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CARDIOVASCULAR DISEASES: TRADITIONAL AND NON-TRADITIONAL RISK FACTORS

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Abstract:
Cardiovascular disease, also known as CVD, is the most common cause of mortality worldwide. The heart's arteries, blood vessels, and heart muscles become susceptible in the majority of CVD cases. The study focuses on the role which hypertension, as well as varying dense triglyceride and cholesterol levels, play in the onset and progression of cardiovascular disease. This review includes covers potential biomarkers such as homocysteine, fibrinogen, plex, the cytokines, and serum amyloid, along with the prognostic effects of thrombin/anti-thrombin III.
KEY WORDS: Cardiovascular disease, Diabetes, Fibrinogen, HDL, LDL

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INTRODUCTION:

Cardiovascular diseases (CVD) which mainly include coronary heart disease (CHD), stroke, rheumatic heart disease (RHD) and cardiomyopathy comprise the largest cause of death worldwide[1].When the 20th century began, less than 10% of deaths globally were attributable to cardiovascular disease (CVD); by 2001, that number had risen to 30%.Countries like low and middle-income have 80% deaths due to CVD . The annual death rate from CVD is approximately 9%[2]. Cardiovascular diseases (CVD) comprise a broad spectrum of ailments, including those affecting the vascular and cardiac muscles. Diabetes, high low-density lipoprotein cholesterol, smoking, hypertension, physical inactivity, and a number of linked metabolic risk factors are potential risk factors for CVD[3].Framingham Heart Study in 1961 was the first to present the idea of risk factors which relates the existence of elevated cholesterol, tobacco smoking, hypertension and diabetes mellitus to future CVD[4].The majority of CVDs are brought on by both infections and atherosclerosis.

TRADITIONAL RISK FACTORS

Even though early research identified high blood pressure, diabetes, and high cholesterol as conventional CVD risk factors, quite a few of researchers had stated their absence in a large portion of people suffering from clinical vascular events. In fact, nearly 50% of those with their first clinical vascular events don't follow the standardCVD risk factors[5]. But these results might not be applicable to any demographic, researchers from the according to FHS, 50% of the CHD patients had total cholesterol (TC) values of less than 240 mg/dl and 20% TC was less than 200 mg/dl[6].

Based on data from the Women's Health Study (WHS), 45% of coronary events occur in women with normal LDL cholesterol levels (<130 mg/dl), and 75% occur in 27,939 women without high LDL cholesterol levels (<160 mg/dl)[7]. As may be expected, when several big studies on CVD were reviewed, the majority of participants had one or more conventional risk factors[8]. On the other hand, a fifth lacked any of the conventional risk factors. In addition, the prevalence of traditional cardiovascular risk factors were similarly slightly elevated among the cohort participants who did not experience CHD[9]. Considering these results, recent research have concentrated on methods of improving our capacity to forecast CVD. Still, Many of these are most commonly utilised and show promise in standard medical procedures.

Cardiovascular disease and Hypertension

In the Joint National Committee's Sixth Report, the Prevention, identification, assessment, and management categorical in High Blood Pressure (1997) hypertension defined as a systolic blood pressure of at least 140 mmHg or 90 mmHg. Diastolic blood pressure in millimetres or the amount of antihypertensive medication currently used medicines. A number of observational studies have revealed firmly established a strong correlation between high CHD and BP[10-12]. This partnership is valid for both men and women, as well as young and old. Occasionally those with high BP are at higher risk of CHD[13].

Cardiovascular disease and Diabetes

Patients with type 1 and type 2 diabetes mellitus have a significantly higher risk of developing all forms of cardiovascular disease[14,15].The death rate among people who do not have diabetes was lower than those of diabetes patients who experienced increased CHD[16,17].Hyperglycemia is thought to be the possible risk factor even though it is independent based on the traits typically seen in diabetics similar to dyslipidemia and obesity. Good glycemic control lowers the chance of microvascular issues of diabetes. But in those with diabetes, significant inadequate glucose regulation has not been lowering the while a trend, macrovascular disease (CHD) towards advantage has been noted[18].

Cardiovascular disease and Total cholesterol,low-density lipoprotein cholesterol

Nearly every cell in the body can synthesise cholesterol, and an important portion of it can be absorbed by diet. The lipid hypothesis states that elevated concentrations of LDL cholesterol or abnormally high cholesterol levels (hypercholesterolemia) are known to be the main lipid risk factors[19]. Blood temperature levels have been shown in numerous studies to have an exponential effect on cardiovascular and overall mortality, with the relationship being stronger in younger participants. Higher cholesterol does have a more negative impact on health in older adults[20].

The dose-response relationship between TC and the risk of CHD has been repeatedly verified by various research. After evaluating more than 300,000 males, the Multiple Risk Factor Intervention Trial (MRFIT) found an upward trend between TC and age-adjusted CHD mortality rate among MRFIT screeners who have a TC 240 mg/dL, relative risk (RR) of coronary heart disease In contrast to individuals with TC <182 mg/dL,It had a 3.4 death rate[21]. However, aside from

TC, there the risk of coronary heart disease (CHD) is influenced by strongly established by research with 25 years of follow-up as reported in the Seven Countries Study (SCS)[22].

Research carried out on many populations shows that people with higher cholesterol had greater rates of atherosclerosis and CHD than people who have at a lower level (Keys et al., 1984). The advantage correlation between the amount of cholesterol in serum and the beginning of the first or subsequent episode of CHD, was found to be caused by high LDL cholesterol;The risk increases as the level rises[24]. Prospective information suggested that the chance of CHD at reduced cholesterol, and it's clear that this has showed up in larger investigations[23,24.]

There is evidence to support multiple stages in the relationship between high LDL cholesterol and the start of CHD[25].The initial step in atherogenesis, or the fatty streak, is the presence of cholesterol-filled macrophages, the majority of which are derived from low-density lipoprotein (LDL) cholesterol. The second stage consists of fibrous plaques, which are scar tissue covering a lipid-rich core. The growth of plaque is further influenced by additional risk factors. In the third stage, plagues that are unstable and prone to rupture and luminal thrombosis development are shown to have begun. Plaque rupture accounts for the majority of acute coronary syndromes (ACS)[26,27].

Cardiovascular disease and Triglycerides, very low–density lipoprotein cholesterol

A glycerol molecule containing an OH group is converted to an ester called triglyceride (TG), which is what makes up most fats and is later used by the body for digestion. Fatty acids, monoglycerides, and certain diglycerides are absorbed after the TG has been broken down since the duodenum is unable to absorb lipids in their TG form. High blood TG levels have been connected to atherosclerosis and coronary heart disease (CHD) in humans.

The majority of observational research and analyses that were published in previous years support TG as a separate risk factor for CHD. Numerous nations with widely disparate incidences of CVD have participated in these trials, with populations spanning a wide range of ages [28-31].Historically, univariate research has used increased TG to predict CHD events after adjusting for other covariates such as plasma glucose and HDL cholesterol, with which it has a strong and negative relationship[32]. A thorough evaluation of population based prospective studies has revealed an independent effect of TG on CHD occurrences, even after adjusting for HDL cholesterol[33].Together with the understanding that both elevated LDL cholesterol and TG alone do not considerably outweigh the combined hyperlipidaemia ability to induce CHD[34].

The liver makes a kind of lipoprotein known as very l owdensity lipoprotein (VLDL), that helps in the tran sport of cholesterol and lipids into the bloodstream.It is a combination from cholesterol and apolipoproteins , which collect in the liver and then transform into lo wdensity lipoprotein, or LDL, cholesterol in the bloo d.Whereas chylomicrons carry exogenous (dietary) pr oducts, VLDL cholesterol contains internal metabolit es (which include TG, phospholipids, cholesterol, and cholesteryl esters).

Relic lipoproteins are the most probable candidates for atherogenic TG-rich lipoproteins (TGRLP). Small VLDL cholesterol and lipoproteins of intermediate density, or IDL, are two types of these lipoproteins. Reviews[35–37]provided strong evidence in favour of the remnants' atherogenicity. It was found that elevation and the precise identification of remnants were powerful predictors of CHD in a number of clinical investigations[38,39].

Cardiovascular disease and elevated high-density lipoprotein cholesterol

One of the five main lipoprotein groups that makes up HDL cholesterol is responsible for allowing lipids like TG and cholesterol to be carried through the water based bloodstream. In healthy individuals, HDL cholesterol carries roughly thirty percent of the blood cholesterol. While decreasing, which raises the risk of heart disease, an elevated amount of HDL cholesterol protects against CVD. When testing cholesterol, some of the material found in HDL particles as opposed to "bad" LDL cholesterol is thought to act as protectors of the body's cardiovascular health.

Low blood HDL is strongly associated with higher CHD morbidity and mortality, according to epidemiological evidence[40,41].On the other hand, elevated HDL cholesterol indicates a lower risk. A 1-3 percent increase in the risk of coronary heart disease is linked to a 1% drop in HDL cholesterol, according to a variety of epidemiological studies taken collectively. Epidemiology studies have shown that low HDL cholesterol is an independent risk factor for CHD, and this conclusion is maintained in multivariate analysis after controlling for other risk variables.

Actually, there is a strong correlation between HDL cholesterol and the risk of coronary heart disease (CHD) in prospective studies[42,43]. When the adult

Treatment Panel II (ATP II) was observed to have a low HDL cholesterol of less than 35 mg/dL, it was noted as one of several significant risk variables that were utilised to lower the LDL cholesterol therapeutic objective. Men and women would be at the same risk from the same level of HDL cholesterol, hence the concept of low-HDL cholesterol was established for both sexes.

NON-TRADITIONAL RISK FACTORS

The epidemiology and fundamental scientific search for greater knowledge of the aetiology of CVD has produced various blood indicators as potential for indicating "nontraditional" risk. Numerous are a part of the inflammatory process, which is now recognised as the primary cause of atherosclerotic disease[44].The following have been proposed as candidates: homocysteine; plasminogen activator inhibitor-1 (PAI-1); fibrinogen; D-dimer; thrombin/ antithrombin III complex; and a number of inflammatory indicators, including adhesion molecule, interleukin (IL), CRP, serum amyloid A (SAA), and MMP. Though several of these markers show potential, the majority are not utilised in standard clinical practice, and it is unknown how predictive many of them are.

Homocysteine

The literature made it abundantly evident what part homocysteine plays as an oxidative stress marker[45,46].Homocysteine levels, a modulator of one carbon metabolism, are linked to CVD[47–49].According to Humphrey et al. (2008), there is a 20% moderate increase in the risk of CVD associated with a high homocysteine level[50].According to Ueland et al.[51],lowering blood homocysteine levels by 3-5 mol/L can lower some types of CVDs, such as deep vein thrombosis and stroke.

Plasminogen activator inhibitor-1 (PAI-1)

The key activator of fibrinolysis is PAI-1. Raiko et al.[52] based on the multivariate analysis, reported that the PAI-1 was associated directly with arterial intima-media thickness, blood pressure, a measure of body mass index (BMI), LDL cholesterol and total cholesterol levels, the glomerular filtration process, and triglycerides. Zhuang et al.[53] reported that the patients with acute ischemic stroke had a significant amount of t-PA, while the level of PAI-1 was reduced significantly. There was a substantial difference in the activities of t-PA and PAI-1 in the control group, convalescent, acute, and chronic groups, and a negative association between the two variables was found. Tofler et al.[54] found that the level of PAI-1 in individuals with CVD was greater (29.1 ng/ml) than in people without CVD (22.1 ng/ml). The results of his experiment likewise showed a strong linear connection between the incidence of CVD and the antigen levels of t-PA and PAI-1.

Fibrinogen

Buchanan initially defined fibrinogen (Fg), the coagulation agent that precedes fibrin, in 1836. The haematological alterations followed by an elevation in Fg include an increase in plasma viscosity, erythrocyte aggregation, and platelet thrombogenesis[55] .Based on epidemiological research, Meade et al.[56] reported that a rise in plasma Fg concentration is associated with a higher risk of CVD, including ischemic heart disease, thromboembolism, and stroke.

D-dimer

One of the key indicators linked to CVD is the fibrin degradation marker, D-dimer. In a long-term cohort analysis with 719 individuals consuming oral anticoagulant medications, Lind et al.[57] found a correlation between increased D-dimer levels and cardiovascular disease. Based on clinical and laboratory data, Fruchter et al.[58] proposed D-dimer as a major prognostic predictor of both short- and long-term survivors who had experienced an acute exacerbation. Additionally, he observed differences in the average D-dimer levels between survivors (1.45 mg/L) and non-survivors (3.18 mg/L).

Interleukin

Based on research studies, interleukin-6, a strong prognostic predictor in the bloodstream, is utilized as an indicator for the early detection of cardiovascular disease[59].According to Reichert et al.[60], the IL-6 c.-174 CC genotype polymorphism was discovered to be a distinct risk factor for coronary heart disease (CHD) in 942 cases. In a similar vein, Buraczynska et al.[61] reported that individuals with type 2 diabetes who carry the C IL-6 G(-174)C allele are at increased risk for cardiovascular disease.

CONCLUSION:

Research indicates that the pathophysiology of disease is influenced by factors such as urbanization, dietary westernization, and rising rates of obesity, diabetes, and smoking. The past several decades have seen a decrease in CVD-related mortality as a result of efforts made to manage the disease. Hypertension, tobacco use, physical inactivity, high-density lipoprotein cholesterol, diabetes, and a number of linked metabolic risk factors are examples of potential risk factors for cardiovascular disease (CVD)[3].Even after these risk factors have been identified, many patients have never gained sufficient control over them. In addition, the increasing rates of obesity and type 2

diabetes mellitus (Type 2 DM) present a threat to the progress achieved in CVD. Significant increases in the prevalence of other critical CVD risk factors, such as insulin resistance, dyslipidaemia, hypertension, and type 2 diabetes, have been attributed to the rising incidence of obesity[3]. Multiple studies have demonstrated that blood cholesterol is the main factor contributing to CVD and the mortality that is associated with it in young people. Low HDL cholesterol levels raise the risk of heart disease, while high HDL cholesterol levels tend to protect against CVD. Homocysteine, coagulation markers like fibrinogen, D-dimer, plasminogen activator inhibitor-1 (PAI-1), and the thrombin/anti-thrombin III complex, along with inflammatory markers such as CRP, interleukin (IL), serum amyloid A (SAA), MMP, and adhesion molecules, are examples of non-traditional risk factors. Pharmacologic therapy, such as endo-cannabinoid receptor antagonists and peroxisome proliferator inhibitors that control the action of glucagon-like peptide-1, is now available to address specific CVD risk factors and is being studied[3].

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