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Cardiovascular Risk Factors and Ischemic Heart Disease

Moataz AbdElmonem Elkot, ElSayed Mohamed Farag, Islam AbdElmonem Elsherbiney, Tareq Abdelrahman Mohamed Gendi

Cardiology Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Tareq Abdelrahman Mohamed Gendi

Email: tareq.elgendy@outlook.com,

Abstract:

Ischaemic heart disease (IHD) remains one of the leading causes of mortality and morbidity worldwide. According to the World Health Organization, a large proportion of cardiovascular disease (CVD)-related deaths are linked to modifiable behavioural and metabolic risk factors such as unhealthy diet, physical inactivity, tobacco use, harmful use of alcohol, elevated blood pressure, raised blood glucose and dyslipidaemia. Many of these risk factors tend to cluster and interact, thereby compounding the burden of disease. For example, the concept of metabolic syndrome (central obesity + hypertension + hyperlipidaemia + insulin resistance) reflects how risk factors aggregate to elevate IHD risk. In the context of IHD, modifiable risk factors (such as hypertension, smoking, diabetes, dyslipidaemia, obesity, sedentary lifestyle) and non-modifiable ones (age, sex, family history, ethnicity) have been well documented. However, emerging evidence points to the importance of non-traditional and emerging risk markers (e.g., psychosocial stress, air pollution, sleep disorders) which may further refine risk stratification and guide preventive strategies. Given the significant global burden of IHD and the fact that many risk factors are potentially modifiable, understanding and addressing these risk factors is critical for effective prevention. Recent studies (for example, from the journal Journal of the American Heart Association) have identified dietary factors, high systolic blood pressure and elevated LDL-cholesterol among the top contributors to IHD burden.

Keywords: Ischaemic Heart Disease (IHD), Cardiovascular Risk Factors, Modifiable Risk Factors, Non-modifiable Risk Factors, Dyslipidaemia / High LDL Cholesterol, Hypertension / High Blood Pressure, Diabetes Mellitus, Obesity / Overweight, Sedentary Lifestyle, Smoking / Tobacco Use, Unhealthy Diet, Psychosocial Stress, Air Pollution / Environmental Risk Factors.

Introduction:

Ischemic heart disease (IHD), also known as coronary artery disease, is a major contributor to global morbidity and mortality, accounting for nearly one in every five deaths worldwide. It results primarily from an imbalance between myocardial oxygen supply and demand due to atherosclerotic narrowing of the coronary arteries. Despite substantial advances in preventive cardiology and acute management, the global burden of IHD continues to rise, especially in low- and middle-income countries, driven by urbanization, lifestyle changes, and increasing life expectancy. Early identification of high-risk individuals and targeted interventions remain essential to reduce disease incidence and improve survival outcomes **(1).**

The pathogenesis of IHD is multifactorial, involving both modifiable and non-modifiable risk factors. Traditional risk factors include hypertension, diabetes mellitus, dyslipidemia, obesity, smoking, and physical inactivity, which interact synergistically to accelerate atherosclerosis and endothelial dysfunction. Non-modifiable factors such as age, sex, family history, and genetic predisposition also influence susceptibility. Notably, modifiable factors account for more than 80% of premature cardiovascular deaths, emphasizing the need for aggressive preventive

strategies. In addition, metabolic syndrome—a cluster of insulin resistance, abdominal obesity, and dyslipidemia—has emerged as a powerful predictor of IHD events **(2).**

Recent research highlights the growing role of non-traditional and emerging risk determinants in cardiovascular disease. Chronic psychosocial stress, air pollution, poor sleep quality, and systemic inflammation have been recognized as novel contributors to ischemic heart disease risk. These findings underscore the importance of a comprehensive approach that integrates lifestyle modification, environmental protection, and public health initiatives. Therefore, a multidimensional prevention strategy addressing both established and emerging factors is crucial to mitigate the global burden of ischemic heart disease **(3).**

Ischemic heart disease, also called coronary heart disease (CHD) or coronary artery disease, is the term given to heart problems caused by narrowed coronary arteries. Although the narrowing can be caused by a blood clot or by constriction of the blood vessel, most often it is caused by buildup of atheromatous plaque. **(4)**

Epidemiology.

➢ Ischemic heart disease(IHD) is a leading cause of death worldwide.

➢ It is estimated that globally, IHD affects around 126 million individuals (1,655 per 100,000), which is approximately 1.72% of the world's population. Nine million deaths were caused by IHD globally. Men were more commonly affected than women, and incidence typically started in the fourth decade and increased with age. **(5)**

➢ The global prevalence of IHD is rising. It is estimated that the current prevalence rate of 1,655 per 100,000 population is expected to exceed 1,845 by the year 2030.

➢ IHD is the number one cause of death, disability, and human suffering globally.

➢ Egypt comes 4th in the Age-standardized prevalence rate of IHD. (**6)**

Classification of Ischemic Heart disease.

➢ IHD can be classified differently according different criteria and most commonly classified to CCS and CAS.

➢ **Chronic Coronary Syndrome (CCS)**

- CCS are a range of clinical presentations or syndromes that arise due to structural and/or functional alterations related to chronic diseases of the coronary arteries and/or microcirculation. These alterations can lead to transient, reversible, myocardial demand vs. blood supply mismatch resulting in hypoperfusion (ischemia), usually (but not always) provoked by exertion, emotion or other stress, and may manifest as angina, other chest discomfort, or dyspnea, or be asymptomatic. Although stable for long periods, chronic coronary diseases are frequently progressive and may destabilize at any moment with the development of an ACS. **(7)**

- Our understanding of the pathophysiology of CCS is transitioning from a simple to a more complex and dynamic model. Older concepts considered a fixed, focal, flow-limiting atherosclerotic stenosis of a large or medium coronary artery as a sine qua non for inducible myocardial ischemia and ischemic chest pain (angina pectoris). Current concepts have broadened to embrace structural and functional abnormalities in both the macro- and microvascular compartments of the coronary tree that may lead to transient myocardial ischemia. **(7)**

- At the macrovascular level, not only fixed, flow-limiting stenoses but also diffuse atherosclerotic lesions without identifiable luminal narrowing may cause ischemia under stress. **(8)** structural abnormalities such as myocardial bridging **(9)** and congenital arterial anomalies **(10)** or dynamic epicardial vasospasm may be responsible for transient ischemia.

- At the microvascular level, coronary microvascular dysfunction (CMD) is increasingly acknowledged as a prevalent factor characterizing the entire spectrum of CCS **(11)** functional and structural microcirculatory abnormalities may cause angina and ischemia even in patients with non-obstructive disease of the large or medium coronary arteries [angina with non-obstructive coronary arteries (ANOCA); ischemia with non-obstructive coronary arteries (INOCA)]. **(11).**

- Finally, systemic or extracoronary conditions, such as anemia, tachycardia, blood pressure (BP) changes, myocardial hypertrophy, and fibrosis, may contribute to the complex pathophysiology of non-acute myocardial ischemia**. (12)**

➢ **Acute coronary syndromes (ACSs):**

- Acute coronary syndrome (ACS) can be divided into subgroups of ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina **(13)**

➢ **Unstable Angina:**

- Unstable angina falls under the umbrella term "acute coronary syndrome" (ACS). ACS affects a large portion of the population and remains the leading cause of death worldwide**.(14)**
- Coronary atherosclerotic disease underlies unstable angina in nearly all patients with acute myocardial ischemia. The primary cause of unstable angina involves coronary artery narrowing due to a nonocclusive thrombus forming on a disrupted atherosclerotic plaque**.(15)**

- A key distinguishing feature of unstable angina from CCS is incomplete resolution of pain with typical relieving factors. Many patients have preexisting CAD, either previously diagnosed or with stable anginal symptoms. These patients often report increased frequency, duration, or severity of chest pain episodes; such changes suggest unstable angina rather than stable or other causes of chest pain. Recognizing these symptoms is critical, as unstable angina may indicate impending myocardial infarction or ST-elevation myocardial infarction. **(16)**

➢ **Non ST segment Elevation Myocardial infarction(NSTEMI):**

- NSTEMI and Unstable angina are very similar, with NSTEMI having positive cardiac biomarkers. And there are several potential causes of this mismatch in NSTEMI. There may be a flow-limiting condition such as a stable plaque, vasospasm as in Prinzmetal angina, coronary embolism, or coronary arteritis. Non-coronary injury to the heart such as cardiac contusion, myocarditis, or presence of cardiotoxic substances can also produce NSTEMI. Finally, conditions relatively unrelated to the coronary arteries or myocardium itself such as hypotension, hypertension, tachycardia, aortic stenosis, and pulmonary embolism lead to NSTEMI because the increased oxygen demand cannot be met**. (17)**

- NSTEMI is diagnosed in patients determined to have symptoms consistent with ACS and troponin elevation but without ECG changes consistent with STEMI. Unstable angina and NSTEMI differ primarily in the presence or absence of detectable troponin leak.

- Cardiac troponin is the cardiac biomarker of choice. Troponin is more specific and more sensitive than other biomarkers and becomes elevated relatively early in the disease process. While contemporary cardiac troponin may not be elevated within the first 2 to 4 hours after symptom onset, newer high sensitivity troponin assays have detectable elevations much earlier. It is also true that the amount of troponin released, and therefore the time to elevation, is proportional with infarct size, so it is unlikely to have a negative initial troponin with larger infarcts. Regardless of infarct size, most patients with true ischemia will have elevations in troponin within 6 hours, and negative troponins at this point effectively rule out infarct in most patients. Most assays use a cutoff value of greater than a 99th percentile as a positive test. In older, contemporary troponin assays, no detectable

troponin is reported in most healthy individuals without the disease. Newer high sensitivity troponin assays often will report a normal detectable range in healthy individuals without the disease**. (18)**

- **ST segment Elevation Myocardial Infarction (STEMI)**

- Myocardial infarction (MI) is commonly defined as cardiomyocyte death caused by substantial and sustained ischemia due to an imbalance of oxygen supply and demand. On the basis of the electrocardiogram (EKG or ECG) trace, MI is differentiated between STEMI and NSTEMI. STEMI is the result of transmural ischemia (that is, ischemia that involves the full thickness of the myocardium). **(19)**
- The epidemiology of patients with STEMI continues to evolve. The Global Registry of Acute Coronary Events (GRACE) **(20)** documented that STEMI accounted for ~36% of ACS cases. Similar findings have been reported in a developing country, with STEMI accounting for ~37% of ACS cases enrolled in the Jakarta Acute Coronary Syndrome (JAC) Registry database **(21)**

- According to an analysis of a large United States database, the age-adjusted and sex-adjusted incidence of hospitalizations for STEMI significantly decreased from 133 per 100,000 person-years in 1999 to 50 per 100,000 person-years in 2008 **(22)**
- These results reflect the situation in the Western world, whereas the prevalence and incidence of cardiovascular disease (CVD) in developing countries are increasing **(23).** Reasons for this increase include expanding life expectancy, changing lifestyles and the adoption of a Western diet (which is typically rich in saturated fats and refined sugars) in these regions. In addition, CVD occurs at a younger age in developing countries than in developed ones. For example, a case–control study found that acute MI occurred at a significantly younger age in individuals living in south Asian countries than in individuals from other countries **(24)**
- The predominant underlying mechanism of the total coronary occlusion in STEMI is thrombosis developing on a coronary atherosclerotic plaque **(25)**.
- A few exceptions exist and include spontaneous coronary artery dissection which is defined as a nontraumatic and noniatrogenic tear within the layers of the coronary vessel wall, with intramural hemorrhage that creates a false lumen. **(26)**
- Coronary spasm which is a variant form of angina and characterized by symptoms of chest pain at rest with ST-segment elevation. Coronary spasm typically occurs in the early hours of the morning during depressed vagal tone and is associated with transient vasoconstriction of the epicardial coronary arteries, resulting in total or subtotal vessel occlusion with consecutive myocardial ischemia. Underlying mechanisms are a mostly localized abnormality of a coronary artery that results in hyper-reactivity to vasoconstrictor stimuli and a vasoconstrictor stimulus capable of inducing the spasm. Most common stimuli are illicit drugs, such as cocaine, but also include some weight-loss products, over-the-counter drugs, chemotherapies, antimigraine medications and antibiotics. **(27).**

- Coronary embolism: however, the reported prevalence of coronary embolism as the cause of ST-segment elevation myocardial infarction (STEMI) ranges from 4% to 13% according to angiographic and autopsy studies. **(28)**
- A vulnerable plaque can be described as an atherosclerotic lesion that has a high risk of rupture and is characterized by a large lipid-rich or necrotic core that is separated from the vessel lumen by a thin fibrous cap (also called thin-capped fibroatheroma). Disruption of a so-called vulnerable plaque has been reported as the most common cause of acute MI. **(29)**
- The working diagnosis is usually based on symptoms consistent with myocardial ischemia, that is, persistent chest pain and new ST-segment elevation. However, it is important to also recognize atypical symptoms, such as pain in neck, back or jaw as well as weakness, nausea or fatigue, which are more frequent in women than in men. **(30)**
- STEMI may occur in the absence of obstructive CAD on angiography and is termed MI with non-obstructed coronary arteries (MINOCA). MINOCA that is associated with ST-segment elevations may be based

on atherosclerotic plaque rupture, ulceration, fissuring, erosion or coronary dissection with non-obstructive or no CAD, but also myocardial disorders such as myocarditis and Takotsubo stress cardiomyopathy. **(31)**

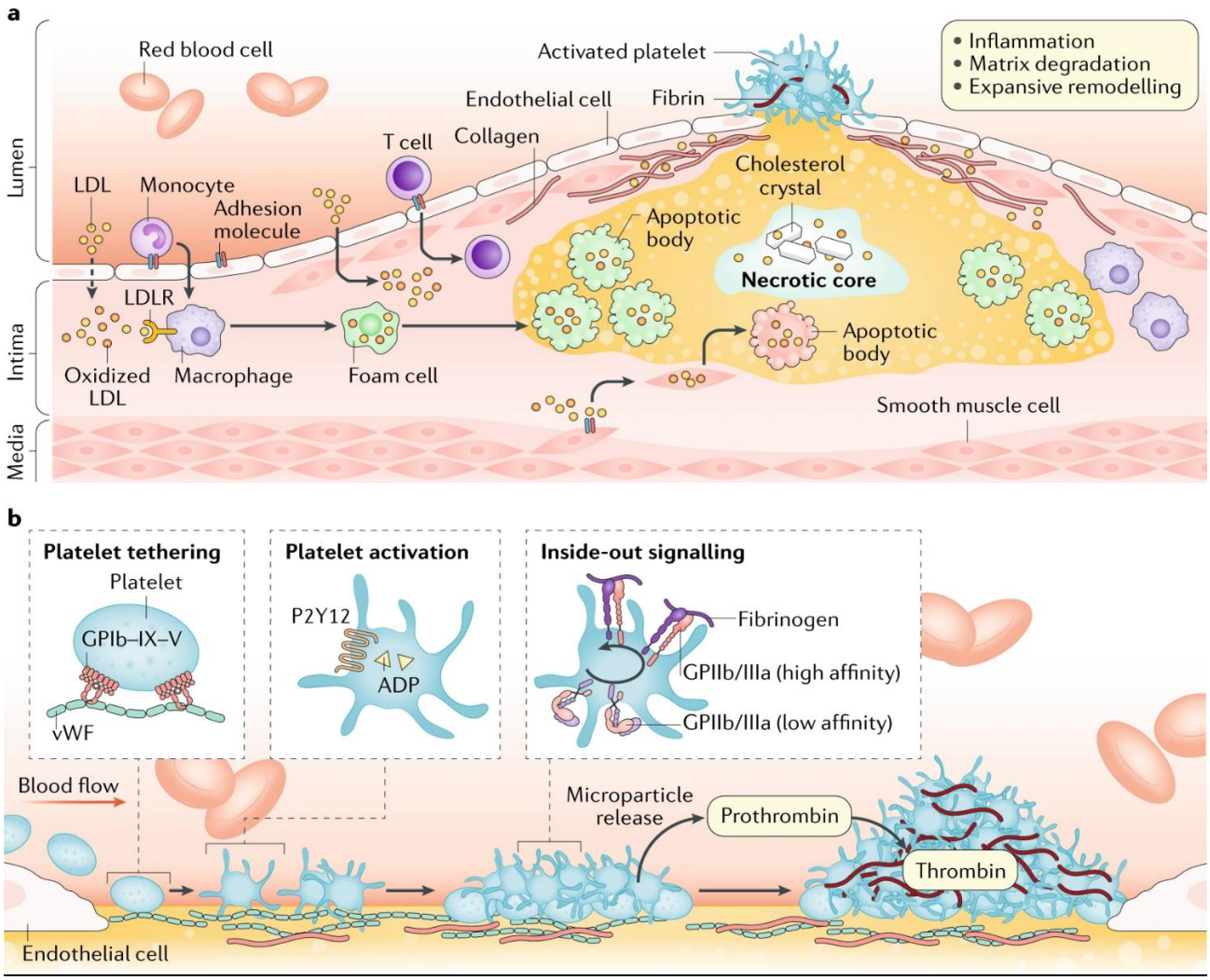

Figure 1 showing Atheromatous plaque development, plaque rupture and thrombus formation.

Risk factors of Ischemic Heart Disease.

➢ **Non-modifiable risk factors:**

- **Age**

CAD prevalence increases after 35 years of age in both men and women. The lifetime risk of developing CAD in men and women after 40 years of age is 49% and 32%, respectively. **(32)**

- **Gender**

Men are at increased risk compared to women. Although men are at higher risk than women of CAD, it is still the leading cause of death among women. Among women, only 54% were aware of this in 2009. Cardiovascular disease caused approximately 1 in 3 female deaths**. (33)**

Women were found to have non-obstructive CAD in 57% of cases, in contrast to men who more commonly had obstructive CAD. Proposed mechanisms for this include coronary microvascular dysfunction (CMD), altered endothelial tone, structural changes, and altered response to vasodilator stimuli **(34)**.

Estrogen is thought to have a protective role in coronary vasoreactivity and is also theorized to promote plaque stabilization via an anti-inflammatory effect on atherosclerosis. **(35)**

- **Ethnicity**

Blacks, Hispanics, Latinos, and Southeast Asians are ethnic groups with an increased risk of CAD morbidity and mortality.**(36)**

- **Family History**

Family history is also a significant risk factor. Patients with a family history of premature cardiac disease younger than 50 years of age have an increased CAD mortality risk**. (37)**
A separate article indicated that a father or brother diagnosed with CAD before 55 years of age and a mother or sister diagnosed before 65 years of age are considered risk factors. **(38)**

- **Modifiable risk factors:**

- **Hypertension**

A major change in the 2017 ACC/AHA guidelines was the implementation of a lower (130/80 mm Hg) threshold defining hypertension. SBP of 130 to 139 or diastolic BP of 80 to 89 mm Hg defined stage 1 hypertension, whereas any values >140/90 mm Hg defined stage 2 hypertension, the 2018 ESC/ESH guideline maintained the 140/90 mm Hg threshold and hypertension classification from the previous 2013 guidelines**. (39)**

About 1 out of every 3 patients have hypertension. Hypertension and smoking were responsible for the largest number of deaths in a 2009 review comparing twelve modifiable risk factors. Yet, only 54% of these patients achieve adequate blood pressure control. **(40)**

Hypertension has long been a major risk factor for heart disease through both oxidative and mechanical stress it places on the arterial wall. **(41)**

- **Hyperlipidemia**

Hyperlipidemia is considered the second most common risk factor for ischemic heart disease. **(42)** According to the World Health Organization, raised cholesterol caused an estimated 2.6 million deaths. **(42)**

A recent cross-sectional study utilizing the coronary calcium score indicated a 55%, 41%, and 20% higher prevalence of hypercholesterolemia, combined hyperlipidemia, and low HDL-c, respectively. **(43)**

Elevated triglycerides have also been implicated in CAD; however, the relationship is more complicated as the association becomes attenuated when adjusted for other risk factors such as central adiposity, insulin resistance, and poor diet. Thus, it is challenging to determine an isolated effect of triglycerides on CAD. **(44)**

- **Obesity**

Obesity prevalence has increased globally. **(45**) In the United Kingdom, the prevalence increased from 15% in 1993 to 27% in **2015 (46),** and more than half of the population could have obesity by 2050. Obesity and overweight increase the risk of developing MI by adversely contributing to risk factors including hypertension, dyslipidemia, chronic inflammatory state, type 2 diabetes mellitus and metabolic syndrome. **(47)**

- **Smoking**

Smoking is one of the major risk factors for the development of atherosclerotic conditions including MI **(48)** and worsens outcomes after intervention. Patients who smoke are at a higher risk of mortality and morbidity following PCI **(49)**.

Several mechanisms by which cigarette smoking leads to CAD have been proposed, including oxidative damage to the endothelium, leading to endothelial damage and accelerating atherosclerosis, platelet activation and thrombosis, reduced oxygen availability and sympathetic nervous system activation, resulting in coronary vasoconstriction**. (50)**

- **Diet**

An unhealthy diet (based on food high in sodium, refined sugar and fat) is associated with an increased risk of MI by inducing weight gain. It also has an adverse effect on other risk factors for MI including hypercholesterolemia, hypertension and type 2 diabetes mellitus **(51)**

High sodium intake has been shown to increase blood pressure, whereas sodium reduction has been shown to decrease CAD, and in particular, elderly patients or individuals with underlying elevated blood pressure may benefit the most from it **(52).**

One of the main forms of sugar in diet is sweetened beverages, and a systematic review has demonstrated a positive association between sweetened beverages and CAD. (**53)** Excessive consumption of saturated and trans-fat is also considered to be a risk factor for coronary heart disease. **(54)**

- **Sedentary Life**

The beneficial effect of physical exercise on coronary heart disease has long been recognized**. (55)**
Many studies have strongly supported the protective effect of physical activity on CAD, with the incidence of CAD halved in the most physically active individuals compared with the most sedentary. **(56)**
The mechanisms by which exercise exerts its protective effect are probably by reducing the risk factors associated with the development of CAD, such as lowering blood pressure**.** and triglycerides· and improving endothelial function, enhancing nitric oxide bioavailability and promoting collateral vessel development **(57)**
The current recommendation is to do physical activity for 150 minutes per week and strength exercises on ≥2 days on a weekly basis· **(58)**

- **Diabetes Mellitus**

The Centers for Disease Control (CDC) reports that more than 1 out of every 3 adult patients in the United States have prediabetes, which puts one at risk of developing type 2 diabetes, heart disease, and stroke.

The heart disease rate is 2.5 times higher in men and 2.4 times higher in women in adult patients with diabetes compared to those without diabetes. **(59)**

A 2017 meta-analysis indicated that patients with diabetes with an A1C > 7.0 had an 85% higher likelihood of cardiovascular mortality compared to those with an A1C < 7.0%. It also revealed that non-diabetic patients with an A1C > 6.0% had a 50% higher likelihood of cardiovascular mortality compared to those with an A1C of < 5.0%. Researchers also reported significant study heterogeneity. **(60)**

Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes. **(61)**

- **Stress**

The aftereffects of extreme and prolonged distress can lead to psychological trauma, which may lead to morbid outcomes **(62)**
The above makes it equivalent to the primary risk factors associated with cardiovascular disease (CVD). Andrew Steptoe in his statistical analysis revealed the prevalence of CVD among socially apathetic populations, which is about 50%. However, a 40% population working in pressured environments is likely to develop CVD **(63).**

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