JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S12

Emerging biomarkers for early detection of diseases (e.g., Alzheimer's, cardiac conditions)

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Background: Biomarkers are quantifiable biological signs that offer vital details about a person's health or illness. Finding new biomarkers for the early diagnosis of illnesses like Alzheimer's and cardiovascular disorders has drawn more attention in recent years. Improving patient outcomes, enabling prompt management, and slowing the progression of the disease all depend on early detection. Early diagnosis and tailored medicine have been transformed by the identification of novel biomarkers made possible by developments in molecular biology, proteomics, and imaging techniques. These new biomarkers, which have the potential to revolutionize diagnostics, include blood-based markers, genetic variations, and imaging-based indicators.

Aim: This study aims to identify and evaluate emerging biomarkers for early detection of Alzheimer's disease and cardiac conditions, understand their mechanisms and clinical relevance, and assess their potential impact on improving diagnostic accuracy and patient outcomes.

Conclusion: A new era in the early detection of diseases such as Alzheimer's and heart issues is dawning, made possible by emerging biomarkers. There is a lot of hope for the therapeutic use of biomarkers like NT-proBNP and amyloid-beta for cardiovascular disorders and tau and amyloid-beta for Alzheimer's. Nevertheless, there are still obstacles to overcome, such as accessibility, cost-effectiveness, and uniformity. If these biomarkers are to become standard in clinical practice, further study and validation of them are required. These innovations have the potential to make healthcare more efficient worldwide by lowering the illness burden, improving patient quality of life, and allowing early detection.

Keywords: Amyloid-beta (Aß), Tau protein, Neurofilament light chain (NfL), High-sensitivity troponin (hs-Tn), N-terminal pro-B-type natriuretic peptide (NT-proBNP) and C-reactive protein (CRP)

Introduction

The key to better prognosis and less healthcare costs is early disease identification. Novel approaches are often required since conventional diagnostic procedures miss diseases in their subclinical phases. Here, biomarkers—tools obtained from biological fluids, tissues, or imaging—have become indispensable. Biomarkers allow for the early prediction of neurodegeneration in Alzheimer's disease and cardiac disorders such as myocardial damage or heart failure, respectively, and can do so for quite some time before symptoms appear. In order to improve the early diagnostic skills of these illnesses, this study explores the developing biomarkers that show promise.[1]

Biomarkers for Alzheimer's Disease

Popular Biomarkers

Progressive cognitive impairment and the buildup of amyloid plaques and neurofibrillary tangles in the brain are hallmarks of Alzheimer's disease (AD), a neurodegenerative condition. When it comes to early diagnosis, tracking the course of disease, and directing treatment plans, biomarkers have become indispensable. Aβ peptides, which stand as amyloid beta, are one of the most extensively researched biomarkers. To be more precise, lower amounts of Aβ42 in CSF suggest that it is being stored in the brain, and the AỤ42/AỤ40 ratio improves diagnostic accuracy by taking into consideration differences in peptide synthesis.[2]

Another characteristic of Alzheimer's disease pathogenesis, tau proteins are also utilized as biomarkers. Phosphorylated tau (p-Tau), especially subtypes such as p-Tau181 and p-Tau217, is directly associated with the development of neurofibrillary tangles, whereas total tau (t-Tau) indicates neuronal damage. Higher concentrations of tau biomarkers in cerebrospinal fluid or blood are highly associated with the advancement of Alzheimer's disease.[3]

Neurofilament light chain (NfL) is another core marker that has recently come to light as a potential sign of axonal injury. Being found in both cerebrospinal fluid and blood, it shows promise as a non-invasive biomarker. Diagnostic imaging for Alzheimer's disease has also advanced. By focusing on tau tangles, amyloid PET imaging can identify the formation of amyloid plaque using radiotracers, and tau PET imaging can provide detailed disease staging.[4]

In contrast, structural MRI reveals shrinkage in the brain, especially in early-stage disease-affected areas such the medial temporal lobe and hippocampus. Some of the neuroinflammation biomarkers that help explain the inflammatory processes in Alzheimer's disease include glial fibrillary acidic protein (GFAP) and YKL-40. The biomarker repertoire is further expanded by the observation that increased concentrations of neurogranin in cerebrospinal fluid (CSF) are indicative of synaptic dysfunction.[5]

Understanding the risk of Alzheimer's disease, especially in cases that manifest later in life, relies heavily on genetic biomarkers like the APOE ε4 allele. There is a correlation between early-onset familial AD and mutations in genes such as APP, PSEN1, and PSEN2. The non-invasive and economical nature of blood-based biomarkers is contributing to their rising popularity. Reliable indications of Alzheimer's pathology are now being established by plasma levels of p-Tau181 and p-Tau217, along with the plasma Aβ42/Aβ40 ratio.[6]

Novel biomarkers are being developed and made possible by multi-modal diagnostic techniques that combine data from CSF, imaging, and blood, thanks to emerging technologies such as proteomics, metabolomics, and artificial intelligence. All things considered, these developments are revolutionizing Alzheimer's diagnostics, which bodes well for the possibility of earlier diagnosis and more efficient treatments.[7]

Biomarkers on the Rise

To develop more precise and earlier diagnostic tools, researchers are constantly exploring new potential biomarkers for Alzheimer's disease (AD). New biomarkers are filling the gaps left by older approaches by making use of developments in data analytics, molecular biology, and neuroimaging. New blood-based biomarkers are among the most encouraging innovations because they provide a less intrusive option to imaging and analysis of cerebrospinal fluid (CSF). One promising marker for Alzheimer's disease pathology and a way to differentiate it from other neurodegenerative diseases is plasma phosphorylated tau (p-Tau), especially p-Tau181 and p-Tau217. These indicators are suitable for extensive screening since they mimic the results of tests that are based on CSF.[8]

Another promising protein is neurofilament light chain (NfL), which is a sign of damage to axons. Being able to be detected in both blood and cerebrospinal fluid, NfL offers valuable information on the advancement of disease and is being investigated as a marker for therapy monitoring. Additionally, there have been notable advancements in imaging biomarkers. The use of tracers such as flortaucipir in tau PET imaging allows for the observation of tau tangles in live patients, providing a direct indicator of disease stage. The advancement of more precise and economical tracers continues to enhance the already-established field of amyloid imaging. The inflammatory processes associated in Alzheimer's disease (AD) can be better understood with the use of neuroinflammation biomarkers including glial fibrillary acidic protein (GFAP) and complement cascade proteins, in addition to amyloid and tau.[9]

The potential of microRNAs (miRNAs) as diagnostic tools is also the subject of cutting-edge methods. The microRNA (miRNA) profile can be identified in both blood and cerebrospinal fluid (CSF) and is known to be dysregulated in Alzheimer's disease (AD). The range of early detection methods is being expanded by the discovery of novel potential biomarkers through proteomic and metabolomic research. Personalized medicine approaches in Alzheimer's diagnoses are being made possible by the integration of multi-omics data with artificial intelligence and machine learning. These new biomarkers are a game-changer; they could lead to more accurate diagnosis, more precise disease monitoring, and more reliable assessments of treatment measures' effectiveness.[10]

Methods for Detection

Multiple state-of-the-art methods, each specifically designed for a different kind and origin of Alzheimer's disease (AD) biomarker, are used in their identification. Since cerebrospinal fluid (CSF) analysis reflects brain biochemistry directly, it is still one of the most dependable procedures. To assess amyloid-beta (Aβ42) and tau proteins, techniques like enzyme-linked immunosorbent assay (ELISA) are commonly employed. Mass spectrometry (MS) allows for the accurate measurement of several biomarkers, which is useful for research and diagnostics.[11]

The use of immunoprecipitation techniques to enrich biomarkers for subsequent analysis significantly improves sensitivity. The non-invasive and easy-to-sample blood-based biomarker detection has been more popular in the past few years. Plasma biomarkers such as phosphorylated tau (p-Tau181 and p-Tau217) and neurofilament light chain (NfL) can be detected using immunoassays such single-molecule array (SIMOA), which provides ultra-sensitive detection capabilities. The breadth of biomarker identification in blood has been further increased by advanced molecular techniques, such as proteomics and microRNA analysis by qRT-PCR and next-generation sequencing (NGS).[12]

To see the structural and molecular alterations linked to Alzheimer's, neuroimaging techniques are crucial. Amyloid PET imaging uses radiotracers like Florbetapir and Pittsburgh Compound B (PiB) to identify amyloid plaques, while tau PET imaging targets tau tangles using tracers such as Flortaucipir. Positron emission tomography (PET) imaging is a gold-standard technology. To round out these approaches, MRI can reveal structural shrinkage in key brain areas including the hippocampus and medial temporal lobe, which are among the first areas impacted by Alzheimer's disease. Diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI) give light on the brain's microstructural integrity and connections in greater detail. Detecting and monitoring Alzheimer's disease biomarkers is made possible by a comprehensive toolkit that includes imaging technologies and fluid-based assays. This allows for earlier diagnosis and more precise therapy interventions.[13]

Indicators of Cardiac Health

Prevalent Biomarkers

The assessment of cardiac health is aided in the diagnosis, monitoring, and management of cardiovascular diseases (CVDs) by use of several biomarkers that reflect various components of cardiac function and pathology. Troponins (cTnT and cTnI) are widely recognized as the most reliable biomarkers for identifying myocardial damage, among many others. When the heart is injured, it releases proteins that are unique to the heart muscle into the bloodstream.[14]

To identify even small cardiac damage, high-sensitivity troponin tests (hs-TnT and hs-TnI) are essential for the early diagnosis of acute coronary syndrome (ACS) and for determining the risk in patients experiencing chest discomfort. Important biomarkers for the diagnosis and management of heart failure include natriuretic peptides, particularly BNP (B-type natriuretic peptide) and its inactive precursor NT-proBNP. These peptides are helpful for prognosis and treatment response monitoring; elevated levels suggest greater ventricular wall stress from volume or pressure overload.[15]

Atherosclerosis is greatly aided by systemic inflammation, which is linked to C-reactive protein (CRP) and its high-sensitivity version (hs-CRP), another significant biomarker. A higher risk of cardiovascular events is associated with elevated levels of hs-CRP. Elevated levels of lipid biomarkers like LDL-C and triglycerides are associated with atherosclerosis, whereas higher levels of HDL-C provide protection; these lipid biomarkers continue to play a crucial role in assessing cardiovascular risk.[16]

Furthermore, galectin-3 has become an important measure of cardiac fibrosis and a predictor of the development of heart failure; elevated levels of this marker are associated with poorer prognoses. ST2, a relatively recent biomarker, provides predictive information in heart failure patients by reflecting cardiac stress and fibrosis. Activated white blood cells release the enzyme myeloperoxidase (MPO), which has been associated with an elevated risk of acute coronary events and atherosclerotic plaque instability.[17]

New microRNAs (miRNAs) like miRNA-208 and miRNA-499 may one day be used as biomarkers to identify myocardial damage and stress, providing information on how genes are controlled in cardiac cells. Although it is less specific than troponin testing, creatine kinase-MB (CK-MB) is nonetheless helpful for diagnosing myocardial damage in certain situations. Lastly, D-dimer is utilized to assess the potential for thrombotic events, such pulmonary embolism and deep vein thrombosis, that frequently occur with cardiovascular disorders. When taken as a whole, these biomarkers paint a complete picture of heart health, which improves the ability to diagnose, stratify risks, and track the efficacy of treatments for cardiovascular disease.[18]

New Biomarkers

In the context of heart failure and other cardiovascular disorders, new biomarkers such as galectin-3, ST2 protein, and microRNAs (miRNAs) offer useful insights into cardiac health. Two important steps in the development of heart failure, inflammation and myocardial fibrosis, are indicated by galectin-3. Galectin-3 may be a diagnostic and therapeutic target because high levels of the protein represent cardiac remodeling and are linked to bad outcomes in individuals with heart failure. Due to its involvement in myocardial fibrosis, keeping tabs on its levels could aid in determining the extent of heart failure and directing therapy choices.[19]

Another key indicator in cardiovascular health is ST2 protein, which stands for soluble suppression of tumorigenicity. In cardiac stress and remodeling, especially in heart failure, it is a critical signal. Patients suffering from chronic heart failure are more likely to experience negative consequences when their ST2 levels rise in reaction to myocardial strain. Clinicians can use ST2

as a prognostic tool to assess the likelihood of disease development and the efficacy of therapies targeted at decreasing cardiac stress and enhancing cardiac function.[20]

One promising indicator of cardiac stress or injury is microRNAs (miRNAs), which are tiny non-coding RNAs that control gene expression. To better understand the role of microRNAs (miRNAs) in cardiac disorders such heart failure and myocardial infarction, researchers are focusing on miRNAs 208 and 499. Understanding the molecular pathways that drive stress, inflammation, and remodeling in the heart can be aided by these microRNAs. Furthermore, they show potential as non-invasive biomarkers that could assist in cardiovascular disease early diagnosis, risk stratification, and therapy efficacy monitoring.[21]

By bringing together galectin-3, ST2, and miRNAs, cardiac biomarker research has entered a new phase, one that promises to improve our capacity to detect, track, and treat diseases like heart failure by providing a more complex picture of the molecular mechanisms underpinning cardiac disease.[22]

Methods of Detection

Advanced techniques, including genetic analysis and protein tests, are used to discover new cardiac biomarkers such as galectin-3, ST2, and miRNAs. Heart failure and other cardiovascular illnesses are rooted in inflammatory processes, myocardial fibrosis, and stress, and these biomarkers shed light on these aspects. Due to the low concentrations or difficulty in quantifying many of these biomarkers, sensitive, specific, and dependable detection procedures are essential.[23]

Galectin-3

Primarily, immunoassays are used to assess galectin-3 levels. Enzyme-Linked Immunosorbent Assay (ELISA) is the gold standard for measuring galectin-3 in blood samples. This approach makes use of antibodies. In clinical settings, this assay is utilized often to evaluate fibrosis and inflammation in patients with heart failure because to its high sensitivity. While other methods like lateral flow assays or Western blotting can also detect galectin-3, the most well-established technique is ELISA because of how versatile and easy it is to use.[24]

ST2 Protein Verification

You can also use immunoassays, like ELISA or chemiluminescent immunoassays, to detect the ST2 protein. These are especially useful for detecting the soluble version of the protein, which is known as sST2. These techniques have been developed for the purpose of highly sensitively quantifying sST2 in blood samples. The high-sensitivity ST2 assay is another well-liked method; it is able to detect even very low plasma ST2 levels, making it ideal for evaluating heart failure patients and determining which ones are most likely to have the disease worsen. Also, cardiac point-of-care assays that measure sST2 levels in real time are in the works for use in hospitals and other medical facilities.[25]

MicroRNA (miRNA) Detection

Blood, serum, and plasma are just a few examples of the bodily fluids that contain microRNAs, which are tiny, non-coding RNA molecules that control gene expression. Quantitative polymerase chain reaction (qPCR) is a sensitivity approach that may amplify and quantify certain microRNAs; it is commonly used for miRNA detection. Because they yield trustworthy results with little sample input, qPCR assays see extensive use. The next-generation sequencing (NGS) method is another popular choice; it provides detailed information on miRNA expression patterns and may profile whole miRNA populations in a single run. Another method for miRNA detection is microarray-based analysis, which is commonly used in research environments for miRNA profiling on a large scale.[26]

New possibilities for the non-invasive, real-time detection of cardiac biomarkers are emerging because of developments in biosensors and nanotechnology, which complement these existing methods. The development of point-of-care diagnostics is underway, and these sensors based on nanoparticles have the potential to detect low-abundance biomarkers such as galectin-3 and miRNAs with great sensitivity. Additionally, due to its non-invasiveness and capacity to detect numerous biomarkers concurrently, liquid biopsy procedures are gaining popularity. These procedures test blood or other bodily fluids for biomarkers.[27]

In general, new cardiac biomarker detection methods are constantly improving, which makes it easier to track the course of heart failure, determine risk, and direct treatment. We will be able to diagnose and manage cardiovascular problems more effectively when protein assays, genetic analysis, and upcoming technologies are combined.[28]

Obstacles and Restrictions

Although there is enormous potential for improving the diagnosis and treatment of cardiovascular disease through the detection of new biomarkers such as galectin-3, ST2, and microRNAs (miRNAs), there are several limits and obstacles that prevent their broad practical use. Some examples of these difficulties include problems with clinical validation and regulatory approval, as well as technical constraints in detection methods.[29]

Precision and Reliability

Making sure biomarker detection is very sensitive and specific is a big deal. Due to their low quantities in blood or plasma, biomarkers like galectin-3 and ST2 might be difficult to detect reliably without extremely sensitive assays. Inadequate specificity of detection methods for the target biomarker might lead to false positives or negatives. Because their levels might be affected by a variety of other conditions or disorders, this poses a special challenge when evaluating biomarkers that are engaged in complicated biological processes, such as inflammation and fibrosis.[30]

Inadequate Regulation

The lack of consensus on how to best measure these indicators using assays is another major roadblock. For instance, whereas chemiluminescent and enzyme-linked immunosorbent assays (ELISA) are frequently employed for galectin-3 and ST2 detection, findings from different laboratories can be affected by variations in assay procedures, reagents, and equipment. Establishing unambiguous diagnostic thresholds and treatment guidelines might be hindered by the difficulty in comparing data across different clinical trials or labs, which is caused by this lack of consistency.[31]

Clinical Validation

Biomarker clinical validation is a laborious and intricate procedure. The therapeutic relevance of new biomarkers, such as galectin-3 and ST2, needs to be confirmed in large-scale, multicenter trials, despite their promising research results. Although several biomarkers show promise in well-controlled lab settings, their utility in the more complex and unpredictable clinical context is debatable. Extensive evidence demonstrating these biomarkers are trustworthy disease indicators, enhance patient outcomes, and provide value above existing diagnostic methods is required for the clinical validation procedure.[32]

Availability and Price

To identify new biomarkers, high-sensitivity immunoassays for ST2 and galectin-3, or next-generation sequencing (NGS) for miRNA profiling, are necessary yet prohibitively expensive. Not everyone has access to the specialist equipment and reagents needed for these tests, especially in areas with limited resources. These technologies may not be widely used in clinical

practice due to their high costs and restricted accessibility, especially in developing regions or healthcare systems with limited resources.[33]

Regulatory Clearance

Another significant obstacle is obtaining regulatory approval from organizations such as the European Medicines Agency or the U.S. Food and Drug Administration. New biomarker tests must pass stringent regulatory reviews to guarantee they are safe, effective, and reliable before they can enter clinical practice. New diagnostic techniques, particularly those relying on developing technology or unique biomarkers, might have a long and expensive road to approval. Furthermore, regulatory requirements for genetic tests like miRNA profiling can be intricate, given the sensitive nature of the genetic information involved and the need to adhere to stringent privacy and ethical guidelines.[34]

Finding Meaning in Results and Making Them Standard

It can be difficult to interpret results in a clinically useful way, even when biomarkers like ST2 and miRNAs are discovered precisely. It is challenging to create precise reference ranges or diagnostic cutoffs for biomarkers because their levels can fluctuate depending on factors such as the stage of the disease and patient demographics (age, sex, comorbidities). Combining several biomarkers, such galectin-3 with ST2 or miRNAs, necessitates sophisticated data analytics and an in-depth familiarity with the interplay between the various biomarkers and the intricate biological systems at work in cardiac illness. This could need the use of complex models and technologies like machine learning and artificial intelligence (AI), neither of which are necessarily available in every healthcare facility.[35]

Privacy and Ethical Considerations

Genetic and molecular biomarkers, particularly microRNAs (miRNAs), are becoming increasingly used, which raises ethical questions about patient privacy and permission. One example is microRNA profiling, which requires the examination of genetic material that may disclose private medical records. Healthcare providers, researchers, and regulatory agencies must all work together to resolve the pressing issues of patient privacy and the security of genetic data.[36]

Conclusion

New biomarkers including microRNAs (miRNAs), galectin-3, and ST2 hold a lot of potential for better cardiovascular disease diagnosis, prognosis, and treatment, especially in heart failure. When it comes to understanding the pathophysiology of heart disease, these indicators are crucial for providing information on inflammation, myocardial fibrosis, and cardiac stress. However, in order for them to be widely used in therapeutic settings, a number of challenges must be resolved. It is still very difficult to provide accurate and dependable diagnostic results due to problems with sensitivity and specificity, assay standardization, and clinical validation. Global integration of these biomarkers into ordinary clinical practice is further impeded by the cost and accessibility of improved detection methods, as well as the complexity of regulatory approval.

It is not easy to interpret biomarker results, particularly when dealing with several biomarkers that necessitate sophisticated data analysis and technological advancements. Despite these obstacles, there are significant potential benefits to integrating these biomarkers into clinical practice. These include the ability to detect diseases earlier, stratify patients based on risk, and provide more tailored treatments. These biomarkers have the potential to become vital resources for the individualized treatment of cardiovascular disorders, which could enhance patient outcomes and healthcare efficiency with further study, better technology, and the establishment of standardized protocols.

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