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Review Article

Biomarkers for early diagnosis and management of cardiovascular diseases

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ABSTRACT

In the last two decades, there has been a significant increase in interest in cardiovascular biomarkers for early diagnosis, primary disease control, and management. This has been fueled by the importation of advanced gene technology for the identification of novel biomarkers, as well as a better understanding of disease pathophysiology. This article provides a thorough examination of available biomarkers as well as their evaluation. A growing number of biomarkers are being used to assess the risk of cardiovascular disease (CVD) and to improve primary prevention. However, clinicians face a difficult task in evaluating and identifying appropriate biomarkers and when they should be used. Since the turn of the century, researchers have been examining the capabilities and limitations of novel biomarkers in the management of CVD. These studies show that much work remains to be done in order to identify novel biomarkers that are more precise and cost-effective for use in early heart disease prevention.

INTRODUCTION

The term "cardiovascular disease (CVD)" refers to the combination of LDL retention and hemodynamic stress that leads to vulnerable plaque, plaque rupture, and thrombosis formation[1]. Lipid-lowering trials are one option for treatment[2,3]. C-reactive proteins are commonly found in bio samples from patients with heart disease (around 30 C-reactive proteins)[4,5]. Some risk factors as causal pathways leading to diseases and risk markers as statistically associated with the disease may exist, but they do not have to be causally linked; it could be due to the disease process itself[6,7]. Some biomarkers from other organs or tissues are also associated with heart diseases, such as renal function, adipose tissues, neurohormonal therapy, unstable plaque, oxidative stress, hypertension, myocyte injury/death, cardiomyocyte/myocardial stretch, inflammation, and extracellular matrix remodeling (Figure 1)[8-11]. As a result, various biomarkers reflect various pathophysiological pathways[12].

Biomarkers are critical tools for testing, diagnosis, and changing prognosis in CVD diagnosis and their use has exploded. At this time, no single biomarker fully satisfies the ideal characteristics. As a result, various biomarkers in clinical use have revealed various pathophysiological conditions[14]. Although the number of CVD biomarkers has been increasing in recent reports, only a small number of them make it into clinical trials and implementation because only a few of them provide clinically useful diagnostic and prognostic information[15-17]. Biomarkers are used for a variety of purposes, including early detection, diagnosis of an acute or chronic syndrome, risk classification, observation of disease progression or responses to therapy (prognostic), and therapy selection for patient benefit[18-21].

RISK FACTORS FOR CVD

These can be classified as a) modifiable and b) non-modifiable depending on heredity and lifestyle. Diet, stress, physical inactivity, tobacco, alcohol, and obesity are all important factors that contribute to the progression of CVDs. Non-modifiable factors such as age, gender, family history, race or ethnicity, and socioeconomic status all play a role in the development of CVDs. Biological factors (unnatural consistency of lipid profile, hypertension, and diabetes) also play a role in the development of CVDs[8].

SELECTION CRITERIA AND CONSIDERATION FOR NOVEL BIOMARKERS

Biomarkers measurement is usually considered as accurate, reproducible, accessible assay, stability, reasonable cost, high throughput, and rapid turnaround when judging novel CVD biomarkers for clinical use[21-25]. Furthermore, whether the biomarker adds new information to existing tests or not, it must provide a strong link between the disease and the

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biomarker[26-28]. Furthermore, the utility of biomarkers in patient management includes higher-ranking functioning compared to existing tests, evidence that confederated is modifiable with precise therapy, and biomarker-guided triage or supervising that improves care[21,29-31]. The evaluation of ideal biomarkers could be a crucial component of screening, prognosis, and diagnostic strategies (Figure 2). A biomarker can sometimes be anything that reflects a natural process, so it could be genetic markers or soluble biomarkers[32].

According to Morrow et al. three specific outlines for evaluating biomarkers in general use, the following important key points must be prioritized. These are (a) simple biomarker measurement and handling, (b) what data it contributes to the biomarker, and (c) how it affects management.[33-35]. The most commonly used biomarker is depicted in the panel below (Figure 3).

The ideal biomarker is used to screen and diagnose a disease, change prognosis, or show how clinical management is affected. In preliminary studies, a few randomized clinical trials may be required for the assessment of biomarkers. However, there is little information about the impact of biomarker-guided strategies on clinical outcomes[33]. Heart failure (B type natriuretic peptides: BNP and N-terminal pro-brain Natriuretic Peptide: NT-proBNP) and acute coronary syndromes (cardiac troponins T and I) are two cardiac markers used in clinical practice (Figure 3)[21,22,29,37-39]. The latter case is used for prognosis estimation, acute patient evaluation, and personalized medicine for therapy guidance and monitoring[40-43].

COVID 19 AND CARDIOVASCULAR DISEASE

COVID-19 was formerly assumed to be a mild form of interstitial pneumonia, but it has now been categorized as a vascular disease owing to substantial consequences and reasons of mortality, including myocardial damage, venous thromboembolism, arrhythmias, and acute coronary syndrome[44,45]. The interaction of the viral spike (S) protein with angiotensin-converting enzyme 2 (ACE2), which mediates virus entry into host cells, is likely to be the cause of COVID-19's cardiovascular disease manifestations[46]. Endothelial cells of the lungs, heart, kidneys, liver, and intestines express ACE2 receptors in high amounts. In humans, the SARS-CoV-2 virus may infect endothelium cells and produce severe illnesses. The discovery of endothelial cell damage in diverse organs' circulatory beds sheds light on hitherto inexplicable symptoms and clinical outcomes mentioned in early COVID-19 pandemic reports[45,46]. The observation of endothelial cell damage in human organs (lungs, heart and kidney) vascular beds sheds light on hitherto unexplained symptoms and clinical outcomes recorded in early COVID-19 pandemic reports. Patients with pre-existing cardiovascular illness are more likely to have negative results in COVID-19, which might be explained by viral endothelium damage[45]. According to recent research, thrombosis has become a common connecting factor for a variety of symptoms that were previously unrelated to COVID-19[47]. Deep vein thrombosis (DVT) was found in 58 percent of COVID-19 autopsies, which was worsened by lethal venous thromboembolism (VTE) in 30 percent of patients. In addition, the other 30% of patients in this initial cohort suffered from sudden cardiac death and renal infarc-

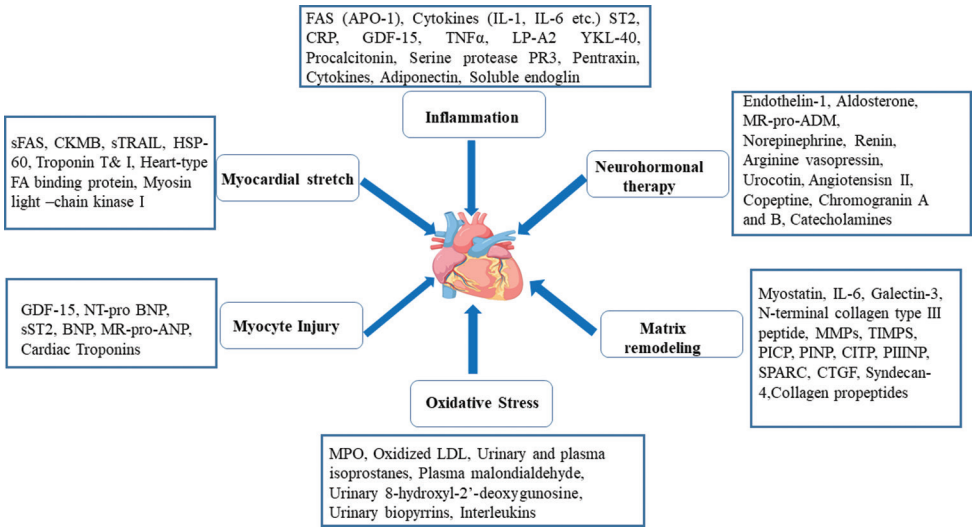

Figure 1. Biomarker classification based on CVD pathophysiological processes. The illustration has been adapted and modified from[13]. Abbreviations: Fetal alcohol syndrome (FAS), Interleukin (IL), Interleukin 1 receptor-like protein/suppression of tumorigenicity 2 (ST2), C-reactive protein (CRP), Growth/differentiation factor 15 (GDF15), Tumor necrosis factor-α (TNF-α), Lipoprotein-associated phospholipase A2 (LP-A2), Chitinase-3-Like Protein 1 (YKL-40), Mid-regional proadrenomedullin (MR-proADM), Tissue inhibitor of metalloproteases (TIMPS), Procollagen 1 C-type terminal propeptide (PICP), C-terminal telopeptide of collagen type I (CITP), Type III procollagen peptide (PIIINP), Soluble protein acidic rich in cysteine (SPARC), Connective tissue growth factor (CTGF), Myeloperoxidase (MPO), Low density lipoprotein (LDL), N-terminal pro b-type natriuretic peptide (NT-proBNP), soluble suppression of tumorigenicity 2 (sST2), Brain natriuretic peptide (BNP), Mid-regional pro atrial natriuretic peptide (MR-proANP), Soluble fetal alcohol syndrome (sFAS), Creatine kinase-MB (CK-MB), Soluble TNF-related apoptosis-inducing ligand (sTRAIL), Heat shock protein -60 (HSP-60)

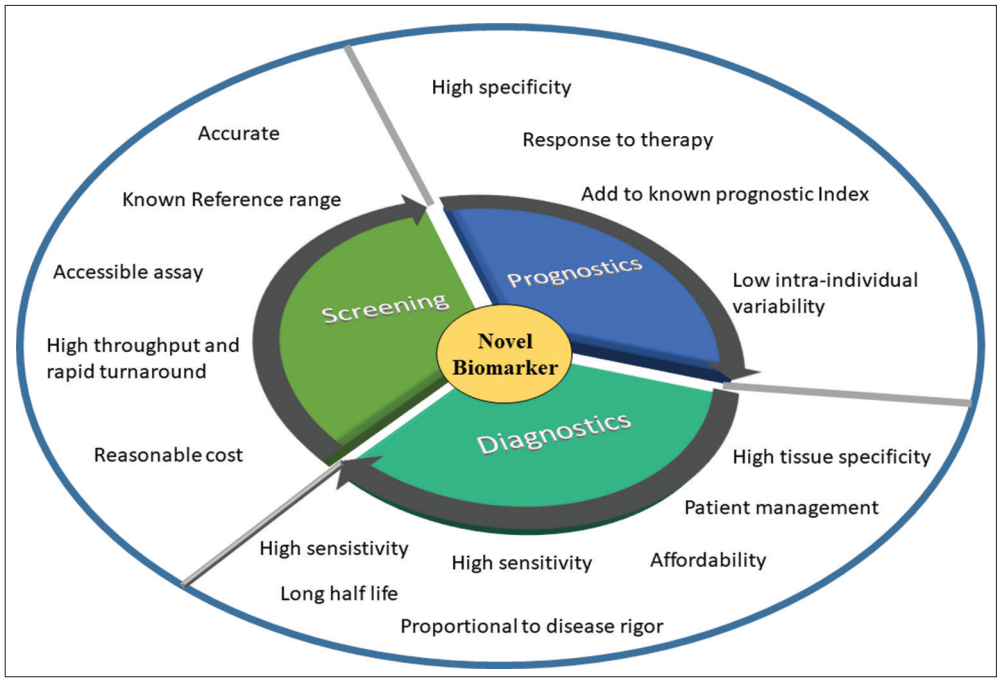

Figure 2. Characteristics of a novel biomarker that are ideal for a specific application. The image has been modified and adapted from[15]

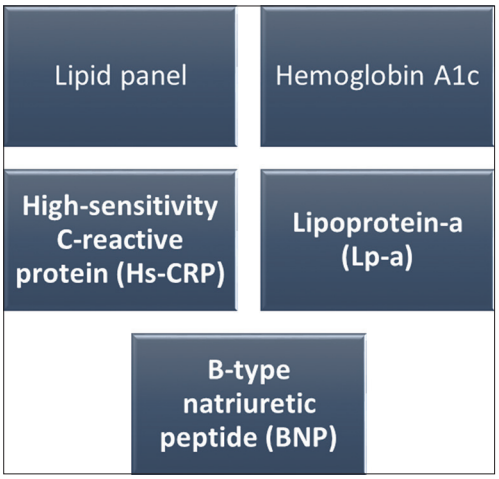

Figure 3. The top five biomarkers for primary detection and prevention of cardiovascular disease are the most widely used. The image has been changed and adapted from[33,36]

tion sequelae[45]. Cardiovascular biomarkers, especially D-dimer and troponin, seems to be exceptionally potent prognostic indicators, suggesting that more proactive treatments and coverings are required to limit arterial/venous occlusion and heart muscle infarction[45,48]. The levels of D-dimer, lactate dehydrogenase (LDH), and the aspartate transaminase to alanine transaminase ratio (AST–ALT) in the blood profile of COVID 19 patients show significant variability, indicating the severity of infection[49].

CONCLUSION

Biomarkers hold out the promise of more precise and earlier risk stratification for CVDs. It also helps with disease screening, such as myocardial infarction and heart failure, and has been extensively researched. It also aids in the early detection and prevention of cardiovascular disease. Unfortunately, no single potential biomarker has emerged to best screen for CVD disease, and none of them has enough sensitivity or precision to be useful. Biomarkers that are currently available are more biased and have a wide range of results during screening and prognosis. As a result, future strategies will primarily focus on unbiased approaches, which means that risk factors will be solved using proteomics or metabolomics approaches, as well as larger biomarker screening[50].

Declarations

The author have no conflicts of interest to declare.

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