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REVIEW

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Innovative biomarkers in cardiovascular disease: Advances in prevention and therapeutics

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ABSTRACT

Cardiovascular disease (CVD) is a leading cause of global morbidity and mortality, with diverse causes including lifestyle, environmental, and genetic factors. Biomarkers have traditionally supported CVD detection, prevention, and management, with LDL-cholesterol, high-sensitivity C-reactive protein (hs-CRP), and troponin offering diagnostic insights. However, their specificity and predictive power are limited. Recent discoveries have identified novel biomarkers like genetic polymorphisms, epigenetic modifications, and circulating microRNAs, which provide deeper insights into CVD pathophysiology. Technologies like metabolomics have introduced biomarkers such as trimethylamine-N-oxide (TMAO), linked to CVD risk and potential therapeutic targeting. These innovations promote a personalized CVD treatment approach, tailoring therapies to individual risk profiles. Pharmacogenomics advancements further enhance drug selection and dosing accuracy. Nonetheless, challenges remain, particularly in validating and integrating these biomarkers into routine clinical practice. This minireview explores established and emerging CVD biomarkers and their role in advancing personalized medicine, potentially revolutionizing CVD management through improved risk prediction, early diagnosis, and precise treatment strategies.

KEYWORDS

Precision medicine; Troponin; Cholesterol; Morbidity; Cardiovascular disease

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Introduction

Cardiovascular disease (CVD) is a leading cause of global morbidity and mortality, affecting millions annually. The onset and progression of CVD are influenced by a complex combination of genetic, environmental, and lifestyle factors. CVD encompasses a range of conditions, including coronary artery disease, heart failure, and hypertension, each contributing significantly to the overall disease burden [1]. Traditional approaches to CVD diagnosis and risk assessment have long relied on well-established biomarkers, such as LDL-cholesterol, high-sensitivity C-reactive protein (hs-CRP), and cardiac troponins. These biomarkers are critical in identifying patients at elevated risk and in guiding initial therapeutic decisions. However, they often lack specificity, particularly for early-stage or asymptomatic cases. Traditional biomarkers have limitations in detecting underlying disease mechanisms, and their predictive accuracy for long-term outcomes is constrained. These limitations underscore the need for more advanced, individualized diagnostic approaches to improve patient outcomes in clinical settings [2].

Recent advancements in biomarker science have introduced new molecular indicators with significant potential to enhance CVD management. Innovations in genetics, epigenetics, and metabolomics have led to the identification of novel biomarkers, including single nucleotide polymorphisms (SNPs), epigenetic modifications, and metabolites such as trimethylamine-N-oxide (TMAO). These biomarkers provide a deeper understanding of the molecular pathways associated with CVD risk and progression [3]. Additionally, biomarkers such as circulating microRNAs and endothelial progenitor cells (EPCs) offer promising applications for early detection, risk stratification, and targeted therapy, allowing for high-risk individuals to be identified before clinical symptoms appear. Unlike traditional markers, which serve primarily as broad indicators of risk, these emerging biomarkers enable tailored treatment plans aligned with the principles of personalized medicine (Figure 1) [4]. By offering insights into individual biological profiles, these markers have the potential to enhance both preventative and therapeutic strategies in cardiovascular care.

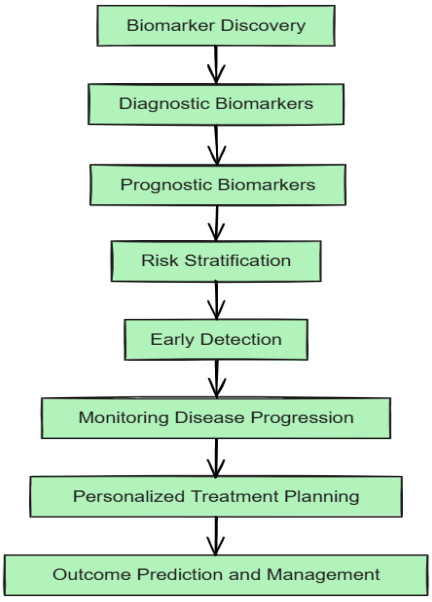

Figure 1. Role of biomarkers in CVD.

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While emerging biomarkers show great promise, several challenges impede their full clinical integration. Traditional biomarkers, despite being widely validated and accessible, lack the specificity needed to distinguish among CVD subtypes or predict long-term risk effectively. For example, hs-CRP is a marker of systemic inflammation that is elevated in a wide range of inflammatory conditions beyond CVD, reducing its diagnostic precision. Conversely, emerging biomarkers, such as genetic and epigenetic indicators, provide a more personalized view of disease risk but are largely confined to research settings due to the need for extensive clinical validation, regulatory approval, and the high costs associated with testing. Additionally, studies examining these biomarkers are in preliminary stages, with an urgent need for standardization across diverse populations to ensure clinical reliability and widespread applicability [5]. Addressing these research gaps is critical to transitioning biomarker discoveries from the laboratory to routine clinical practice, where they can enhance both diagnostic and therapeutic precision.

This mini-review aims to provide a comprehensive overview of both traditional and emerging biomarkers in CVD, focusing on their diagnostic, prognostic, and therapeutic roles, as well as their limitations in current clinical practice. It explores recent advancements in biomarker research that are facilitating a shift toward personalized medicine, particularly through individualized risk assessment and therapy. By examining the strengths and limitations of these biomarkers, this review highlights the transformative potential of emerging biomarkers to improve risk prediction, enable early diagnosis, and support customized therapy in CVD management. Furthermore, it underscores the future directions and challenges in integrating these biomarkers into clinical practice to optimize cardiovascular health outcomes.

Traditional Biomarkers in CVD

In the past, several biomarkers have been essential for evaluating and controlling cardiovascular health. Understanding the metabolism of cholesterol and how it contributes to the development of plaque in arteries requires knowledge of LDL-cholesterol, one of the most often tested lipids and an indicator of atherosclerosis [6]. An elevated risk of coronary artery disease has been consistently associated with elevated levels of LDL cholesterol. Another well-known inflammatory biomarker that reflects systemic inflammation linked to cardiovascular risk is high-sensitivity C-reactive protein (hs-CRP) [7]. Because inflammation is widespread in other disorders as well, hs-CRP lacks specificity even though it can signal an increased risk for conditions like myocardial infarction. Troponin and other cardiac-specific markers have shown promise in the diagnosis of myocardial injury, particularly in acute coronary syndrome, when increased levels indicate damage to the heart muscle. However, because of these conventional biomarkers' shortcomings, especially in terms of specificity and predictive power, new biomarkers must be created to fill these gaps and enhance therapeutic outcomes [8]. Table 1 compares the traditional biomarkers with the emerging biomarkers.

Table 1. Comparative study of traditional biomarkers with emerging biomarkers.

Aspect	Traditional Biomarkers	Emerging Biomarkers
Biomarkers	LDL-cholesterol, high-sensitivity C-reactive protein (hs-CRP), troponin	Genetic polymorphisms, microRNAs (e.g., miR-21, miR-208), TMAO, endothelial progenitor cells (EPCs)
Primary Clinical Use	Diagnostic and prognostic evaluation of CVD risk and myocardial injury, particularly in acute settings	Personalized risk assessment, prognostic stratification, potential therapeutic targets
Mechanism of Action	Measures lipid levels, inflammation, and cardiac muscle damage	Involves gene expression changes, metabolic byproducts, and molecular signaling markers
Specificity	Moderate; non-specific indicators like hs-CRP are influenced by various inflammatory processes	High; genetic and molecular markers are often disease-specific, offering better-targeted CVD insights
Sensitivity	Variable; for instance, troponin shows high sensitivity for myocardial injury	High; can detect subtle changes in risk factors, even at pre-clinical stages
Predictive Value	Limited; often reflects current state rather than long-term risk	Higher predictive value due to their ability to provide insights into underlying pathophysiological processes
Advantages	- Widely validated and accepted in clinical practice - Cost-effective - Easily accessible in labs	- Offers insights into individualized risk - Capable of detecting preclinical disease states - Supports precision medicine approaches
Limitations	- Lack of specificity for CVD (e.g., hs-CRP is elevated in various inflammatory states) - Limited predictive power for long-term risk assessment	- Expensive and requires specialized labs - Validation required for diverse populations - Integration into routine practice is still limited

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Regulatory Approval	Commonly approved and integrated into clinical guidelines (e.g., LDL-cholesterol for lipid management)	Limited approval; many are in the experimental phase or require further validation before routine clinical use
Influence of External Factors	External factors like diet, age, and lifestyle can significantly affect levels (e.g., LDL levels impacted by diet)	Less impacted by lifestyle factors in many cases, especially genetic markers; however, some (e.g., TMAO) are diet-sensitive
Role in Personalized Medicine	Low; traditional markers are often general and may not reflect individual disease mechanisms	High; emerging biomarkers provide tailored information on individual risks, enabling precise intervention strategies
Examples of Clinical Applications	- LDL-cholesterol for assessing atherosclerotic risk - hs-CRP for inflammation-linked CVD risk - Troponin for myocardial injury	- Genetic polymorphisms (SNPs) to tailor drug choices (e.g., pharmacogenomic testing) - miRNAs for prognosis in heart failure - TMAO for metabolic risk assessment
Diagnostic Timeline	Primarily used for acute or immediate diagnostics (e.g., troponin for myocardial infarction)	Useful in both acute and chronic settings; some emerging markers (e.g., epigenetic markers) track long-term risk
Cost and Accessibility	Generally low cost; widely accessible in clinical labs	Higher cost; limited accessibility to specialized laboratories
Research and Development Status	Well-established; ongoing research focuses on refining thresholds and improving accuracy	Actively researched with focus on clinical validation, particularly in multi-omic and machine learning integration

Emerging Biomarkers and Their Clinical Applications

Recent advances in research and technology have led to the discovery of new biomarkers, which hold great potential for providing personalized and thorough insights into CVD [9]. These new biomarkers have the potential to increase our knowledge of disease mechanisms, leading to possible improvements in patient management strategies. - Innovative biomarkers such as genetic polymorphisms, endothelial progenitor cells (EPCs), and circulating microRNAs are found among them [10]. Genetic variations offer important insights into a person's predisposition to CVD, allowing healthcare professionals to customize prevention plans as needed. EPCs, essential for vascular repair and regeneration, act as markers of endothelial well-being and help evaluate a patient's cardiovascular risk [11]. Moreover, there is a growing interest in circulating microRNAs due to their durability in bodily fluids and capacity to indicate different pathophysiological processes. Together, these new biomarkers help with better risk evaluation, enhance treatment tracking, and support the creation of personalized treatment methods for effectively managing CVD [12].

Genetic biomarkers

Genetic differences have a major impact on a person's likelihood of developing CVD [13]. Recent advances in genetics have enabled scientists to identify multiple genetic loci linked to vulnerability to different cardiovascular diseases, notably coronary artery disease. GWAS have been crucial in discovering these relationships, uncovering distinct genetic markers that influence the risk of CVD. Of all these indicators, SNPs have attracted interest for their importance in clinical settings. Certain SNPs can assist healthcare providers in determining an individual's risk of developing cardiovascular disease, allowing for timely intervention [14].

Moreover, the information obtained by discovering these genetic markers allows healthcare providers to create and execute more specific preventative plans. For instance, knowing a patient's genetic tendencies can help choose lifestyle changes or medications to lower the risk of cardiovascular issues [15]. Furthermore, genetic biomarkers can also act as predictive tools for assessing a patient's reaction to certain medications. This information is crucial for tailoring treatment plans, as it enables the enhancement of therapeutic effectiveness while reducing possible negative consequences. In general, incorporating genetic biomarkers into clinical practice is a major step forward in the personalized management of cardiovascular disease [16]. Table 2 explains about the types of genetic biomarkers and their applications.

Table 2. Types of genetic biomarkers.

Type of Genetic Biomarker	Target Area	Application
Single Nucleotide Polymorphisms (SNPs)	Variants in specific genes like APOE, PCSK9, and LDLR, affecting lipid metabolism and inflammation pathways	SNPs are used for predicting susceptibility to CVD. Specific SNPs (e.g., in APOE) influence lipid profiles and risk for coronary artery disease (CAD) and hypertension. SNPs in PCSK9 gene are associated with LDL-C levels, impacting cholesterol management strategies.

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Gene Mutations (e.g., MYH7, MYBPC3)	Cardiac muscle proteins, particularly in genes linked to cardiomyopathies	Mutations in genes such as MYH7 (myosin heavy chain) and MYBPC3 (myosin-binding protein C) are predictive of familial hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM). These mutations guide risk assessment and early intervention strategies for high-risk families.
Copy Number Variants (CNVs)	Genes involved in endothelial function and vascular tone, such as NOS3	CNVs influence endothelial nitric oxide synthase (eNOS) levels, impacting vasodilation and vascular health. CNVs in NOS3 can guide personalized strategies for vascular disease prevention and management, particularly in patients with predisposing vascular conditions.
MicroRNAs (miRNAs)	Regulatory RNAs involved in gene expression in cardiac cells and endothelial cells	miRNAs (e.g., miR-21, miR-126, and miR-208) serve as non-invasive biomarkers for myocardial infarction, heart failure, and atherosclerosis. miR-21, for instance, is associated with fibrosis in cardiac tissue, while miR-126 is linked to endothelial repair, aiding in risk stratification.
Epigenetic Modifications (e.g., DNA Methylation)	Genes regulating lipid metabolism, inflammation, and cell cycle	DNA methylation patterns, particularly in genes linked to inflammation and lipid metabolism (e.g., CPT1A), provide insights into environmental and lifestyle influences on CVD risk. Methylation profiling is used for risk assessment and targeted prevention strategies.
Genome-Wide Association Studies (GWAS)	Various loci associated with CAD, hypertension, and arrhythmias identified through large population studies	GWAS identify multiple loci associated with CVD risk factors, including CAD and arrhythmias. This data is applied in population screening to identify high-risk individuals and to inform lifestyle modifications or preventive measures based on genetic susceptibility.
Transcriptomics	Gene expression levels in myocardium and vascular tissue	Transcriptomic profiling is used to understand gene expression changes in response to CVD and drug treatment. Helps in identifying potential therapeutic targets and understanding disease progression at the molecular level.
Long Non-Coding RNAs (lncRNAs)	Regulate gene expression in heart and vascular tissues	lncRNAs such as ANRIL and MALAT1 play roles in vascular remodelling and atherosclerosis. These are being studied for their potential in diagnosing plaque stability and CVD progression, aiding in early diagnosis and tailored interventions.
Circulating Tumor DNA (ctDNA)	DNA fragments from necrotic cardiac cells in the blood	Though primarily used in oncology, ctDNA in cardiovascular research is emerging for assessing cardiac injury and tissue necrosis in heart failure and acute myocardial infarction. Provides a non-invasive method to monitor cell damage and treatment efficacy.
Proteomics of Genetic Variants	Protein-coding genes affected by genetic mutations linked to heart disease (e.g., TITIN)	Proteomic analysis of variants such as those in TITIN provides insights into structural heart diseases like DCM. Assists in developing targeted therapies by understanding how genetic mutations affect protein expression and function in heart muscle cells.
Pharmacogenomic Variants	Genes involved in drug metabolism (e.g., CYP2C19, SLCO1B1)	Genetic variations in enzymes like CYP2C19 and SLCO1B1 influence response to antiplatelet drugs (e.g., clopidogrel) and statins, respectively. Pharmacogenomic testing guides personalized medication selection, optimizing drug efficacy and reducing adverse effects.

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Epigenetic biomarkers

Epigenetic modifications, such as DNA methylation and histone acetylation, alter gene expression without changing the underlying DNA sequence. These modifications can be influenced by environmental factors and lifestyle choices, making epigenetic biomarkers useful for understanding how non-genetic factors contribute to cardiovascular health. For example, DNA methylation changes in genes regulating lipid metabolism and inflammation are associated with an increased risk of CVD [17]. Epigenetic biomarkers thus offer the potential to uncover how environmental exposures affect cardiovascular risk and highlight potential targets for therapeutic intervention.

Circulating microRNAs

MicroRNAs are tiny, non-coding RNA molecules that control post-transcriptional levels of gene expression. Heart failure and myocardial infarction are two cardiovascular diseases that have been connected to particular miRNAs, including miR-21, miR-126, and miR-208. The stability of circulating miRNAs in the bloodstream, their simplicity of detection, and their capacity to provide light on tissue-specific disease processes make them particularly appealing as biomarkers [18]. Certain miRNA profiles are useful tools in clinical practice because they are linked to specific cardiovascular illnesses, providing a promising route for risk assessment and early identification.

Inflammatory biomarkers

Atherosclerosis and other CVDs begin and progress mostly due to chronic inflammation. Although hs-CRP is still a common inflammatory marker, other inflammatory markers such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) have become important predictors of the risk of CVD. Unfavorable cardiovascular events and worse outcomes are linked to elevated levels of these markers [19]. Targeting inflammatory pathways may be a promising therapeutic strategy for managing CVD since it may reduce the risk of subsequent cardiovascular events by lowering systemic inflammation.

Endothelial dysfunction markers

Keeping the endothelium, which lines the inside of blood arteries, healthy is essential to preserving cardiovascular health. Biomarkers including circulating endothelial cells (CECs) and asymmetric dimethylarginine (ADMA) offer information on endothelial health, and endothelial dysfunction is an early sign of atherosclerosis. Inhibited nitric oxide generation is associated with elevated ADMA levels, which leads to endothelial dysfunction. In individuals with high cardiovascular risk, monitoring these indicators can help determine vascular health and forecast unfavorable cardiovascular outcomes [20].

Metabolomics-based biomarkers

Metabolomics, the study of small molecule metabolites within biological systems, offers a comprehensive understanding of metabolic processes involved in disease [16]. Specific metabolites, such as TMAO, have been implicated in CVD risk. Elevated TMAO levels are associated with a higher risk of atherosclerosis and other cardiovascular conditions. Metabolomics-based biomarkers offer unique insights into metabolic pathways associated with CVD, potentially serving as novel targets for therapeutic intervention and improving personalized medicine in cardiovascular care [21].

Natriuretic peptides and cardiac troponins

Biomarkers specific to the heart, such as high-sensitivity troponin and B-type natriuretic peptide (BNP), are widely used for evaluating heart failure and myocardial injury. Improved highly sensitive tests enable the identification of heart damage earlier, assisting in prompt diagnosis and treatment of heart failure and other heart conditions. These biomarkers are also crucial in tracking the success of treatment, allowing for modifications to treatment strategies as necessary to achieve the best outcomes for patients [22].

The Importance of Biomarkers in Cardiovascular Treatments

Biomarkers help diagnose CVD early and can also lead to the creation of personalized treatment plans. For example, pharmacogenomics can assist in pinpointing genetic differences that impact how a patient reacts to drugs such as anticoagulants, improving medication dosage and lowering the chance of negative outcomes. Biomarkers play a crucial role in directing targeted treatments, especially for diseases such as heart failure and atherosclerosis, by enabling healthcare providers to personalize interventions based on each person's risk characteristics [23]. Innovative personalized medicine methods, made possible by the identification of biomarkers, are revolutionizing cardiovascular treatment by providing customized therapies based on individual genetic and molecular characteristics.

Current Limitations and Future Prospects

Innovative biomarkers hold significant promise in advancing CVD management, yet current research reveals several limitations. Many emerging biomarkers, such as microRNAs and genetic polymorphisms, lack thorough validation across diverse populations, limiting their integration into routine clinical practice. Issues with specificity further complicate clinical utility; for instance, markers like high-sensitivity C-reactive protein (hs-CRP) are elevated in multiple inflammatory conditions, not solely CVD, which risks misinterpretation in diagnosis [24]. The inconsistency of assay techniques remains a challenge, as variations in methodologies lead to unreliable results across studies. Additionally, the high cost and limited accessibility of advanced biomarker testing constrain broader clinical adoption, especially in resource-limited settings. Ethical concerns surrounding genetic privacy and the potential for genetic discrimination also underscore the need for careful consideration in the application of genetic biomarkers [25].

The future of CVD biomarkers is promising, with advancements in multi-omics approaches integrating genomics, proteomics, and metabolomics expected to yield comprehensive biomarker panels that enhance diagnostic precision and predictive power. Artificial intelligence and machine learning technologies are increasingly being utilized to analyse complex biomarker data, facilitating early detection and accurate risk stratification. A shift toward non-invasive biomarkers, such as circulating cell-free DNA and RNA, aims to

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provide safer, easier patient monitoring options [26]. To ensure reliability and generalizability, collaborative efforts are underway to establish standardized protocols and validate biomarkers across diverse populations. As personalized medicine gains traction, research is focusing on predictive biomarkers to optimize individualized therapy responses, reducing adverse effects and improving outcomes. Overcoming current limitations through rigorous validation, technological advancement, and ethical guidelines holds the potential to transform CVD management, paving the way for precision medicine in cardiology [27].

Conclusions

The quick progress of new biomarkers in CVD is set to revolutionize prevention, diagnosis, and treatment in this extensive and influential field. These new biomarkers offer special understanding of the root causes of CVD, uncovering the molecular processes that contribute to disease progression. This knowledge is key for progress in customized medical care, enabling more accurate, specific treatments designed for individual risk factors. With the ongoing advancement of technology and molecular biology, it is becoming more and more possible to translate these biomarkers from research to actual clinical applications. Thorough validation and continued research are crucial in confirming the effectiveness and dependability of these biomarkers, backing their incorporation into regular practice. In the end, these advancements are projected to result in substantial benefits: improved patient results, decreased healthcare expenses, and enhanced cardiovascular care standards worldwide. The potential for managing CVD in the future is very promising, as there is a move towards precision medicine to enhance care tailored to individual patients.

Disclosure statement

The authors declare that there are no conflicts of interest that could affect the results or conclusions of this study.

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