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Recent overview: Recent medications use for cardiovascular disorder

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Abstract
The Cardiovascular diseases (CVDs) continue to be a leading global health challenge, requiring innovative pharmacological strategies for effective management. Recent advancements in medication use for CVD focus on integrating novel therapeutic agents, refining guideline-directed medical therapy (GDMT), and addressing treatment disparities. The Recent approval of Semaglutide for weight management in cardiovascular patients highlights the importance of obesity control in reducing cardiovascular risks. Innovations such as sodium-glucose co-transporter 2 (SGLT2) inhibitors and angiotensin receptor-neprilysin inhibitors (ARNIs) have redefined heart failure management, improving morbidity and mortality outcomes. Despite these advances, gaps in care persist, particularly in the under treatment of women with coronary artery disease and the inappropriate use of Aspirin for primary prevention in older adults. Comprehensive pharmacotherapy now emphasizes tailored combinations of antiplatelet agents, anticoagulants, statins, and blood pressure-lowering medications. Emerging therapies, including chelation therapy, hold potential but require further validation.
This overview article provide a comprehensive overview of cardiovascular disorder, encompassing its structure, Risk Factors, Physiology, Types, Causes, Medication. It also give insight into medicines and treatment used for treatment of cardiovascular disorder, exploring classes of drugs which are used to treat the cardiovascular disorder, their targets, agents, mechanisms of action, and notable side effects.

Keywords: Cardiovascular disease, pharmacotherapy, heart failure, sodium-glucose co-transporter 2 inhibitors, angiotensin receptor-neprilysin inhibitors, Semaglutide, chelation therapy, Aspirin, obesity management, personalized treatment.

Introduction

The World Health Organization predicts that by 2015, over 700 million adults would be obese and almost 2.3 billion adults will be overweight. With over 68 percent of the population being overweight or obese, the United States (US) is currently the largest single market for weight loss medications. The UK and other European nations follow. More than 9 million children and teenagers are obese in the United States alone. Furthermore, the number of fat people in China, Russia, India, and Brazil may soon start to overtake that of Western nations. [1]

Throughout the 20th century, people's lifestyles have drastically changed all across the world. These changes, which are commonly referred to as the epidemiological shift, are the result of several scientific and technological advancements that today impact every aspect of human life. Fast food and sedentary lifestyles have replaced agrarian diets and active lifestyles in the majority of human societies. These changes, together with rising tobacco use, have contributed to the epidemic of cardiovascular diseases (CVD), diabetes, obesity, hypertension, and dyslipidemia. Due to a protracted period of epidemiological shift, the burden of CVD increased over several decades in developed countries. In India, epidemiological changes have occurred over a considerably shorter period of time, possibly due to the country's rapid economic development. Consequently, coronary heart disease (CHD) strikes Indians at least five to six years earlier than it does in the West, and cardiovascular disease has become the country's top cause of death.

According to current estimates from several cross-sectional research, the prevalence of CHD in India is between 2 and 7 percent in rural areas and 7 to 13 percent in urban areas. Numerous studies conducted throughout India have shown that the rates of modifiable risk factors for CHD are rising at an exponential rate across both rural and urban segments of our population. Additionally, the incidence of risk factors including diabetes and obesity has increased as a result of migration and urbanization. In 2005 alone, the predicted economic impact of these changes was 9 billion dollars in national income from premature deaths from diabetes, heart disease, and stroke; by 2015, that amount is expected to rise to 237 billion dollars. The percentage of households that paid for their own medical care went from 31.6% in 1995 to 47.3% in 2004. According to modeling research, the GDP would have increased by 4–10% annually if non-communicable diseases (NCDs) had been totally eradicated. The CHD epidemic's causes and management approaches are multifaceted, intricate, and interconnected. We now know that modifiable risk factors that can be decreased with easy measures are what drive the rise in CHD and its risk factors in a variety of contexts. In order to increase secondary prevention, the majority of these preventive techniques fall under the purview of policy, health system intervention, health promotion, and basic quality improvement initiatives. [2]

In India, non-communicable diseases, such as type 2 diabetes and coronary heart disease, are on the rise and account for around 5.8 million deaths annually. Nutrition and changes in lifestyle are the main causes of the increase in NCDs in India. Additionally, Asian Indians have a higher metabolic and cardiovascular risk due to their lower lean mass and higher body fat, stomach fat, liver fat, and pancreas fat compared to white people. Crucially, Asian Indians are more likely than white people to go from pre-diabetes to diabetes more quickly, and they have a harder time returning to normal glucose regulation with the right lifestyle choices. Numerous individuals with diabetes and its consequences raise morbidity and mortality rates and present a significant financial burden. Reducing the fast growing NCD juggernaut in India is challenging, but not impossible. The only things that could help overcome this increasingly challenging obstacle are coordinated efforts from several stakeholders, continuously honest efforts, fiercely focused attention from health officials, and evident political will. Last but not least, all management and preventative strategies ought to be economical, realistic, and targeted at children and disadvantaged groups. [3]

The primary source of disease burden and mortality worldwide is cardiovascular disease. Concerned by the growing prevalence of non-communicable diseases and the higher rates of disease severity and case-fatality in low- and middle-income nations relative to high-income nations, the UN recognized in 2012 that one of the main risks to 21st-century sustainable development was the growing burden of NCDs. In 2013, WHO created targets for NCD prevention and control, including a 25% relative decrease in the overall mortality rate from cardiovascular diseases, a 25% relative decrease in the prevalence of high blood pressure, a halt to the rise in diabetes and obesity, and a guarantee that by 2025, at least 50% of patients with cardiovascular diseases have access to appropriate medications and medical advice. By 2030, the sustainable development goals aim to reduce premature deaths from NCDs to one-third of all premature deaths, highlighting the necessity of multi sectoral national policies to support NCD burden prevention and control. In addition to screening and treating 80% of hypertension patients by 2025, the National Health Policy 2017 of India seeks to minimize 25% of premature deaths from cardiovascular illnesses, which account for a significant portion of NCDs. [4]

Physiology of Heart

The body's blood supply is provided by the cardiovascular system. The speed and volume of blood flowing through the veins can be controlled by reacting to different stimuli. The heart, arteries, veins, and capillaries make up the cardiovascular system. All bodily parts receive enough blood flow thanks to the complex interactions between the heart and arteries. Numerous stimuli, such as shifting blood volume, hormones, electrolytes, osmolarity, drugs, the kidneys, the adrenal glands, and much more, control the cardiovascular system. The cardiovascular system is also heavily regulated by the parasympathetic and sympathetic nervous systems.

The organ responsible for pumping blood through the vessels is the heart. It circulates blood straight into arteries, either the pulmonary or aortic arteries. Because they regulate the volume of blood flow to particular body parts, blood arteries are essential. Veins, capillaries, and arteries are examples of blood vessels. Arteries can split into large and tiny arteries and transport blood out from the heart. Because they are thicker and more elastic to withstand the high pressures, large arteries receive the highest blood flow pressure. More smooth muscle, found in smaller arteries like arterioles, contracts and relaxes to control blood flow to particular body parts. Because arterioles have lower blood pressure, they don't require as much elasticity. Since arterioles are more stiff than bigger arteries, they are responsible for the majority of the resistance in the pulmonary circulation. In addition, the capillaries are a single-cell layer that emerges from arterioles. This thin layer interacts with tissues and organs to exchange waste, gasses, and nutrients. Additionally, blood is returned to the heart via the veins. They have valves to stop blood from flowing backward.

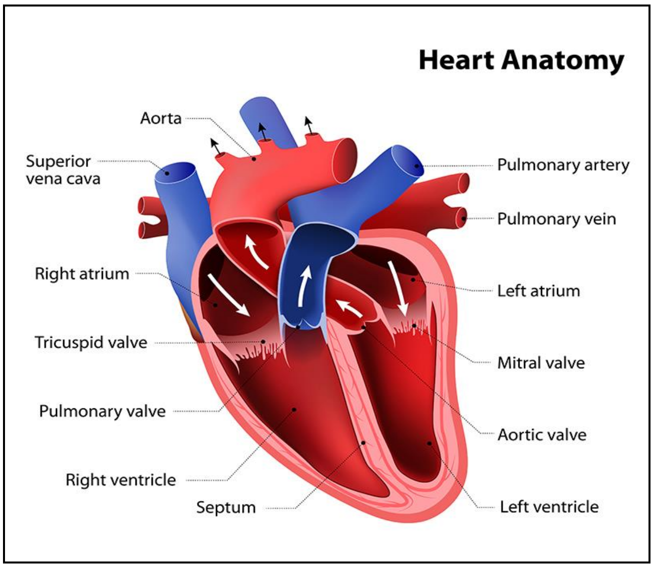

Fig 1: Diagram of Heart

The Cardiac Cycle

The flow of blood through the heart is described by the cardiac cycle. The order it operates in is as follows: Constriction of the atrium Mitral valve closure

1. Phase of Isovolumetry
2. The aortic valve opening
3. Phase of ejection (rapid and decreased ejection), left ventricular emptying
4. The aortic valve closing
5. Relaxation isovolumetric
6. When the mitral valve opens
7. The left ventricle's filling phase (rapid and reduced filling) [5]

Risk Factors of Cardiovascular Disease

1. Hypertension

Two significant risk factors for the occurrence and development of heart failure are hypertension and coronary heart disease. In the general population, these two risk factors often coexist and have additive and synergistic effects that encourage heart failure and left ventricular re-modeling. Depending on age, gender, and ethnicity, these two risk variables may contribute differently to the burden of heart failure in the population. Generally speaking, it is improper to attribute heart failure in the general population to just one of these two risk factors. In the twenty-first century, preventing heart failure requires preventing coronary disease and hypertension. [6]

2. Diabetes

The type 2 diabetes mellitus (T2DM), the most common form of the risk factor for diabetes, has a unique correlation with coronary heart disease. Persons with diabetes are two to four times more likely to develop coronary heart disease than persons without the condition, and 65 to 75 percent of deaths in diabetics are caused by CVD. But more importantly, it was discovered that diabetes patients without coronary artery disease had the same age- and sex-adjusted mortality risk as non-diabetic people who had previously experienced myocardial infarction (MI). The mechanism of thrombogenesis is thought to be based on insulin resistance, visceral obesity, and excess inflammation, as a result of these striking findings about increased mortality risk, which have raised suspicion that common antecedents predispose to diabetes and CHD. [7]

3. Hyperlipidemia

One of the main risk factors for cardiovascular diseases (CVDs) is thought to be hyperlipidemia. One third of all fatalities worldwide are attributed to CVDs, and by 2020, it is predicted that CVDs would overtake all other causes of mortality and disability globally. Increases in one or more plasma lipids, such as triglycerides, cholesterol, cholesterol esters, and phospholipids, as well as plasma lipoproteins, such as very low-density lipoprotein and low-density lipoprotein, and decreased levels of high density lipoprotein, are referred to as hyperlipidemia. The primary cause of atherosclerosis, which is closely linked to ischemic heart disease (IHD), is hypercholesterolemia and hypertriglyceridemia. The high mortality rate and IHD are strongly correlated. Furthermore, about four million fatalities annually are attributed to increased plasma cholesterol levels. [8]

4. Smoking

The largest avoidable cause of cardiovascular disease and death is cigarette smoking. Smoking has been linked to an increased risk of sudden death, a coronary heart disease excess mortality rate of over 70%, and a two to fourfold increased risk of coronary heart disease. These risks are increased when diabetes, hypertension, hypercholesterolemia, and glucose intolerance are present. These condition all work in concert with smoking. It is also commonly known that smoking increases the risk of peripheral vascular disease. [9]

5. Obesity

One of the most often mentioned risk factors for coronary heart disease is obesity. This argument is often supported by epidemiologic studies, especially those that concentrate on patients with central obesity. However, these studies lack precision and are susceptible to bias in misclassification. Except in cases of abdominal obesity, angiograms and post mortem examinations have shown minimal to no association between total fat mass and coronary atherosclerosis. Obesity, especially central obesity, is strongly linked to conventional risk factors for coronary heart disease, including dyslipidemia, type II diabetes, and hypertension. Obesity may also be linked to a number of non-traditional risk factors, including higher Lp(a) levels, hyperhomocystinemia, and thrombogenesis-promoting variables. Additionally, obesity may change endothelial function. [10]

6. Physical Inactivity

Numerous illnesses, including type 2 diabetes, osteoporosis, obesity, cardiovascular disease, respiratory disorders, colon cancer, and breast cancer, can be adversely affected by physical inactivity. According to recent polls, the proportion of sedentary people in Italy fell below 39% in 2010 compared to the previous year, while the age range of 6 to 10 years old saw a 3% rise in physical activity in 2009. By encouraging calorie balance, helping to reduce overweight, improving cardiovascular system efficiency, and fostering a sense of psychological well-being, this will enable future generations to protect their health through consistent physical activity. [11]

7. Diet and Nutrition

With CVD epidemics spreading over many parts of the world that are going through a rapid health transition, cardiovascular diseases are becoming a larger contributor to the global disease burden. In addition to being associated with other cardiovascular risk factors like diabetes, high blood pressure, and obesity, diet and nutrition have been thoroughly studied as risk factors for major cardiovascular disorders like coronary heart disease (CHD) and stroke. A rigorous evaluation of methodological concerns pertaining to exposure measurement, outcome variable nature, research design types, and the meticulous separation of cause, consequence, and confounding as the foundation for observed connections must be part of the evidence interpretation process. There is sufficient data from research done both within and between populations to associate a number of nutrients, minerals, food groups, and dietary patterns with a higher or lower risk of cardiovascular disease. Trans fats and saturated fats are dietary lipids linked to a higher risk of coronary heart disease, whereas polyunsaturated fats are known to offer protection. While dietary potassium reduces the risk of hypertension and stroke, dietary sodium is linked to an increase in blood pressure. Consuming fruits and vegetables on a regular basis helps prevent stroke, coronary heart disease, and hypertension. [12]

Diagnosis

1. Electrocardiogram (ECG)

Measures the heart's electrical activity to diagnose arrhythmias, coronary artery disease, and cardiac chamber enlargement. The noninvasive technique for identifying different arrhythmias is the electrocardiogram (ECG). Because deadly arrhythmias can result in abrupt cardiac death, it is critical to identify and diagnose them as soon as possible. Atrial fibrillation and other arrhythmias raise the risk of stroke and thromboembolic events. Millions of cardiac cells' depolarization potentials add up to produce an ECG. The ECG wave can be used to diagnose the heart abnormalities. However, a physician utilizing a manual method will find it difficult to consistently and precisely detect its amplitude and frequency components. Therefore, ECG screening with computer-aided diagnosis will greatly aid doctors in managing cardiovascular illnesses. Even for a skilled cardiologist, visually inspecting an ECG analysis takes a lot of time and effort. According to reports, using computer software to diagnose the ECG classes is both economical and greatly enhances both patient recovery and diagnostic accuracy. [13]

2. Echocardiography

It uses sound waves to evaluate heart structure and function, diagnosing conditions like heart failure, valvular disease, and cardiomyopathy. For the assessment of cardiac anatomy and hemodynamics in a variety of cardiac conditions, echocardiography is regarded as a crucial test. The test's special qualities make it ideal for repeated patient screening and monitoring during cardiotoxic treatment and pregnancy. Stress echocardiography, as opposed to exercise ECGs, has diagnostic accuracy and prognostic potential comparable to that of male coronary artery disease patients. However, more imaging data about the patient's myocardial perfusion status could be required in individuals who have chest discomfort but do not have considerable coronary stenosis. This data could comprise deformation imaging of the multilayer left ventricular wall motion, myocardial contrast echocardiography for assessing myocardial perfusion, or Doppler imaging for measuring coronary flow velocity. [14]

3. Stress Testing

Evaluates heart function during physical activity, diagnosing coronary artery disease and cardiac arrhythmias. Acute cardiac events and the long-term development of coronary heart disease are two stages of cardiovascular disease that are influenced by psychological stress. Short-term psychological stress is likely to cause acute myocardial infarction through disruptions of inflammatory, hemostatic, and autonomic processes. According to prospective observational studies, there is a 40–50% rise in the incidence of coronary heart disease when people experience chronic stress at work and in their personal lives. Patients with established coronary heart disease have a worse prognosis when they exhibit signs of increased long-term stress, such as social isolation and stress at work. [15]

4. Cardiovascular Magnetic Resonance

It uses magnetic fields and radio waves to evaluate heart structure and function, diagnosing conditions like cardiomyopathy and cardiac tumors. A crucial imaging method for cardiac phenotyping with a significant clinical use is cardiovascular magnetic resonance imaging (CMR). Although it can evaluate scar load, other myocardial tissue properties, and advanced elements of cardiac shape and function, new information is now derivable. [16]

Perfusion imaging and stress-induced wall motion abnormalities imaging are the two primary approaches used in stress cardiac MRI, which has recently become a noninvasive method for the identification of CAD. [17]

5. Biomarkers

An imaging test (echocardiogram or CT scan), a recording taken from a human (blood pressure, ECG, or Holter), or a biosample (blood, urine, or tissue test) can all be used to measure a biomarker. The degree or kind of exposure to an environmental element, genetic predisposition, genetic reactions to exposures, markers of subclinical or clinical disease, or indicators of response to treatment are just a few of the health or disease characteristics that biomarkers might reveal. Thus, biomarkers can be thought of simply as indicators of illness state (preclinical or clinical), disease feature (risk factor or risk marker), or disease rate (progression).

Thus, biomarkers can be categorized as prognostic (predicting future disease course, including recurrence and response to therapy, and monitoring efficacy of therapy), diagnostic (recognizing overt disease), staging (classifying disease severity), screening (screening for subclinical disease), or antecedent (identifying the risk of developing an illness). [18]

Types of Cardiovascular Disease

1. Coronary Artery Disease

One of the main cardiovascular conditions impacting people worldwide is coronary artery disease (CAD). It has been established that this illness is the leading cause of death in both developed and developing nations. Risk factors for the development of cardiovascular disease include genetic, environmental, and lifestyle variables. The likelihood that CAD may develop in the near future is explained by the presence of risk factors in healthy people. According to genome-wide association studies, chromosome 9p21.3 may be linked to the early development of CAD. Diabetes mellitus, hypertension, smoking, obesity, hyperlipidemia, homocystinuria, and psychological stress are risk factors for coronary artery disease (CAD). Extensive research and experiments have established the management and eradication of CAD. Among the few medications used to treat CAD-related symptomatic angina are antiplatelet medicines, nitrates, β-blockers, calcium antagonists, and Ranolazine. [19]

2. Heart Failure

The pathophysiologic condition known as heart failure occu rs when the heart is unable to pump blood at a rate that is ap propriate for the needs of the tissues that are metabolizing it due to an anomaly in cardiac function.Heart failure is an abn ormal condition where the heart's inability to pump blood at a rate appropriate for systemic metabolic needs is mostly ca used by disrupted cardiac performance.Pulmonary congestio n and peripheral hypoperfusion are the two main categories of clinical symptoms that best characterize heart failure in pr actice.Insufficient cardiac output is known as cardiac failure ; that is, aberrant myocardial function (such as an abnormal i ncrease in ventricular filling pressure and/or enddiastolic ve ntricular volume) may exist during rest or exercise despite n ormal cardiac output.[20]

Medications for Cardiovascular Disorders

A. Hypertension

1. Angiotensin-Receptor Neprilysin Inhibitors (ARNIs)

Sacubitril/Valsartan (Entresto) has been shown to reduce mortality and hospitalization in patients with heart failure. The first of a brand-new class of medications known as angiotensin receptor–neprilysin inhibitors is Valsartan/Sacubitril. Since ARBs are not enzyme inhibitors, the class name is misleading. Angiotensin receptor antagonist/neprilysin inhibitors might be a more appropriate term for the class. Two pathophysiological pathways behind heart failure were addressed by the development of the combination angiotensin receptor antagonist/neprilysin inhibitor: reduced sensitivity to natriuretic peptides and activation of the renin-angiotensin-aldosterone system (RAAS).

Reduced natriuretic peptide degradation has been ascribed to the positive effects of neprilysin inhibition. Natriuretic peptides stimulate particulate guanylate cyclase to generate cGMP, which results in vasodilation. Valsartan/sacubitril treatment in heart failure raised brain natriuretic peptide (BNP) while decreasing N-terminal pro-brain natriuretic peptide (NT-proBNP), which suggests that BNP breakdown was reduced indirectly. Furthermore, cGMP increased significantly at all valsartan/sacubitril doses when compared to baseline in a dose-escalation trial conducted on healthy volunteers. By attaching to the natriuretic peptide receptor C and being broken down by neprilysin, natriuretic peptides are removed from the bloodstream. Compared to BNP7, neprilysin is more receptive to atrial natriuretic peptide (ANP) and C-type natriuretic peptide. [21]

2. Direct Renin Inhibitors

Aliskiren (Tekturna) has been used in combination with other antihypertensive agents to achieve better blood pressure control. Researchers determined that the best pharmacologic strategy for blocking the renin–angiotensin pathway was renin inhibition fifty years ago. The rate-limiting step in the production of angiotensin II is catalyzed by the monospecific enzyme renin. Renin and pro-renin bind to the (pro) renin receptor, resulting in increased enzymatic activity and other physiological effects. The creation of renin inhibitors with therapeutic efficacy was elusive until recently. Aliskiren, a strong, low-molecular-weight, nonpeptide, direct renin inhibitor with adequate bioavailability to cause long-lasting inhibition of plasma renin activity following oral treatment, was developed using molecular modeling.

Up to a dose of around 300 mg once day, aliskiren reduces blood pressure (BP) in individuals with hypertension in a dose-dependent manner and controls blood pressure for 24 hours; at these levels, aliskiren exhibits tolerability comparable to that of a placebo. Its antihypertensive effectiveness is comparable to that of diuretics, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers. Following a sudden stop, there is a sustained suppression of plasma renin activity and a persistent drop in blood pressure. Combined with diuretics, a totally additive drop in blood pressure is observed. Aliskiren significantly lowers blood pressure when taken with an angiotensin receptor blocker, indicating complementary pharmacology and more thorough renin-angiotensin system inhibition. Long-term end point trials are planned, and clinical trials are now being conducted to evaluate the impact of aliskiren in combination with an angiotensin receptor blocker on intermediate markers of end organ damage. The role of aliskiren and renin inhibition in the management of hypertension and associated cardiovascular diseases will ultimately be determined by the findings of these investigations. Investigations into aliskiren's impact on receptor-bound renin and pro-renin are ongoing. [22]

3. Calcium Channel Blockers

Amlodipine (Norvasc) and other CCBs remain a cornerstone in the treatment of hypertension. Among the most often recommended medications for the treatment of essential hypertension are calcium channel blockers (CCBs), which include both non-dihydropyridines (Verapamil and Diltiazem) and dihydropyridines (Nifedipine and Amlodipine). According to a number of extensive meta-analyses and large outcome risk trials, CCBs lower the cardiovascular morbidity and mortality linked to uncontrolled hypertension, including stroke. However, when it comes to preventing myocardial infarction and heart failure, CCBs seem to be less effective than diuretics and angiotensin-converting enzyme inhibitors. In guidelines for managing hypertension, CCBs are one of the medications mentioned as possible first-line treatments, either by themselves or in conjunction with other medications.

Additionally, CCBs can be used as an adjuvant therapy in conjunction with angiotensin-converting enzyme inhibitors, angiotensin-II receptor blockers, and diuretics. Patients with isolated systolic hypertension (dihydropyridine), angina pectoris (non-dihydropyridine), or concomitant Raynaud's disease may be partially eligible for CCBs. Although they are not yet available in the US, the more recent inherently long-acting dihydropyridine medications (such as lacidipine and lercanidipine) seem to be just as effective as the more established members of the dihydropyridine class. However, they may have a better tolerability profile, particularly when it comes to peripheral edema. Among the most often recommended medications for the treatment of hypertension, calcium channel blockers (CCBs) have been in use for over 25 years. Although their effectiveness is well-established, over the past ten years, there has been discussion regarding these drugs' safety as well as their impact on cardiovascular (CV) and non-CV morbidity and mortality. The effect of CCBs on CV morbidity and mortality in hypertensive patients has been further clarified by the publication of numerous large outcome studies and thorough meta-analyses in recent years. The most recent national and international guidelines for the management of hypertension have taken these findings into consideration. [23]

B. Dyslipidemia

Endothelial damage is a consequence of dyslipidemia, a powerful predictor of cardiovascular disease. The lack of physiological vasomotor activity that follows endothelial damage might show up as elevated blood pressure (BP). Thus, endothelial dysfunction brought on by conditions like dyslipidemia may result in hypertension. A correlation between aberrant lipids and hypertension has been proposed by cross-sectional studies. A few research have looked at the relationship between plasma lipids and the development of hypertension in the future. They have found that there is a connection between the two. Lipid reduction's impact on blood pressure has been examined in small studies. We can better understand the relationship with the help of more prospective data on the relationship between lipids and hypertension. Therefore, in order to determine if total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C are linked to the risk of hypertension in men who were initially free of it, we conducted a prospective study. [24]

1. Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors

Alirocumab (Praluent) and evolocumab (Repatha) have been shown to significantly reduce LDL cholesterol levels. A serine protease called Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) is involved in maintaining cholesterol homeostasis. Serum LDL clearance is decreased when PCSK9 binds to the complex low-density lipoprotein (LDL) receptor and causes its intracellular breakdown. Although the liver is the primary organ that secretes PCSK9, other tissues also express it to a lower degree. In addition to its widely recognized role in the hepatic LDL receptor-mediated pathway, PCSK9 has been suggested to have the ability to disrupt vascular inflammation in atherogenesis. It has been shown that vascular smooth muscle cells, particularly in an inflammatory milieu, generate more PCSK9 than endothelial cells. Higher shear stress progressively decreased PCSK9 expression in SMCs, whereas low shear stress regions increased PCSK9 expression.

Additionally, an interaction between reactive oxygen species and PCSK9 has been reported. It has been demonstrated that oxidized LDL increases PCKS9 expression by affecting the release of IL-1α, IL-6, and tumor necrosis factor-α in a dose-dependent manner. Following the discovery of gene loss-of-function mutations and the absence of detectable quantities of circulating protein, PCSK9 has gained a lot of attention as a promising target for treatments aimed at decreasing cholesterol. To counteract the effects of intracellular and circulating PCSK9, various tactics have been used. The most promising strategy is to use monoclonal antibodies, of which alirocumab and evolocumab have been licensed for clinical usage in patients with familial hypercholesterolemia and have shown good outcomes. Future research on the "pleiotropic" effects of PCSK9 inhibitors may reveal therapeutic potential for cardiovascular outcomes apart from their ability to decrease cholesterol. [25]

Cholesteryl Ester Transfer Protein (CETP) Inhibitors
Anacetrapib (Kynamro) has been used to raise HDL cholesterol and lower LDL cholesterol. Patients with dyslipidemia still have a residual cardiovascular risk even after taking statins to reduce low-density lipoprotein cholesterol, especially if their high-density lipoprotein (HDL) levels are low. One of the main causes of low HDL cholesterol is increased activity of the cholesteryl ester transfer protein (CETP). In individuals already on statin medication, CETP inhibition with anacetrapib, evacetrapib, and dalcetrapib results in plasma HDL increases of roughly 140%, 80%, and 30%, respectively. Recent studies question whether increasing HDL cholesterol is advantageous in and of itself unless it improves HDL's anti-atherogenic qualities, which include removing cholesterol from artery walls, promoting the synthesis of endothelial nitric oxide, or providing protection from oxidation and inflammation.

The processes by which CETP inhibitors work are showing potentially significant differences, which could result in variations in their anti-atherogenicity that are unrelated to the HDL-cholesterol alterations they cause. Therefore, the processes by which CETP inhibitors inhibit CETP may influence the results of clinical trials involving them. [26]

C. Heart Failure
Fatigue, shortness of breath, and congestion are all part of heart failure, a combination of symptoms linked to insufficient tissue perfusion during exertion and frequently fluid retention. The heart's inability to adequately fill or drain the left ventricle is its main cause. [27]

1. Angiotensin-Converting Enzyme (ACE) Inhibitors
Enalapril (Vasotec) and other ACE inhibitors remain a mainstay in the treatment of heart failure. In patients with CHF receiving approved dosages of ACE inhibitors, angiotensin (Ang) II type 1 receptor (AT1) blocking (ARB) improves hemodynamic parameters and functional ability. Despite ACE inhibitor medication, the additional advantages of ARB point to ongoing Ang II production. Despite ACE suppression, Ang II production may persist due to a number of reasons. In cases where the renin-angiotensin system (RAS) is significantly active, recommended dosages of ACE inhibitors may cause inadequate ACE suppression. Alternatively, Ang II production may be facilitated by enzymatic mechanisms other than ACE. Determining the degree of ACE inhibition attained by the highest prescribed dosages of ACE inhibitors was the goal of the current investigation. The pressor response to increasing dosages of Ang I was used to measure the degree of ACE inhibition.

The conversion of Ang I to Ang II determines the pressor's reaction to Ang I. Only circulating and endothelium-bound ACE can promote conversion to Ang II in the intravascular area. ACE activity in the arterial lumen and, thus, the degree of inhibition attained by ACE inhibitors are reflected in the pressor response to Ang I. As a result, 42 individuals receiving maximally indicated doses of ACE inhibitors for durations varying from 3 to 120 months had their pressor response to Ang I evaluated. The pressor response to Ang I was assessed both before and after the administration of an ARB (Valsartan) in order to evaluate the full inhibition of ACE. Following treatment with twice the maximum prescribed dosages of ACE inhibitors, the pressor response to Ang I was also assessed in 11 patients. [28]

2. Beta Blockers
Slow the heart rate and reduce blood pressure. One of the most significant developments in clinical medicine throughout the 20th century was the introduction of beta-blockers for the treatment of cardiovascular disorders. Because beta-blockers have a negative inotropic effect, they were long thought to be contraindicated in individuals with chronic heart failure. The possible use of beta-blockers in the management of chronic heart failure has drawn attention due to mounting evidence of neurohormonal activation in heart failure patients. Beta-blockers have been demonstrated to have positive effects on mortality and morbidity in heart failure patients with reduced systolic function in a number of major randomized placebo-controlled clinical trials. It's unclear if people with maintained left ventricular systolic function will benefit from it.

One of the many ways beta-blockers help people with chronic heart failure is by lowering their heart rate. This article discusses heart rate as a therapeutic goal in individuals with chronic heart failure and presents findings from significant clinical trials looking at beta-blocker medication in these patients. [29]

3. Diuretics
Remove excess fluid from the body, reducing swelling. During an inpatient stay, diuretic resistance (DR), which can range in relative severity, exacerbates acute heart failure (AHF). This review highlights the existing literature on the predictive significance of diuretic efficiency and predictors of natriuretic response in AHF and provides an overview of the mechanisms of DR with an emphasis on loop diuretics. Although the causes of DR in AHF are poorly understood, the pharmacokinetics of diuretics are compromised in chronic heart failure. Within-dose DR may develop, and nearly all diuresis following a loop diuretic dose takes place in the initial hours following administration.

According to recent research, nephron-level DR might be more significant than issues with the tubule's ability to receive diuretics. Urine sodium (UNa) content may be a direct, physiological, and functional indicator of diuretic responsiveness to a specific loop diuretic dosage since loop diuretics promote natriuresis. [30]

Abbreviations

GDMT - Guideline Directed Medical Therapy
SGLT2 - Sodium Glucose Co-Transporter 2 Inhibitors
NCDs - Non Communicable Diseases
CVD - Cardiovascular Disease
T2DM - Type 2 Diabetes Mellitus
CHD - Coronary Heart Disease
CMR - Magnetic Resonance Imaging
ECG - Electrocardiogram
ARNIs - Angiotensin Receptor Neprilysin Inhibitors
IHD - Ischemic Heart Disease
CCBs - Calcium Channel Blockers
RAAS - Renin Angiotensin Aldosterone System
CV - Cardiovascular
PCSK9 - Proprotein Convertase Subtilisin/Kexin Type 9
TC - Total Cholesterol
HDLC - High Density Lipoprotein Cholesterol
RAS - Renin Angiotensin System
DR - Diuretic Resistance
AHF - Acute Heart Failure
UNa - Urine Sodium

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Conclusion

In conclusion, this article provide a comprehensive overview of cardiovascular disorder, encompassing its structure, risk factors, physiology, types, causes, medication. It also give insight into medicines and treatment used for treatment of cardiovascular disorder, exploring classes of drugs which are used to treat the cardiovascular disorder, their targets, agents, mechanisms of action, and notable side effects. Additionally, it focuses on the current therapies and treatment options, including drug & its dosage forms along with its route of administration. Furthermore, it explores the innovative realm of drug delivery methods. Incorporating novel drug delivery systems for enhanced medical intervention. Recent advancements in cardiovascular pharmacotherapy have significantly improved patient outcomes, with novel medications and refined treatment guidelines playing a pivotal role. The integration of therapies such as SGLT2 inhibitors, ARNIs, and Semaglutide demonstrates the evolving approach to managing cardiovascular diseases, addressing not only heart-specific conditions but also associated factors like obesity and diabetes. However, challenges persist, including disparities in treatment access, particularly among women, and the inappropriate use of certain medications like aspirin in older adults.

Conflict of Interest

All Authors declared that there is no conflict of interest.

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