensitivity troponins (hs-cTnI/hs-cTnT) are currently the gold standard for detecting early myocardial injury. Complement components, TNF-α, and IL-6, IL-1β are immune mediators that contribute to CVD and are increasingly being included in multi-marker models (Sipos et al., 2021; Lee, 2024; McGurk et al.,2021). Lipid and metabolic indicators such as oxylipins, ceramides, and lipoprotein-associated phospholipase A2 can predict the risk of atherosclerosis and metabolic syndrome (Liu et al., 2024; Pluta et al., 2022).

Circulatory microRNAs (e.g., miR-1, miR-133, miR-145, miR-208, and miR-499), long non-coding RNAs, and PIWI-interacting RNAs have emerged as very sensitive biomarkers at the genomic and transcriptome levels. Machine learning-based transcriptome markers have demonstrated high predictive accuracy for CVDs (Pamies et al., 2025; Searles & Charles, 2024). Furthermore, biological and functional markers such as circulating progenitor cells, platelet-leukocyte aggregates, and extracellular vesicles (such as exosomes and microparticles) provide non-invasive methods for monitoring inflammation, thrombosis, and heart injury (Pluta et al., 2022). Furthermore, mass spectrometry-based proteome and metabolomic profiling has transformed biomarker discovery by allowing for the simultaneous, high-throughput identification of low-abundance proteins, peptides, and metabolites (Ammar et al., 2025). When considered as a whole, these new and developing biomarkers improve traditional approaches, represent the complicated pathophysiology of CVD, and pave the way for more accurate diagnosis and personalized cardiovascular treatment.

Clinical Applications of Biomarkers:

Biomarkers are critical for the diagnosis, prognosis, risk assessment, and therapeutic management of CVDs, as they bridge the gap between pathophysiological processes and clinical judgments. While natriuretic peptides (BNP and NT-proBNP) are important for diagnosing and tracking heart failure because they reflect ventricular stress and remodeling, cardiac troponins, particularly high-sensitivity assays (hs-cTnI/hs-cTnT), remain the gold standard for the rapid and precise diagnosis of acute MI (Netala et al., 2025; Wang et al., 2020; Haller et al., 2021). In addition to these established tools, new protein markers like heart-type fatty acid-binding protein (H-FABP), galectin-3, copeptin, soluble suppression of tumorigenicity 2 (sST2), GDF-15, and others are increasingly used in early diagnosis and differential diagnostic approaches (Antonopoulos et al., 2022; Haller et al., 2021). Examples of inflammatory mediators that can forecast cardiovascular events and offer information about vascular inflammation and its long-term impacts include CRP, IL-6, TNF-α, and GDF-15 (Schwarz et al., 2023). Examples of genomic and transcriptomic biomarkers that are more sensitive to early detection, risk stratification, and therapeutic targeting include long non-coding RNAs and a circular microRNA, particularly in diseases where there are limited protein biomarkers (Cao et al., 2022; Schulte et al., 2020). Although the evidence of antiplatelet therapy and the predictor of intervention outcomes may be done with cellular markers, such as platelet-leukocyte aggregates, serial biomarker measurements, such as NT-proBNP in acute HF, could be used to guide therapy and monitor therapeutic response (Pluta et al., 2022). More importantly, the multi-marker technologies and proteomics-metabolomics-transcriptomics integration, which is frequently powered by mass spectrometry and machine learning, are transforming biomarker-based precision medicine (Ghantous et al., 2020). These applications underscore the importance of biomarkers in modern cardiovascular practice since they allow assessment of risks more accurately, diagnose them earlier, and tailor treatment plans to specific patients, which improves their outcomes.

Key Clinical Biomarkers and Their Applications:

Biomarker Category	Key Examples	Clinical Applications	Citations
Myocardial Injury	Cardiac troponins (cTnI, cTnT), H-FABP, and myosin-binding protein-C	The diagnosis of acute myocardial infarction, the early detection of heart diseases, and risk stratification	(Netala et al., 2025; Ghantous et al., 2020; Wang et al., 2020)

Myocardial Stress	BNP, NT-proBNP, MR-proANP, MR-proADM, copeptin	Heart failure diagnosis and prognosis, evaluation of ventricular stress, and change.	(Netala et al., 2025; Haller et al., 2021)
Inflammation	CRP, IL-6, TNF-α, GDF-15, galectin-3, sST2	Risk assessment, prognosis, and monitoring of chronic inflammation and fibrosis	(Antonopoulos et al., 2022; Jaworska et al., 2024)
Platelet Activation	Soluble CD40 ligand, P-selectin, platelet–leucocyte aggregates	Analysis of thrombosis risk, monitoring antiplatelet therapy, and prognosis following interventions	(Schwarz et al., 2023)
Plaque Instability	Lipoprotein-associated phospholipase A2, MMP-9	Analysis of atherosclerotic plaque susceptibility and risk of acute coronary artery disease.	(Netala et al., 2025; Ghantous et al., 2020)
Lipid/Metabolic Markers	Oxylipins, ceramides, TMAO, Lp-PLA2	Assessment of atherosclerosis, metabolic risk, and cardiovascular event prediction	(Jaworska et al., 2024)
Redox/Oxidative Stress	3-nitrotyrosine, oxidized DNA/RNA bases	Prognosis, assessment of comorbidities (e.g., diabetes, hypertension)	(Daiber et al., 2021)
Genomic/ Transcriptomic	microRNAs, lncRNAs, transcriptomic panels	Early detection, risk stratification, personalized therapy, especially where protein markers are lacking	(DeGroat et al., 2024)
Hormonal/ Neurohormonl	Copeptin, endothelin-1	Diagnosis and prognosis in heart failure, neurohormonal activation	(Li et al., 2023)

Calcium Homeostasis	Secretoneurin	Assessment of arrhythmia risk, cardiac stress	(Plášek et al., 2022)

Challenges and Limitations:

In spite of the advances in medicine and technology, CVDs are still a serious health issue in every part of the world (Afzal et al., 2025; Jafri et al., 2025). Irrespective of the diagnostic instruments, there exist numerous obstacles when dealing with patients with progressive HF (Samanidis, 2024). Their complexity causes them to be very difficult to diagnose and treat uniquely because they are caused by a combination of behavioural, environmental, and genetic factors (Pandey et al., 2025; Quer et al., 2024). An ageing population and the occurrence of chronic disease conditions increase the risk of dying and make treatment more difficult (Dai, 2024; Hu et al., 2022). Socioeconomic differences and access to healthcare, specifically in low-income localities, exacerbate the problem (Chaturvedi et al., 2024). Also, inadequate adherence to treatment, cultural concerns, and inappropriate lifestyle practices impede prevention efforts (Isiaho et al., 2025; Kang et al., 2025). The use of artificial intelligence and smart health technology can enhance the process of monitoring and prediction, and these applications can be constrained by barriers such as data privacy, implementation within clinical workflows, and legal provisions (Pandey et al., 2025; Ullah et al., 2023). Absence of dependable early biomarkers, as well as the challenges of the implementation of new treatments, including gene and miRNA-based therapy, in clinical practices, also hinder development (Benincasa et al., 2024).

Future Perspectives:

Artificial Intelligence, novel biomarkers, and the most recent biosensing technologies are transforming the future diagnosis of CVD to an improved and more accurate, personalised, and accessible approach (Srinivasan and Sharma, 2025; Gupta et al., 2025). The mechanism of disease diagnosis is evolving, as AI and machine learning automate the process of image interpretation of various types of tests, including Magnetic Resonance Imaging (MRI), Computed Tomography (CT) Scan, Electrocardiogram (ECG), and others (Zahid et al., 2025). This results in improved and precise outputs compared to outdated techniques (Khera et al., 2024; Giaj Levra, 2025; Willemink et al., 2021). AI systems are capable of detecting minor symptoms of an illness, anticipating threats before they happen, and tailoring treatment particular patient (Khera et al., 2024; Pantelidis et al., 2025). At the same time, new biomarkers, such as peptides, microRNAs, piRNAs, and extracellular vesicles, have better sensitivity and specificity in diagnosing at the earliest stage (Omran et al., 2022; Liu et al., 2024). The biosensors of the next generation (optical and electrochemical wearables) will be able to monitor cardiac health in real-time and in a non-invasive manner (John et al., 2022). By adopting such new technologies in combination with multi-omics approaches that incorporate proteomics, metabolomics, and genomic data, they lead to a new age of precision cardiology, which enables the management of diseases individually, continuous monitoring, and early intervention (DeGroat et al., 2024; Bastos et al., 2025).

Conclusion:

The changing field of cardiovascular research supports the growing importance of laboratory biomarkers in the diagnostics of diseases, risk assessment, and follow-up monitoring of the treatment. Such technologies are transforming our approach to cardiovascular pathophysiology and are informing the strategy of precision medicine. These strategies will involve traditional ones such as troponins, natriuretic peptides, and CRP and emerging ones of molecular and genetic markers. The combination of proteomics, metabolomics and genomics could help to develop new biomarker panels to improve the diagnostic and prognostic accuracy. Nevertheless, issues still remain, particularly in regard to standardisation, validation and translation of the experimental biomarkers into clinical use. The most appropriate research areas in the future are massive, multi-center studies, the ethical use of data, and the use of artificial intelligence to enhance predictive modelling. Finally, the collaboration of physicians, researchers, and data scientists will lay the groundwork on the way to the personalized approach to cardiovascular care. This will lessen the disease burden in the world by making interventions and the detection of disease easier.

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