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Biomarkers in cardiovascular disease: Insights into diagnosis, risk stratification, and emerging therapeutic approaches

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ABSTRACT

Cardiovascular disease (CVD) continues to constitute a significant global health concern, playing a significant role in premature deaths and increasing healthcare expenditures. Its complex etiology and varied clinical manifestations present substantial challenges to both healthcare systems and individual health outcomes. Despite the numerous diagnostic methodologies available for the management of CVD, further extensive research is needed to elucidate the complex interrelationship between distinct factors, optimize biomarkers for early detection, and understand the critical role of certain proteins in CVD pathogenesis. Biomarkers such as cardiac troponins, hFABP, c-MyC, ANP, BNP, MRproADM, copeptin, CRP, IL-6, GDF-15, soluble ST2, galectin-3, soluble CD40 ligand, P-selectin, Lp-PLA2, MMP-9, catecholamines, granin proteins, and secretoneurin have significant diagnostic value for numerous CVDs. This review concisely summarizes the global impact of cardiovascular diseases and their risk factors and discusses the roles of biomarkers in cardiovascular diagnostic processes. This review further discusses various therapeutic approaches, both current and emerging, that are applicable for curtailing different CVDs in the future.

Keywords: biomarkers; CVD; risk factors; therapies; epidemiology

1. INTRODUCTION

Cardiovascular disease (CVD) continues to be a significant contributor to early death and increasing healthcare expenses (GBD 2019 Diseases and Injuries Collaborators, 2020). CVD remains a formidable challenge to global public health, as it poses significant burdens on healthcare systems and individual well-being. Owing to its multifactorial etiology and diverse manifestations, CVD encompasses a spectrum of conditions, including coronary artery disease (CAD), heart failure (HF), stroke, and peripheral artery disease (Mensah et al., 2019). While advancements in medical science have improved our understanding of CVD and expanded treatment options, the prevalence and impact of CVD continue to rise, driven by an aging population, sedentary lifestyles, and a rising prevalence of risk factors such as obesity, hypertension, and diabetes mellitus.

Many epidemiological studies have shed ample light on how several genetic, environmental, and behavioral factors interactively contribute to the onset and progression of CVD, with well-established risk factors for CVD that exert

deleterious effects on the cardiovascular system through various mechanisms, including endothelial dysfunction, inflammation, and oxidative stress. Furthermore, emerging evidence suggests that psychosocial factors, such as depression (Rajan et al., 2020), inadequate sleep (Makarem et al., 2022), and psychological stress (Hall et al., 2018), may also influence cardiovascular health, emphasizing the importance of a comprehensive approach to CVD prevention and management.

In recent years, there has been growing recognition of the bidirectional relationship between mental health and CVD, with conditions such as depression and anxiety exhibiting significant associations with adverse cardiovascular outcomes (Lichtman et al., 2014). Moreover, sleep disturbances, including insomnia and sleep apnea, have emerged as potential contributors to CVD risk, highlighting the intricate connections between sleep quality and cardiovascular health (Jarrin et al., 2018). Additionally, metabolic disorders, such as dyslipidemia, insulin resistance, and metabolic syndrome, play pivotal roles in the pathogenesis of atherosclerosis and contribute to the development of CVD (Mathew et al., 2008).

As our understanding of the complex interplay between risk factors and cardiovascular health continues to evolve, there is a pressing need for comprehensive strategies to mitigate CVD risk and improve outcomes for affected individuals. By addressing modifiable risk factors through lifestyle modifications, pharmacological interventions, and targeted therapies, healthcare providers can play a pivotal role in reducing the burden of CVD and promoting cardiovascular health across populations.

2. EPIDEMIOLOGY OF CVD

The primary cause of death worldwide and a significant contributor to disability are CVDs, primarily ischemic heart disease, stroke, heart failure, peripheral arterial disease, and several other cardiac and vascular conditions (Mensah et al., 2019). According to the 2013 Global Burden of Disease Study, CVD accounts for more than 30% of all deaths globally (GBD 2013 Mortality and Causes of Death Collaborators, 2015). Nonetheless, new data from Europe indicate that in many nations, cancer has surpassed CVD as the primary cause of mortality (Nichols et al., 2014).

The number of deaths from CVD climbed significantly from 12.1 million in 1990 to 18.6 million in 2019, and the rate of development of all CVD nearly doubled from 271 million in 1990 to 523 million in 2019 (Roth et al., 2020), with North Africa, the Middle East, and Central and Eastern Europe having the highest age-standardized rates of cardiovascular disease mortality because of elevated systolic pressure and countries in Australia having the lowest (Walther, 2023). However, there was a noticeable decline of one-third in the death rate from 1990–2019. Although this difference is not consistent across the globe, females (0.204% deaths) are reported to have lower age-standardized cardiovascular death rates than males (0.2808% deaths) (Cesare et al., 2023).

3. RISK FACTORS ASSOCIATED WITH CVD

CVD refers to a range of conditions that affect the heart and blood vessels. These conditions include coronary artery disease (which leads to heart attack), stroke, heart failure, congenital heart defects, peripheral artery disease, and other disorders. Essentially, any condition that affects the heart's function or the blood vessels throughout the body falls under the umbrella of CVD. These disorders are known to be caused either spontaneously or systemically by a range of factors extending from lifestyle to both simple and complicated medical conditions. In older individuals, however, high blood pressure, body mass index, and blood cholesterol and glucose levels are more prevalent risk factors than in younger individuals (Andersson & Vasan, 2018). This trend arises because these risk factors accumulate and worsen as individuals age.

Insufficient sleep duration has become a significant concern, with its effects on health and overall well-being being particularly profound. Lifestyle changes, such as extended working hours, social late outings, and technology, have led to a reduction in recommended sleep durations for young adults and older adults (Covassin & Prachi Singh, 2017). Sleep loss negatively impacts quality of life, mood, cognitive function, and health, potentially leading to cardiovascular complications such as hypertension and metabolic syndrome (Khan & Aouad, 2022).

Depression, a psychiatric condition, is linked to CVD and depressive disorders, which are the leading causes of disability in high-income countries (Rajan et al., 2020). Women are more susceptible to depressive disorders, and depression exacerbates cardiovascular morbidity and mortality (Bucciarelli et al., 2020). The fundamental mechanisms relating depression to CVD are complex and likely involve multiple factors (Vaccarino et al., 2020).

Obesity has increased dramatically on a global scale, reaching epidemic levels (Bastien et al., 2014). Obesity is strongly linked to various CVDs, such as hypertension, heart failure, coronary heart disease, stroke, atrial fibrillation, and sudden cardiac death (Poirier et al., 2006). Both directly and indirectly, obesity contributes to CVD morbidity and mortality by worsening coexisting CVD risk factors (Mathew et al., 2008). Recent findings emphasize that abdominal obesity serves as an independent marker for cardiovascular disease risk, distinct from body mass index. Lifestyle modifications and weight loss not only ameliorate metabolic syndrome but also mitigate systemic inflammation and endothelial dysfunction (Powell-Wiley et al., 2021).

4. BIOMARKERS ASSOCIATED WITH CVD

4.1 Cardiac troponins

Three components comprise the muscle protein complex known as troponin, which is present in striated muscle: troponin C, T, and I. In 2000, it was added to the definition of acute myocardial infarction (AMI), and patients who are suspected of having acute coronary syndrome (ACS) still rely heavily on it for their diagnostic needs (Alpert et al., 2000). A cardiac troponin reading above the 99th percentile of the specified assay and a notable shift between two tests in cardiac troponin concentrations are needed for the diagnosis of AMI (Thygesen et al., 2018).

An increasing number of strategies have been presented for the early identification of ACS due to the sensitivity of diagnostic troponin testing (Cervellin et al., 2016). Rapid diagnostic techniques could reduce the time it takes to diagnose and treat patients with chest pain,

which would reduce total expenses. The primary benefit of higher sensitivity is a speedier rule-out because the window of opportunity after AMI when cardiac troponins cannot be detected is closing (Morrow, 2017).

AMI diagnosis cutoffs have been significantly lowered by measuring cTnT and cTnI concentrations owing to the evolution of highly efficient cardiac troponin tests. These modest levels of cardiac troponin in the blood are linked to both conventional cardiovascular risk factors and measures of left ventricular anatomy and function (de Lemos et al., 2010). An ideal biomarker for primary prevention would reveal both the response to a risk-reducing strategy and the likelihood of a disease developing (Lyngbakken et al., 2018).

4.2 Heart-type fatty acid-binding protein (hFABP)

Transporting fatty acids through membranes is the function of fatty acid-binding proteins, such as hFABP, the most common isoform in the heart and skeletal muscle. hFABP is released into the circulation after acute myocardial ischemia and is particularly specific for the myocardium; it might offer diagnostic data for early AMI diagnosis. The clinical significance of hFABP is greatest in early presenters because of its rapid clearance from peripheral circulation; it may also aid in differentiating chronically elevated cardiac troponin concentrations from AMI (Januzzi et al., 2012). However, the diagnostic qualities of hFABP are not as good as those of CT, and the present guidelines do not support its use in AMI diagnosis (Roffi et al., 2015).

4.3 Cardiac myosin binding protein-C (c-MyC)

c-MyC is a protein in the sarcomere and is the basic unit of muscle contraction. It plays a vital role in normal heart function (Offer et al., 1973). When the heart muscle is damaged, c-MyC is released into the blood faster than cardiac troponin, another protein marker of heart injury (Baker et al., 2015). Scientists have developed high-sensitivity tests for c-MyC that can measure very low levels of this protein in more than 95% of people who do not have heart problems (Marjot et al., 2016). Studies suggest that c-MyC can help rule out acute myocardial infarction (AMI) or heart attack faster than can cardiac troponin. This could be useful for emergency care in the field, where c-MyC might diagnose AMI symptoms better than cardiac troponin and allow for faster decision-making (Kaier et al., 2017). However, there is no widely available commercial test for c-MyC.

4.4 A-type natriuretic peptides (ANP)

The atria and ventricles produce natriuretic peptides, which, when the heart wall is strained, increase renal sodium excretion. These peptides include A-, B-, and C-type natriuretic peptides. When patients have dyspnea and chronic heart failure, ANP concentrations are highly correlated with the diagnosis of acute heart failure (Maisel et al., 2010). ANP concentrations are strong indicators of mortality and dire consequences in patients with stable coronary artery disease, chest discomfort and AMI (Khan et al., 2008; Sabatine et al., 2012; Tzikas et al., 2013).

4.5 B-type natriuretic peptide (BNP)

In cardiovascular research and clinical cardiology, BNP and inert 76-amino acid N-terminal prohormone of brain natriuretic peptide (NT-proBNP) are often utilized. Ventricular cardiomyocytes create BNP, which cleaves into proBNP and a signal peptide. Thereafter, biologically active BNP and NT-proBNP are produced (de Lemos et al., 2003). BNP stimulates natriuresis/diuresis and arterial vasodilatation while inhibiting the action of the renin-angiotensin aldosterone and adrenergic systems (Braunwald, 2008). In individuals without known ventricular dysfunction, natriuretic peptides are strongly linked to the likelihood of incident heart failure and are employed in the diagnosis and prognosis of heart failure patients (deFilippi et al., 2010). NT-proBNP concentrations help determine the prognosis and risk of atrial fibrillation, and they are highly correlated with the risk of CVD and death (Folsom et al., 2013).

4.6 Mid-regional proadrenomedullin

Cardiovascular disease is a condition that causes the release of adrenomedullin, a 52-amino acid natriuretic and vasodilatory peptide. Patients who have heart failure are more likely to have heart failure. Serum concentrations of mid-regional pro-adrenomedullin (MRproADM), a stable precursor to adrenomedullin, are correlated with age, body mass index, current smoking status, renal function, HbA1c, c-reactive protein, and NT-proBNP (Krintus et al., 2018). As a biomarker for targeted cardiovascular risk prediction, it is limited by its specificity and generalizability (Morgenthaler et al., 2005).

4.7 Copeptin

After myocardial damage, copeptin is a prohormone that rises and falls swiftly. It is the only biomarker available for the diagnosis of myocardial infarction other than ST-segment elevation, and when paired with traditional tests, it improves the diagnostic performance of AMI (Roffi et al., 2016). Because of the quick drop, it is most helpful for early presenters. Copeptin levels have been linked to poor outcomes in individuals suffering from sepsis (Struck et al., 2005), AMI (Khan et al., 2007), and heart failure (Voors et al., 2009).

4.8 C-reactive protein (CRP)

An elevated level of the hormone CRP, which the liver produces in response to inflammation, increases the risk of cardiovascular disease. Elevated CRP levels have been linked to peripheral arterial disease, ischemic stroke, AMI, and cardiovascular death. However, compared with indicators specific to the heart, such as NT-proBNP and cardiac troponin, the correlation is less pronounced (Oluleye et al., 2013). High-sensitivity CRP assays have made it possible to perform more sensitive statistical analyses of relationships with cardiovascular disease. Significant reductions in cardiovascular morbidity and death have been observed with immunomodulatory therapy, concomitant with decreases in CRP levels (Ridker et al., 2018). Establishing the causative role of CRP in coronary heart disease was the goal of the C-Reactive Protein Coronary Heart Disease Genetics Collaboration. Genetic variations in CRP did not significantly correlate with clinical outcomes, but a Mendelian randomization meta-analysis conducted in 2011 confirmed a substantial correlation (Wensley et al., 2011).

4.9 Interleukin 6 (IL-6)

In response to infections and injuries, macrophages and T cells release the gene-encoded cytokine IL-6, which

increases cardiovascular risk and has a negative effect on the prognosis of ACS patients (Kaptoge et al., 2014). The incidence of recurrent AMI is greatly decreased by the inhibition of interleukin 1β, an IL-6 inductor (Ridker et al., 2017).

4.10 Growth differentiation factor 15 (GDF-15)

Oxidative stress and inflammation are signaled by cytokine GDF-15 (Böttner et al., 1999). It accumulates with age, obesity, diabetes, and deterioration of kidney function (Farhan et al., 2016). It is expressed in multiple tissues. In both acute and chronic heart injury, GDF-15 upregulation might represent a protective mechanism (Kempf et al., 2006). In the general population, ACS, and heart failure populations, it is a powerful predictor of adverse events, although it has less diagnostic power than cardiac troponins and natriuretic peptides in some patients (Chan et al., 2016). Patients using oral anticoagulant medication may benefit from additional information regarding bleeding risk provided by GDF-15 readings (Hijazi et al., 2017).

4.11 Suppressor of tumorigenicity 2 (ST2)

Two variants of the cardiovascular biomarker ST2 exist: soluble ST2 and transmembrane receptor form ST2 (ST2L). While it offers predictive information for heart failure (Pascual-Figal et al., 2009), AMI (Jenkins et al., 2017), stable coronary artery (Dieplinger et al., 2014), and unselected patients with dyspnea, its diagnostic ability for HF is not as good as that of NTproBNP (Januzzi et al., 2007). Although the 2013 American College of Cardiology Foundation/American Heart Association Guidelines for the Management of Heart Failure support sST2, galectin-3 appears to have better predictive qualities for HF patients (Yancy et al., 2013). Guidelines on circulating biomarkers by the European Heart Federation are still tentative (Ponikowski et al., 2016).

4.12 Galectin-3

The animal lectin galectin-3, which binds to β-galactosides, is involved in angiogenesis, apoptosis, cell-to-cell contact, and macrophage phagocytosis (McCann et al., 2008). It is elevated in both acute and chronic decompensated heart failure (Lok et al., 2013) and linked to early fibrotic and inflammatory alterations in the failing heart (Sharma et al., 2004). The predictive qualities of galectin-3 are especially compelling for heart failure patients with an intact ejection fraction. While not included in European guidelines, it is advised in the 2013 ACCF/AHA Guidelines for the Management of Heart Failure (Yancy et al., 2013). While soluble sST2 may be more helpful in tracking the course of heart failure, galectin-3 may be better at establishing left ventricular remodeling (Wu et al., 2013).

4.13 Soluble CD40 ligands (CD40L)

T-cell CD40L activates CD40, a protein present in antigen-presenting cells, which in turn causes endothelial cell activation, tissue factor synthesis, and the release of inflammatory cytokines. The development and progression of cardiovascular disease are linked, and soluble CD40L concentrations have an impact on treatment outcomes and prognosis in ACS patients. It is also involved in B-cell activation pathways (Lyngbakken et al., 2018).

4.14 P-selectin

In response to inflammatory mediators, platelets and endothelial cells express P-selectin, the greatest cell adhesion molecule. It is linked to poor outcomes in patients with peripheral artery disease and subsequent atherosclerosis and causes an increase in atherosclerotic endothelial cells (Lyngbakken et al., 2018). In women in good health, elevated amounts are linked to cardiovascular mortality, stroke, and AMI.

4.15 Lipoprotein-associated phospholipase A2 (Lp-PLA2)

A hormone involved in phospholipid metabolism in artery walls, Lp-PLA2, is generated by inflammatory cells (Lyngbakken et al., 2018). It has been linked to adverse outcomes in patients with existing coronary artery disease, ischemic stroke, and advanced atherosclerotic disease (Hui, 2012).

4.16 Matrix metalloproteinase-9 (MMP-9)

MMP-9 is a zinc-dependent endopeptidase family that breaks down collagen in the basement membrane and interstitial spaces. It is linked to a greater risk of ischemia and plaque rupture in CVD, which includes incident CAD and ischemic stroke (Jefferis et al., 2010). Its clinical significance, however, relates to the prognosis after coronary artery disease, particularly to the progression of heart failure and the onset of post-AMI ventricular remodeling (Ramos-Fernandez et al., 2011). This theory is supported by experimental research using MMP-9-deficient mice and MMP inhibition in rabbits, which results in less ventricular dilatation after myocardial ischemia (Lindsey et al., 2002).

4.17 Catecholamines

In patients with heart failure, norepinephrine has been investigated as a prognostic biomarker. Increased plasma and urine norepinephrine levels have been shown by Jay et al. (1984) to be predictive of mortality in patients with chronic heart failure. Although less strongly than BNP, norepinephrine concentrations were found to be significantly linked with morbidity and mortality in the Valsartan Heart Failure Trial (Latini et al., 2004). There is a temporal correlation between changes in risk and norepinephrine levels (Anand et al., 2003).

4.18 Granin proteins

The secretion of peptides, hormones, neurotransmitters, and growth factors is dependent on chromogranin-secretogranin (granin) proteins (Bartolomucci et al., 2011). Their large size and high quantity of amino acids define them. The only granin protein that is currently being used clinically as a diagnostic marker for neuroendocrine tumors, specifically pheochromocytoma and multiple endocrine neoplasia, is chromogranin A, the index member of the granin family (Kunz et al., 2013). Because it is costored and released with catecholamines during exocytosis from sympathetic nerve terminals, CgA is thought to reflect neuroendocrine activity during stress (Dimsdale et al., 1992). Research has indicated that patients with chronic heart failure have elevated levels of catecholamines and CgA in terms of heart rate variability. Higher levels of CgA are linked to poorer outcomes in ACS and acute heart failure patients but not in chronic heart failure patients (Røsjø et al., 2010) show in Table 1.

Table 1. Biomarkers associated with cardiovascular diseases and their subtype

Biomarkers	Myocardial infarction	Coronary artery disease	Heart failure	Atrial fibrillation	Ischemic stroke
Myocardial injury					
CT	+	+	+	+	+
hFABP	+	-	+	-	-
c-MyC	+	-	-	-	+
Myocardial stress					
ANP	+	+	+	-	-
BNP	+	+	+	+	+
MRproADM	+	-	+	-	-
Copeptin	+	-	+	-	+
Inflammation					
CRP	+	+	+	+	+
IL-6	+	+	-	-	+
GDF-15	+	-	+	+	-
Galectin-3	-	-	+	-	-
Soluble ST2	+	+	+	-	+
Platelet activation					
P-selectin	+	-	-	-	+
Soluble CD40 ligand	+	-	-	-	+
Plaque instability					
Lp-PLA2	+	-	-	-	+
MMP-9	+	+	+	-	+
Systemic stress					
Granin proteins	+	-	+	-	-
Catecholamines	-	-	+	-	-
Calcium homeostasis					
Secretoneurin	-	-	+	-	-

Note: CT, cardiac troponins; ST 2, suppressor of tumorigenicity 2; CD40, cluster of differentiation 40; hFABP, heart-type fatty acid-binding protein; c-MyC, cardiac myosin binding protein-C; ANP, A-type natriuretic peptide; BNP, B-type natriuretic peptide; MRproADM, mid-regional pro-adrenomedullin; CRP, C-reactive protein; IL-6, interleukin-6; GDF-15, growth differentiation factor 15; Lp-PLA2, lipoprotein-associated phospholipase A2; MMP-9 matrix metalloproteinase-9

4.19 Secretoneurin

A conserved peptide from SgII called secretoneurin is linked to the management of Ca^{2+} in cardiomyocytes. Secretoneurin is a key endogenous regulator of Ca^{2+}/calmodulin-dependent protein kinase II d (CaMKII), a protein implicated in inflammation, cardiac hypertrophy, excitation–contraction coupling, and cell death, according to in vitro research (Anderson et al., 2011). It phosphorylates the Ca^{2+} release channel in cardiomyocytes by directly inhibiting CaMKII. The expression of the secretoneurin gene is increased tenfold in animals suffering from heart failure (Røsjø et al., 2012) and is also elevated in individuals experiencing acute myocardial dysfunction, including sepsis, cardiac arrest, and acute heart failure (Røsjø et al., 2018). Secretoneurin's advantageous effects on myocardial Ca^{2+} handling point to a compensatory mechanism that is comparable to that of natriuretic peptides and natriuresis in heart failure patients (Lyngbakken et al., 2018).

4.20 Other Biomarkers for CVD

Uric acid, a byproduct of purine metabolism, is a significant factor in gout and other cardiovascular diseases (Saito et al., 2021). Mahomed (1879) suggested an association between uric acid and CVD approximately 140 years ago. However, the causality remains uncertain, with the challenge of determining whether elevated uric acid directly contributes to CVD pathophysiology or serves as a marker for increased cardiovascular risk. Despite efforts to elucidate causality, conclusive evidence supporting a direct causal relationship between elevated uric acid and CVD remains elusive (Kleber et al., 2015).

Lactate, a metabolic byproduct, plays a multifaceted role in organ growth, vascular development, and progenitor cell activities (Dong et al., 2022). Its levels serve as prognostic markers in heart failure and are implicated in atrial structural remodeling during atrial fibrillation (Hu et al., 2021).

Lipoproteins and lipids have been linked to atherosclerotic CVD (ASCVD) for more than fifty years (Chait & Eckel, 2016). Recent research has suggested that lipoprotein(a) plays a causal role in the development of CVD, including coronary heart disease, peripheral artery disease, aortic valve stenosis, and possibly ischemic stroke (Langsted et al., 2019). However, further research is needed to confirm causality and evaluate the effectiveness of new therapies aimed at lowering lipoprotein(a) levels.

5. PHARMACOLOGICAL, NONPHARMACOLOGICAL AND DEVICE-BASED THERAPIES

Pharmacotherapy is still considered one of the most essential strategies in the modality of CVD, especially for hypertension, coronary artery disease heart failure and atrial fibrillation. Consequently, new developments have presented improved and specific drugs with side effects. Recent studies have shown that novel mineralocorticoid receptor antagonists (MRAs) play a significant role in CVD. Finerenone is a third-generation nonsteroidal MRA that targets heart failure and chronic kidney disease because its properties are related to a decrease in the level of oxidative stress and improvement in endothelial function. In contrast to earlier MRAs such as spironolactone, finerenone provides a safer profile with a lower risk of hyperkalemia and kidney complications and would benefit the management of CVD (Zhai et al., 2024). Another intervention involves direct oral anticoagulants (DOACs), which have revolutionized the treatment of atrial fibrillation and venous thromboembolism by offering satisfactory anticoagulation with less monitoring than vitamin K antagonists do. Current investigations concerning their use in patients with other diseases, including cancer, have revealed rather complex attitudes toward the control of bleeding and the choice of therapy (Angeli et al., 2024).

Technically integrated interventions such as pulsed field ablation (PFA) for atrial fibrillation (AF) are now being applied in the treatment of chronic cardiovascular diseases, especially in patients who do not respond to drug therapy. PFA is a new nonthermal ablation technique aimed at the treatment of atrial fibrillation. Conventional radiofrequency ablation has been found to be dangerous in many ways because it is known to affect many tissues around cardiac tissue, whereas PFA is more accurate in its search for cardiac tissue in the body. A study performed in Japanese patients demonstrated the effectiveness and safety of PFA and therefore suggested its suitability as a standard for AF therapy (Yamane et al., 2024). Another two nonpharmacological approaches that are currently under study for individuals with resistant hypertension include renal denervation and baroreflex activation therapy. Such strategies are especially effective in patients who remain hypertensive when they are on their best medical treatment plan (Tolu-akinnawo et al., 2021).

Personalized medicine and AI have recently been combined to provide a greater level of risk assessment and individualized treatment in the management of CVD. Several works have focused on AI-based models intended for predicting the prognosis of heart failure. For example, a genetic programming model has been designed for diagnosing patients prone to experiencing further deterioration of heart failure and initiating treatment accordingly (Visco et al., 2024). Recent technological advancements worldwide have led scientists to discover several approaches that have proven fruitful in dealing with cardiovascular diseases. One such advancement is the discovery of factor XI inhibitors used in a novel anticoagulation method, an alternative to the use of anticoagulation drugs currently used in the prevention of thrombosis. These inhibitors present a compelling case for treating and preventing venous thromboembolism and potentially address unmet therapeutic needs in the field of cardiovascular medicine (Santagata et al., 2023). Several minimally invasive approaches exist, such as transcatheter aortic valve replacement. Through this treatment, some patients can avoid open heart surgery by receiving a new heart valve through a catheter in place of their malfunctioning heart valve (van Baal et al., 2019). Improvements in existing strategies, such as coronary artery bypass grafting into robotic-assisted CABG, are being explored to potentially reduce surgical trauma and recovery time (Jonsson et al., 2023).

Medical treatment of cardiovascular disorders typically begins with lipid-lowering medications, most commonly statins. Statins reduce LDL cholesterol and either prevent or slow the development of plaque in arteries. In patients who cannot tolerate statins, or if side effects are intolerable, other classes of medications to lower lipids may be utilized (Chou et al., 2016). Anticoagulants, more colloquially referred to as “blood thinners,” along with antiplatelet medications, are some of the most important medications in the prevention of strokes associated with AF. These medications exert their effects through the inhibition of harmful blood clot formation that could lead to stroke; however, this may concurrently promote bleeding through the prevention of beneficial clot formation (Pundi et al., 2021). Antihypertensive medications represent another cornerstone in the treatment of cardiovascular diseases. For example, medications such as beta-blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors lower blood pressure due to dilation of blood vessels, reducing the workload of the heart.

A wide range of medications exist for the treatment and maintenance of pain or other symptoms emanating from various cardiovascular conditions; selected drug classes, along with their brand names as available on the market, are listed in the Table 2 below, each targeting a particular aspect of cardiovascular disease management.

Table 2. Drugs used for cardiovascular disease

Generic/Brand name(s)	Target	References
1. Sotagliflozin (*Inpefa*)	Sodium/glucose cotransporter 1 and 2	(Bhatt et al., 2021)
2. Dimethyl sulfoxide (*Rimso-50*)	Interleukin-5 receptor subunit alpha, Mucin-16, and Myc proto-oncogene protein	(Huang et al., 2020)
3. Arbutamine	Beta-1,2 and 3 adrenergic receptors	(Ginzton et al., 1996)
4. Bempedoic acid (*Nexletol, Nexlizet*)	ATP-citrate synthase	(Nissen et al., 2023)
5. Perindopril (*Aceon, Coversyl, Prestalia, Viacoram*)	Angiotensin-converting enzyme and Secreted frizzled-related protein 4	(Dinicolantonio et al., 2013)
6. Colchicine (*Colcrys, Gloperba, Lodoco, Mitigare*)	Tubulin beta chain	(Deftereos et al., 2022)
7. Rosuvastatin (*Crestor, Ezallor, Roszet*)	3-hydroxy-3-methylglutaryl-coenzyme A reductase and Integrin alpha-L	(Jin et al., 2020)
8. Vericiguat (*Verquvo*)	Guanylate cyclase soluble subunit beta-1	(Armstrong et al., 2020)
9. Mexiletine	Sodium channel protein type 5 subunit alpha and Aryl hydrocarbon receptor	(Olleik et al., 2023)
10. Guanadrel	Sodium-dependent noradrenaline transporter	(Dunn & Dunlap, 1981)
11. Eprosartan (*Teveten HCT*)	Type-1 angiotensin II receptor	(Cheng-Lai, 2002)
12. Telmisartan (*Actelsar Hct, Micardis, Micardis-hct, Pritor, Twynsta*)	Type-1 angiotensin II receptor and Peroxisome proliferator-activated receptor gamma	(Weber, 2010)
13. Cilazapril (*Inhibace*)	Angiotensin-converting enzyme	(Deget & Brogden, 1991)
14. Torasemide (*Demadex, Soaanz*)	Solute carrier family 12 members 1 and 2	(Manolis et al., 2021)

6. CONCLUSION

In the context of CVD, the future holds promise for significant advancements across various fronts. First, there is an increasing emphasis on personalized medicine, leveraging genomic insights to tailor treatments and preventive strategies to individuals' unique genetic profiles, lifestyle factors, and risk profiles. Additionally, emerging technologies such as AI and machine learning are revolutionizing CVD diagnosis and management, offering more accurate risk prediction models, early detection of disease, and precise treatment recommendations. Furthermore, there is growing recognition of the importance of holistic approaches to CVD management, integrating lifestyle modifications, such as diet, exercise, stress management, and social support, alongside pharmacological and interventional therapies. Moreover, ongoing research into novel biomarkers, genetic markers, and therapeutic targets discussed in this study promises to uncover new avenues for early detection, risk stratification, and targeted treatments for CVD. Finally, concerted efforts in public health initiatives, education, and policy interventions are crucial for addressing the social determinants of health, reducing health disparities, and promoting cardiovascular wellness across populations; thus, these efforts are recommended.

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