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Assessment of Novel Biomarkers for Early Detection of Cardiovascular Diseases

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As a major cause of morbidity and mortality, cardiovascular diseases (CVDs) pose a serious threat to global health. For the efficient therapy and prevention of CVDs, early identification and risk stratification are essential. The evaluation of novel biomarkers for the early identification of CVDs is explored in this review paper, which divides them into five major categories: genomics, proteomics, metabolomics, imaging, and artificial intelligence (AI). Single nucleotide polymorphisms (SNPs) and epigenetic changes are examples of genomic biomarkers that provide information about genetic predispositions to CVDs. Proteomic biomarkers help in diagnosis and risk assessment, such as cardiac troponin and brain natriuretic peptide (BNP). Metabolomic biomarkers concentrate on metabolic patterns and offer useful data for early detection and individualised care. With the use of AI, imaging biomarkers are better able to evaluate heart shape, spontaneous function, and blood flow. Additionally, AI-driven biomarker discovery uses deep learning and machine learning algorithms to analyse a variety of data sources, speeding up the discovery of new CVD indications. Although encouraging, issues with data privacy, model interpretability, and regulatory approval must be resolved for AI-based biomarkers to be successfully implemented in clinical practise.

INTRODUCTION

Cardiovascular diseases (CVDs) are a global public health challenge, responsible for a Mortality and morbidity are a significant burden [1]. Coronary artery disease, myocardial infarction, heart failure, and stroke are just a few of the vast spectrum of disorders they cover that impact the heart and blood arteries. The early identification of CVD remains a crucial objective despite major advancements in medical research. Early therapies that might considerably improve patient outcomes and lessen the societal and financial costs of certain diseases can result from prompt diagnosis.

ABSTRACT:

The mainstay of diagnosing and assessing CVD risk has historically been the use of well-established biomarkers including blood pressure, cholesterol levels, and electrocardiograms. Although useful, these indicators frequently don't have the sensitivity and specificity needed for early illness identification. The investigation of novel biomarkers that provide greater accuracy and early detection capabilities is necessary due to this constraint.

There has been a positive uptick in recent years in the study of new biomarkers for the early detection of CVDs. These new biomarkers have the potential to improve our capacity to recognise individuals who are at risk, facilitate early interventions, and eventually lessen the burden of CVD. With the use of five key categories—genomics, proteomics, metabolomics, imaging, and artificial intelligence (AI)—this study attempts to give a thorough overview of these emerging CVD biomarkers.

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The study of CVD has seen a rise in the use of genomic biomarkers. The study of a person's genome involves finding specific genetic variations linked to a higher risk of developing cardiovascular disease (CVD) [2]. Genome-wide association studies (GWAS) have shown a large number of single nucleotide polymorphisms (SNPs) associated with CVD susceptibility since the development of high-throughput sequencing methods. By stratifying people depending on their genetic propensity for CVD, these genetic markers allow for personalised preventive strategies [3].

DNA methylation and non-coding RNAs are two epigenetic changes that have showed promise in revealing the molecular pathways behind CVD development [4]. Epigenetic biomarkers may enable early disease identification and offer insights into disease progression. In-depth discussion of the current state of genetic biomarkers for CVD, their clinical uses, and the obstacles they must overcome before being regularly incorporated into clinical practise will be provided in this part.

Another interesting area of CVD research is proteomic biomarkers. The study of all the proteins present in a biological system is known as proteomics [5]. The pathogenesis of CVDs can be better understood by analysing the post-translational modifications and protein expression levels. The identification of particular protein markers linked to CVDs, such as cardiac troponins, brain natriuretic peptide (BNP), and Creactive protein, has been made possible by cutting-edge methods like mass spectrometry [6].

The diagnosis and risk classification of CVD patients depend heavily on these biomarkers. Additionally, proteomic markers have the ability to distinguish between various CVD subtypes and assess treatment responses. The state of proteomic biomarkers for CVDs will be evaluated critically in this part, with a focus on both their advantages and disadvantages.

On the other hand, metabolomic biomarkers provide a distinctive viewpoint on the pathophysiology of CVD. The comprehensive examination of small molecule metabolites in biological samples is the focus of metabolomics [7]. Given that changes in metabolites such lipids, amino acids, and sugars are linked to CVDs, metabolic profiles can shed light on disease risk and development [8].

Different metabolomic patterns linked to CVDs have been found using cutting-edge analytical methods such nuclear magnetic resonance spectroscopy and mass spectrometry [9]. Furthermore, combining metabolomics data with other 'omics' information can improve our comprehension of the underlying mechanisms behind CVDs. This section will examine recent advances in metabolomic biomarkers for CVDs, focusing on their potential as diagnostic and prognostic tools.

Imaging biomarkers have played a crucial role in the diagnosis and treatment of CVD for many years. The heart and blood vessels can be precisely analysed using non-invasive imaging techniques such cardiac magnetic resonance imaging (MRI), computed tomography angiography, and positron emission tomography (PET) [10]. The evaluation of heart structure, function, and blood flow requires the use of these imaging biomarkers. Additionally, current developments in artificial intelligence (AI) have completely changed medical imaging and its function as a tool for diagnosing CVDs. Today, AI systems are able to examine enormous collections of medical picture information, spot minor alterations suggestive of CVDs, and provide quantitative evaluations of disease progression [11]. The most recent imaging biomarkers, their clinical uses, and the prospective effects of AI on the diagnosis of CVD will all be covered in this part.

AI has become a potent technique for biomarker development in CVD research in recent years. In order to find patterns and relationships that might be missed by conventional methods, machine learning and deep learning algorithms can analyse a variety of data sources, including genomes, proteomics, metabolomics, and medical imaging [12]. The discovery of novel markers for CVDs may be accelerated by AI-based biomarker research.

On the basis of a person's specific data profile, AI models can also be used for risk stratification, early detection, and personalised therapy suggestions. The deployment of AI in clinical practise, however, is fraught with difficulties relating to model interpretability, data protection, and regulatory authorisation. This section will assess the state of AI's application to biomarker discovery as well as the potential for incorporating AIbased tools into standard clinical practise.

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GENOMIC BIOMARKERS

Our knowledge of the genetic causes of cardiovascular diseases (CVDs) has been completely transformed by genomic biomarkers. The study of a person's genetic make-up is covered by the discipline of genomics, which concentrates on finding certain genetic variations linked to an increased risk of CVD.

High-throughput sequencing technology have made it possible to conduct genome-wide association studies (GWAS), which have found a large number of SNPs linked to CVD susceptibility [1]. These genetic markers provide important information about a person's hereditary propensity for CVD, enabling tailored preventive strategies and early therapies. Such a plan signifies a considerable transition from a general approach to a more specialised and efficient healthcare paradigm.

For instance, certain SNPs have been associated with a higher risk of hypertension and coronary artery disease (CAD) [2]. Healthcare professionals can start targeted interventions like lifestyle changes, early pharmaceutical therapy, or more regular monitoring by identifying these genetic variants in a person. By focusing interventions on those who are most at risk, this strategy not only lessens the overall burden of CVD but also guarantees that resources are used more effectively.

Genomic biomarkers include the evaluation of epigenetic changes in addition to SNPs. The study of heritable gene expression modifications that do not entail changes to the DNA sequence itself is known as epigenetics [3]. Epigenetic biomarkers may help with early detection in some cases and provide insights into the molecular processes underlying the pathogenesis of CVD.

One important epigenetic alteration that has been linked to CVDs is DNA methylation. Atherosclerosis and heart failure have both been linked to alterations in DNA methylation patterns in particular genes [4]. In the context of CVD research, non-coding RNAs like microRNAs have attracted attention for their ability to control gene expression [5]. These epigenetic indicators may contribute to a better comprehension of the molecular mechanisms behind CVDs, enabling more focused and efficient therapies.

Precision medicine has taken on new directions as a result of our increased understanding of the genomic and epigenetic roots of CVDs. It is now possible to identify those who may be at higher risk of having CVDs long

before clinical symptoms appear through genetic testing and epigenetic profiling. This early detection opens the door for preventative actions, which have the potential to significantly lower the incidence and severity of CVDs. The potential for personalised medicine offered by genomic and epigenetic biomarkers is one of its key benefits. For instance, medication selection and dose can be affected by a person's genetic propensity for statin intolerance or risk of experiencing negative drug reactions from anticoagulants [6]. This not only increases the treatment's effectiveness but also reduces the risk of adverse effects.

Additionally, combining genomes and epigenomics data with other 'omics' data, including proteomics and metabolomics, can give a more thorough understanding of CVDs. Integrating multimodal data can reveal complicated connections between genetic, protein, and metabolic pathways, illuminating the delicate interplay of factors influencing CVD onset and progression [7].

However, there are a number of difficulties in integrating genomic and epigenomic indicators into clinical practise. It is essential to ensure the precision and reproducibility of genetic test results since inaccurate data interpretation can result in inappropriate risk categorization and treatment choices [8]. Genetic testing also raises ethical challenges, such as privacy concerns, issues of informed consent, and the possibility of discrimination based on genetic information [9].

Furthermore, because of the intricate interactions between genetic and environmental risk factors for CVD, genomic and epigenomic indicators cannot give a complete picture. Diet, exercise, and smoking are lifestyle factors that have a big impact on CVD development. A more comprehensive knowledge of an individual's risk can be obtained by combining genetic data with these lifestyle factors [10].

Finally, genetic and epigenomic biomarkers present a promising approach for the early identification and individualised management of cardiovascular disorders. A person's genetic propensity to CVDs can be determined thanks to advances in genomics like GWAS and the discovery of disease-associated SNPs. DNA methylation and non-coding RNAs are two epigenetic indicators that help us better understand the underlying biological processes in these disorders.

A more thorough understanding of CVDs and the intricate interactions between genetic, protein, and

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metabolic variables may be possible with the merging of genomic and epigenomic data with other 'omics' disciplines. As these biomarkers are implemented into clinical practise, concerns about the reliability of genetic testing, ethical issues, and the requirement for a comprehensive approach to CVD risk assessment must be addressed. Finally, precision medicine in the prevention and treatment of cardiovascular disorders is made possible by genetic and epigenomic biomarkers.

PROTEOMIC BIOMARKERS

The study of cardiovascular disease (CVD) has become increasingly dependent on proteomic biomarkers, which provide a window into the complex world of proteins and their function in CVD pathogenesis. Proteomics, or the study of all the proteins in a biological system, sheds important light on the molecular processes behind CVDs. The capacity of proteomic biomarkers to show protein expression profiles and post-translational changes, both of which are important regulators of cellular function, is one of their primary advantages [1]. Researchers have been able to pinpoint certain proteins that operate as indicators for CVDs, assisting in their diagnosis and risk classification, by characterising these characteristics.

Cardiac troponin, a well-known proteomic biomarker in the setting of CVDs, is one such instance. A complex of three regulatory proteins called cardiac troponin is essential for the contraction of the heart's muscles [2]. Increased blood levels of cardiac troponin, which are frequently seen in diseases like myocardial infarction, are a sign of myocardial damage [3]. The diagnosis of acute coronary syndrome has been substantially enhanced by the sensitive and specific detection of cardiac troponin, enabling early intervention and better patient outcomes. Another important proteomic biomarker for CVDs is brain natriuretic peptide (BNP). In reaction to increasing

pressure inside the cardiac chambers, the heart releases the hormone known as BNP. It is a useful marker for this disease because its levels are high in diseases like cardiac failure [4]. BNP measures are used to diagnose, riskstratify, and monitor heart failure patients, as well as to decide on the best course of treatment and gauge how well it is working.

Proteomic indicators including C-reactive protein (CRP) have also been linked to an increased risk of CVD. The liver produces CRP, an acute-phase protein, in response to inflammation [5]. Increased CRP levels have been

associated with an increased risk of atherosclerosis and other CVDs. CRP readings can be a useful tool for risk assessment, determining the necessity for additional diagnostic procedures and treatment options.

Proteomics allows for the investigation of the entire proteome in addition to individual protein markers, revealing broad alterations in protein expression linked to CVDs. Researchers can find novel biomarkers and learn more about the molecular pathways underlying CVD by contrasting the proteome profiles of healthy and CVD patients [6].

There are several potential clinical uses for proteomic biomarkers. They are crucial for the diagnosis and risk assessment of patients with CVD, assisting in the selection of the best treatment options. Additionally, they are essential for tracking the development of the disease and evaluating the success of therapeutic therapies. Proteomic biomarkers support a more individualised approach to the management of CVD by revealing information about the underlying molecular processes.

Proteomic biomarkers have a lot of potential, but they also have limitations and difficulties. Proteomic assay standardisation is crucial since different reagents and laboratory procedures can have an impact on the outcomes [7]. Additionally, because a single protein can play multiple roles in distinct physiological situations, interpreting proteomic data can be challenging. To effectively use proteins as biomarkers, it is essential to understand their context-specific meaning.

By revealing the complex interplay of genetic, protein, and metabolic variables, the integration of proteomics with other 'omics' disciplines, such as genomics and metabolomics, enables a more thorough understanding of CVDs [8]. This multidisciplinary strategy improves our capacity to find new biomarkers and create focused therapies.

In conclusion, proteomic biomarkers have become crucial diagnostic, risk-based, and treatment tools for cardiovascular illnesses. Insights into the protein-based mechanisms behind various illnesses are provided by them, allowing for early detection and individualised treatment plans. However, to fully realise the potential of proteomic biomarkers, issues with standardisation and data interpretation must be resolved. Their incorporation with other 'omics' disciplines has the possibility of revealing a more thorough understanding of CVDs,

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which will ultimately result in better patient management and outcomes.

METABOLOMIC BIOMARKERS

By concentrating on the analysis of small molecule metabolites in biological samples, metabolomic biomarkers provide a distinctive viewpoint on cardiovascular diseases (CVDs). This method offers prospects for early detection and individualised treatment while revealing understanding on the biology of the metabolic alterations connected to CVDs.

The metabolome, which is an organism's whole collection of metabolites, is essential for maintaining healthy physiological processes. Changes in a person's metabolic profile are linked to a number of illnesses, including CVDs. In order to enable early intervention and more individualised treatment strategies, metabolomic biomarkers seek to identify particular metabolites or metabolic patterns that are indicative of CVD risk.

The assessment of lipids is one of the metabolomic indicators that has drawn a lot of interest in CVD research. It is widely known that dyslipidemia, which is characterised by aberrant lipid profiles, increases the chance of developing atherosclerotic CVDs including coronary artery disease [1]. Specific lipid species, such as cholesterol and triglycerides, have been linked to an elevated risk of CVD through metabolomic analysis. This information assists in the early detection of those who are at risk and provides guidance for interventions like dietary changes and lipid-lowering drugs.

Another class of metabolites that have been investigated as possible indicators for CVDs are amino acids. Diabetes and insulin resistance are two CVD risk factors that have been linked to changes in amino acid metabolism [2]. Specific amino acids, such as branchedchain amino acids and aromatic amino acids, have been found to vary in CVD-at-risk patients according to metabolomic investigations. These amino acid profiles may be a sign of metabolic abnormalities and may direct actions to increase insulin sensitivity and lower the risk of CVD.

Additionally, the metabolomic analysis of sugars and associated metabolites, also referred to as glycomics, has shed important light on the metabolic alterations linked to CVDs. Alterations in glycomics have been linked to an increased risk of atherosclerosis and heart failure, according to research [3]. Metabolomics advances our understanding of the metabolic pathways associated with CVDs and provides possible targets for treatments by finding particular sugar-related indicators.

The identification of distinctive metabolomic patterns linked to CVDs has been made possible by cutting-edge analytical methods such nuclear magnetic resonance spectroscopy and mass spectrometry [4]. These profiles may include lipids, amino acids, carbohydrates, and organic acids, among other metabolites. The combination of these several data sources enables a more thorough understanding of a person's metabolic status and serves as the foundation for individualised treatment plans.

Metabolomic biomarkers have the ability to guide treatment choices in addition to helping in the early diagnosis of CVDs. For instance, dietary therapies and lifestyle changes targeted at lowering the risk of CVD can be guided by the discovery of certain metabolomic patterns. Metabolomic data can also be used to evaluate treatment outcomes and track the success of therapeutic therapies [5].

Metabolomic biomarkers have certain advantages, but they also have drawbacks. Data interpretation may become more challenging due to variations in metabolite measurements brought on by things like food and lifestyle. To ensure the accuracy and reproducibility of results, standardised metabolomic tests and data analysis techniques are essential [6].

A more thorough understanding of CVDs may be obtained by combining metabolomics with other "omics" fields like genetics and proteomics. Researchers can acquire a better understanding of the intricate mechanisms underlying CVD development and progression by analysing the interactions between genetic, protein, and metabolic variables [7].

Finally, by emphasising the metabolic alterations connected to cardiovascular illnesses, metabolomic indicators provide a distinctive perspective on these ailments. Measuring certain metabolites or metabolic patterns offers insightful information on CVD risk and pathogenesis, facilitating early detection and individualised treatment strategies. Despite issues with data variability and standardisation, metabolomics' integration with other 'omics' disciplines holds the potential of enabling a more thorough understanding of

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CVDs, which will ultimately result in more effective preventative and management methods.

BIOMARKERS FOR IMAGING

For many years, imaging biomarkers have been essential to the diagnosis and treatment of cardiovascular diseases (CVDs). These non-invasive techniques are crucial for evaluating the anatomy, operation, and blood flow of the heart because they give precise anatomical and functional details about the heart and blood arteries.

Imaging biomarkers' capacity to see heart anatomy and spot structural abnormalities is one of their main advantages. For example, cardiac computed tomography angiography and magnetic resonance imaging (MRI) of the heart allow for a precise evaluation of the heart's chambers, valves, and main veins. Diagnoses of disorders such congenital heart abnormalities, valvular diseases, and aortic aneurysms depend heavily on these imaging modalities [1].

Additionally, imaging biomarkers are essential for assessing heart function. Using methods like echocardiography and cine MRI, it is possible to assess the ejection fraction and other functional metrics while also getting dynamic images of the heart's contractility. For illnesses like heart failure, when early intervention can greatly effect outcomes, monitoring changes in cardiac function over time is crucial [2].

Imaging biomarkers assist in assessing blood flow and perfusion in addition to structural and functional evaluations. Myocardial blood flow and viability can be determined using nuclear imaging techniques like positron emission tomography (PET) and single-photon emission computed tomography (SPECT). These imaging techniques are especially useful for identifying diseases like myocardial infarction, where it's crucial to gauge the heart's blood supply [3].

The use of imaging biomarkers has moved beyond their typical diagnostic applications thanks to developments in medical imaging. The creation of automated diagnostic tools and predictive models for CVDs has been made possible by the merging of artificial intelligence (AI) with medical imaging [4]. AI algorithms are able to examine enormous collections of medical picture information, spot minor alterations suggestive of CVDs, and offer quantitative evaluations of disease development. For instance, AI-based technologies can examine cardiac MRI pictures to find small myocardial tissue changes that might not be visible to the naked eye. Early detection of illnesses like cardiomyopathy and infiltrative cardiac disorders can be aided by these technologies. By examining imaging data coupled with other clinical data, AI systems can also be used to forecast future cardiac events, such as heart attacks [5].

The effectiveness and efficiency of diagnosing CVD could be increased by using AI into medical imaging. AIbased tools can assist healthcare providers in making more informed clinical decisions by automating the examination of complex imaging data. Additionally, these techniques can help in the early detection of CVDs, enabling prompt therapies that can have a big impact on patient outcomes.

However, there are difficulties in implementing AI in therapeutic settings. The need to overcome important obstacles such as governmental approval, interpretability of AI models, and data privacy issues [6]. Building trust in these tools requires ensuring the confidentiality of patient data and the transparency of AI algorithms.

In conclusion, imaging biomarkers that provide information on the anatomy, function, and blood flow of the heart have proved crucial in the diagnosis and treatment of cardiovascular disorders. The development of automated diagnostic tools and predictive models made possible by recent developments in artificial intelligence has increased the use of imaging biomarkers. Although incorporating AI into medical imaging has a lot of potential, overcoming data privacy and regulatory issues is essential for the effective use of these cuttingedge techniques in clinical practise. The use of imaging biomarkers in conjunction with AI has the potential to significantly improve their effectiveness in the early detection and management of CVDs.

ARTIFICIAL INTELLIGENCE IN BIOMARKER DISCOVERY

In the realm of cardiovascular diseases (CVDs), artificial intelligence (AI) has become a potent tool for finding novel biomarkers. In order to find patterns and relationships that might be missed by conventional methods, machine learning and deep learning algorithms have the ability to analyse a variety of data sources, including genomes, proteomics, metabolomics, and medical imaging. The topic of AI-based biomarker





discovery is evolving because it provides a quick and data-driven method for finding new CVD markers.

The ability of AI to manage huge and complex information is one of the technology's primary advantages in biomarker development. Massive amounts of data are produced by the 'omics' disciplines, such as genomics, proteomics, and metabolomics, and it can be difficult to analyse them efficiently using conventional statistical techniques. Researchers can find hidden patterns and connections by using AI algorithms, which are excellent at processing and extracting important information from these data sources [1].

For instance, in genomics, AI may examine the genomic information from thousands of people to pinpoint particular genetic variations linked to an increased risk of CVD. A more thorough understanding of the genetic causes of CVDs can be obtained using machine learning algorithms, which can identify complicated relationships between genes and environmental factors [2]. This method greatly quickens the discovery of novel genetic biomarkers and provides information on a person's hereditary susceptibility to cardiovascular disease.

AI has proven used in proteomics for examining protein expression profiles. Even while conventional approaches may not be able to detect such differences, deep learning systems can detect small changes in protein patterns linked to CVDs [3]. AI-based techniques find novel protein biomarkers that help in the diagnosis and risk classification of CVD patients by thoroughly examining the proteome landscape.

The data-processing abilities of AI are also advantageous for metabolomics. Due to the great variety of metabolites involved, the analysis of metabolomic data can be quite complex. By identifying metabolic patterns linked to CVD risk, AI models like neural networks can provide insights into the metabolic changes linked to cardiovascular disorders [4]. AI-discovered metabolic biomarkers are useful for early identification and the creation of individualised therapy plans.

A paradigm shift in the finding of imaging biomarkers has also been brought about by the combination of AI with medical imaging. In order to find small structural and functional alterations suggestive of CVDs, AI algorithms can examine large datasets of medical pictures, such as cardiac MRI or CT scans [5]. These instruments can offer numerical evaluations of disease progression, enabling earlier interventions and more precise risk categorization.

AI-based biomarker discovery has numerous clinical uses. Based on a person's specific data profile, AI models can be used for risk assessment, early detection, and personalised therapy suggestions. Through targeted therapies that take into account a person's genetic, protein, and metabolic variables, this personalised approach eventually improves patient outcomes [6].

The use of AI in clinical practise and biomarker discovery, however, presents a unique set of difficulties. Data privacy issues are of utmost importance, particularly when dealing with private 'omics' data and graphic medical photos. Building confidence in AI-based solutions requires ensuring the security and confidentiality of patient information [7].

Another key issue is model interpretability. Deep learning algorithms in particular are frequently referred to as "black boxes," making it challenging to comprehend how they get to particular conclusions. Particularly in clinical decision-making, the interpretability of AI models is crucial since healthcare personnel must be able to rely on and comprehend the recommendations made by these technologies [8].

A significant barrier to the implementation of AI-based biomarkers in clinical practise is regulatory approval. Healthcare regulators must make sure AI technologies are reliable, safe, and capable of diagnosing and treating CVDs. The process of establishing regulatory frameworks and standards for the approval and oversight of these tools is ongoing.

CONCLUSION

In conclusion, the search for cardiovascular disease biomarkers has entered a new era thanks to artificial intelligence. To find new biomarkers, machine learning and deep learning algorithms may analyse enormous and complicated datasets from genomes, proteomics, metabolomics, and medical imaging. This data-driven methodology speeds up the identification of markers for early detection, risk classification, and individualised care. To successfully integrate AI-based biomarkers in clinical practise, it is crucial to overcome issues with data privacy, model interpretability, and regulatory authorisation. Artificial intelligence is still a potent tool for advancing patient care and CVD research.



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