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Atherosclerosis: Pathophysiology, risk factors, diagnosis and treatment

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Abstract

Atherosclerosis is a chronic inflammatory disease characterized by the buildup of lipid-rich plaques in the arteries, leading to cardiovascular diseases such as myocardial infarction, stroke, and peripheral artery disease. The pathophysiology of atherosclerosis involves the interplay between vascular and immunological cells, with oxidative stress, inflammation, and endothelial dysfunction playing key roles. Lifestyle-related risk factors, such as diet, smoking, and physical activity, contribute to the development of atherosclerosis. Diagnosis is typically made using imaging techniques such as ultrasound, magnetic resonance, and computed tomography. Treatment strategies focus on reducing low-density lipoprotein levels, managing risk factors, and preventing clinical events. This article provides an overview of the current understanding of atherosclerosis, highlighting its pathophysiology, risk factors, diagnosis, and treatment

Keywords: Atherosclerosis; Cardiovascular Diseases; Cholesterol; Endothelial Dysfunction

1. Introduction

Mercury is classified by environmental health authorities as a very hazardous heavy metal that poses a risk to human health. Mercury has harmful effects on the environment that are widespread across the planet [1]. It includes ischemic stroke or sudden myocardial infarction. Reversing the disease process is crucial for both prevention and treatment, as many individuals who exhibit their initial symptoms already have severe atherosclerosis. The illness is based on a long-term inflammatory process that involves immune and vascular cells [2]. Numerous cell types and cytokines are involved in the chronic inflammatory disease known as atherosclerosis [3]. Both the innate and adaptive immune systems are essential for the development and subsequent progression of atherosclerosis, a chronic inflammatory disease [4]. Mature vascular smooth muscle cells (VSMCs) control blood vessel diameter, which in turn controls blood pressure and blood flow distribution [5]. The mechanisms of innate and adaptive immunes can either promote or quell atherosclerosis [6], according to genome-wide association, clonal lineage tracing, and clinical trials. Over the past 20 years, key propagators like Peter Libby, Göran Hansson, and Paul Ridker eventually consolidated this evidence and successfully translated much of the basic knowledge into meaningful clinical studies, identifying residual inflammation as a potent risk factor and major contributor to clinical morbidity and mortality on par with low-density lipoprotein (LDL) cholesterol [7]. Both vascular and immunological cells are involved in atherosclerosis, a complicated inflammatory disease that is brought on by the build-up of lipoproteins high in cholesterol in the walls of big and medium-sized arteries. Experimental atherogenesis has been causally linked to both innate and adaptive immune responses [8]. Throughout the many clinical phases of atherosclerosis development, functional alterations in all kinds of vascular cells are driven by transcriptional modifications. Histone modification and DNA methylation are two enzyme-mediated epigenetic processes that epigenetics uses to regulate transcriptome alterations [9].

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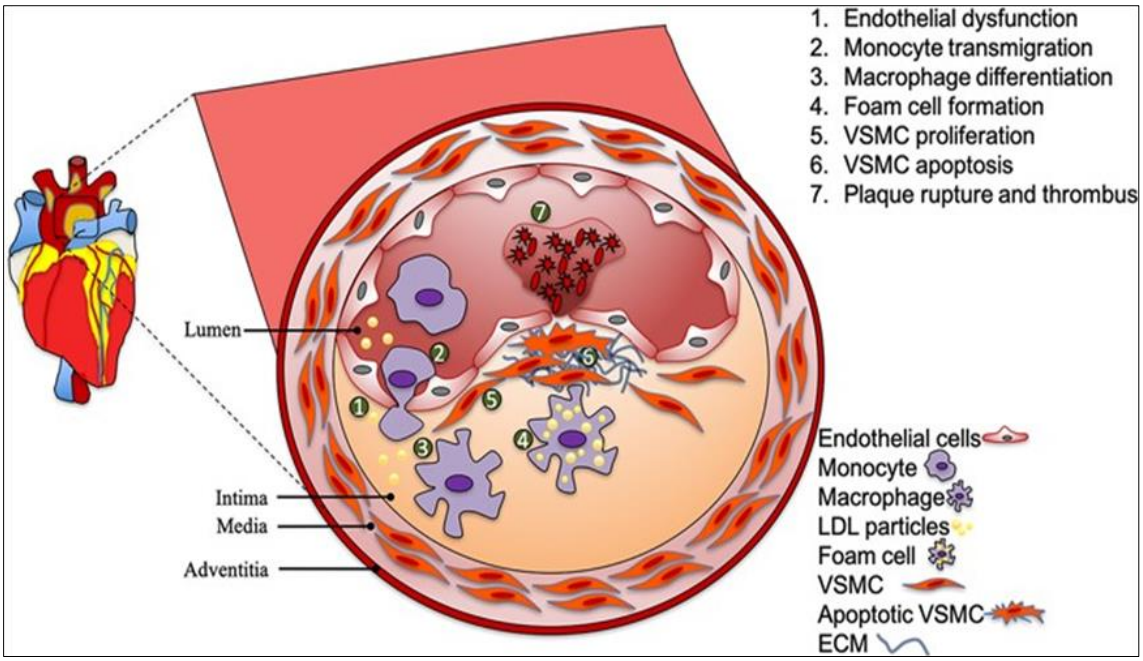

Figure 1 Atherosclerotic plaque development [9]

2. Pathophysiology

Humans have been aware of metallic mercury and its inorganic salts since ancient times, when this element was used in medicine. Mercury compounds were employed as a dependable germicide [1]. Endothelial cells, the lining of cells exposed to blood flow, respond sensitively to even the smallest variations in hemodynamic flow. Other biological processes also depend on this kind of mechanosensing [2]. Various cells inside the atherosclerotic lesion are activated by local inflammatory responses in atherosclerosis. Lipids stimulate endothelial cells, and Various cells inside the atherosclerotic lesion are activated by local inflammatory responses in atherosclerosis. Various cells inside the atherosclerotic lesion are activated by local inflammatory responses in atherosclerosis [10]. Numerous pathogenic mechanisms seem to link atherosclerosis with diabetes mellitus. Studies on diabetic individuals have demonstrated an increased risk and hastened development of atherosclerosis [11]. Severe cardiovascular events such as myocardial infarction, ischemic stroke, and sudden cardiac arrest can also result from blood clots forming in the vasculatures [12]. Atherosclerosis may occur because of aberrant signalling in the disturbed network of vascular endothelial cells, which causes the vascular function to deteriorate in prediabetes. These results offer a fresh method for examining the vascular dysfunction associated with prediabetic obesity [13]. For decades, the biological rationale for employing glycolysis rather than oxidative phosphorylation for energy production was unclear because the latter is a much less efficient technique for ATP synthesis. [14]. Atherosclerosis, a condition in which lipid-rich plaques develop in the arteries, is primarily responsible for ischemic CVD. Atherosclerosis is a widespread, chronic inflammatory disease of the vasculature, as demonstrated by decades of research into the processes of atherogenesis and plaque development in several pre-clinical animal models. The endothelial cells (EC) that line the vasculature become dysfunctional and lose their typical anti-inflammatory and anti-thrombotic qualities in response to damage brought on by cardiovascular risk factors, such as smoking, diabetes, hypertension, and dyslipidemia [15]. Depending on a number of factors, such as lifestyle, each individual may have a diverse range of gut microbes. The microbiota is known to fluctuate greatly throughout the first year of life before stabilizing as an adult like consortia [16].

Acute thrombotic blockage of a coronary artery causes myocardial infarction (MI), which affects the heart muscle that depends on the artery for oxygen and nutrition. Even though it is now standard medical practice to lessen the damage by reopening the affected coronary artery through Percutaneous Coronary Intervention (PCI), a considerable number of patients still suffer from serious heart damage for a variety of reasons, such as presenting to their doctor with unusual symptoms or too late, which is especially problematic for women [18]. One critical early proatherogenic event that may also be significant later in the course of the illness is the oxidation of LDL and the generation of free radicals inside the endothelium [19].

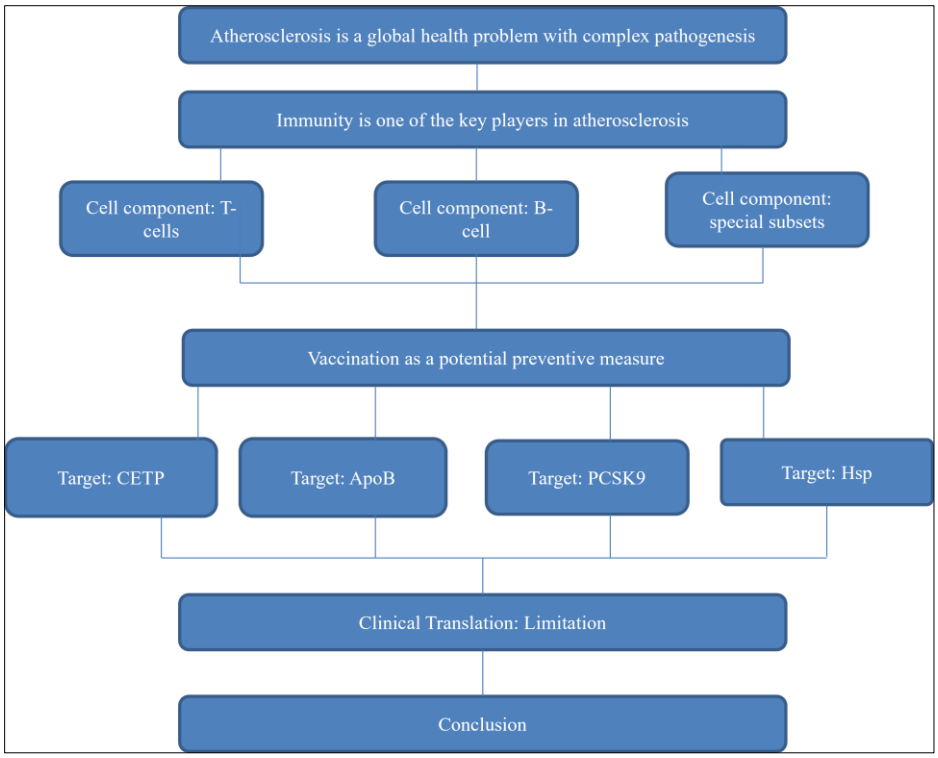

Figure 2 Pathophysiology of Atherosclerosis [17]

3. Risk factor of Atherosclerosis

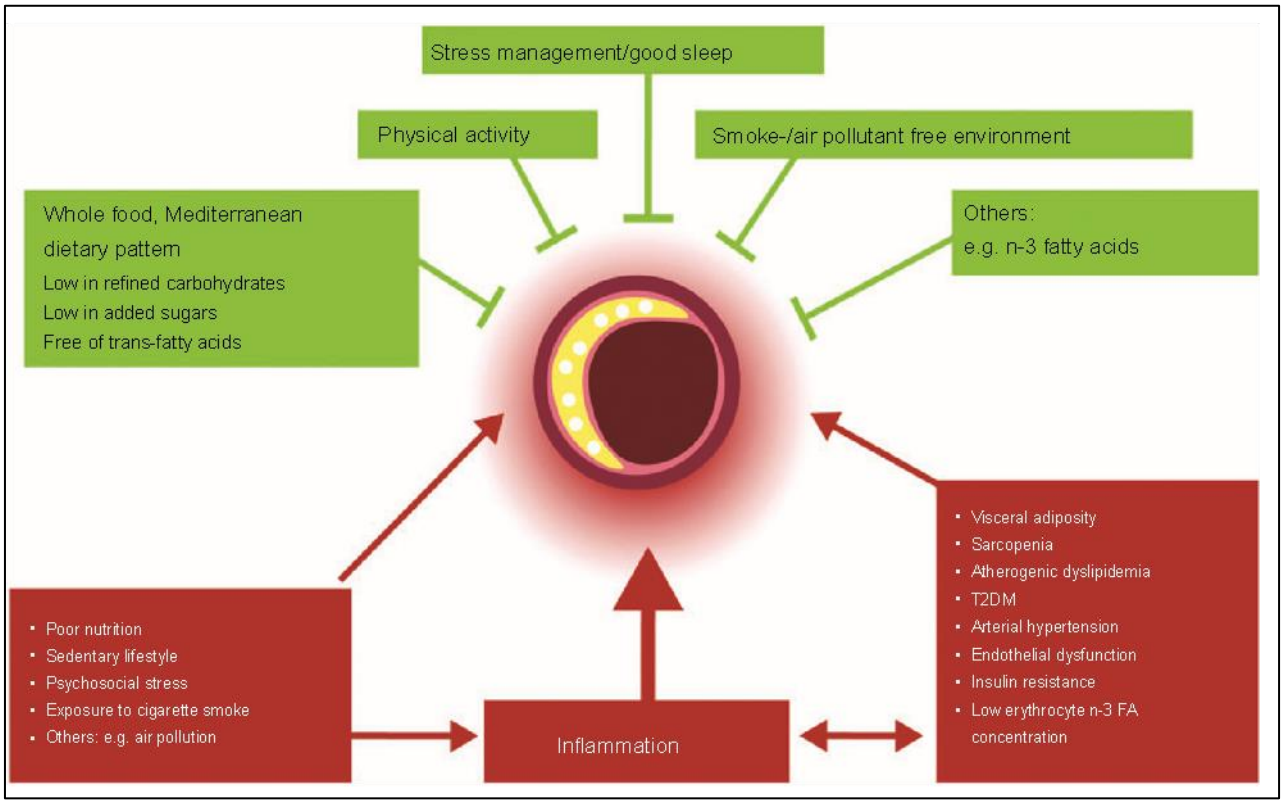

Figure 3 Lifestyle and high-risk atherosclerosis [20]

The production of digestive enzymes like matrix metalloproteinases increases with plaque inflammation, causing the fibrous cap that holds the plaque and its atherogenic debris together to thin out. This, in turn, creates the possibility of plaque rupture and intraluminal coronary thrombosis [10]. Because of their contractile qualities, vascular smooth muscle cells (VSMCs), the predominant constituent of the artery wall, are in charge of preserving vascular tone and controlling blood pressure [21]. Just ahead of COVID-19 and cancer, cardiovascular diseases (CVDs) continue to be the world's biggest cause of mortality. Myocardial infarction (MI), peripheral artery disease, and stroke are all included in the wide category of cardiovascular disease (CVD) [22]. The incidence of cardiovascular disease has sharply increased, leading to its development. Its causes are mostly lifestyle-related (diet, smoking, physical activity), while its developmental factors include things that are out of human control (age, gender, family history, and genetic markers) and things that can be changed (lipid disorders, diabetes, hypertension, obesity, metabolic syndrome, and inflammatory markers) [23]. Men often have a poorer risk factor profile than women, which probably contributes to the higher chance of early negative occurrences in men. Nonetheless, women are more affected by the majority of risk factors when it comes to increased cardiovascular risk [15]. The strong linkage between stroke and atherosclerosis is highlighted by the fact that both conditions are linked to shared risk factors such metabolic syndrome, hypertension, and type 2 diabetes [24]. Because of the magnetic field, metal implants provide a serious risk when using MRI imaging. Other disadvantages of MRI are its long operating time, high cost, and limited sensitivity [25]. The only proven method to lower the prevalence of CV illnesses is to restrict exposure to environmental risk factors, such as pollutants and dietary variables [26]. Given that elevated oxidative stress is linked to atherosclerotic risk factors, the theory seems likely [27]. According to their plasma metabolites profile, a recently published study demonstrates that probiotic supplements improve endothelial functions in people with coronary artery disease (CAD) without changing the microbiota population or conventional cardiovascular risk factors, only their transcriptional activity [28]. Research has indicated that among Mexican women, long-term stress is a risk factor for carotid atherosclerosis [29]. Because to the formation of fibrous tissue, calcification, inflammation, artery wall ulceration, and even bleeding, plaques grow into far more complicated lesions. Although the rupture or erosion of the plaque is what causes the thrombi that result in myocardial infarction, occlusion by plaque development is a significant risk factor [30]. In this area, triglycerides have garnered less attention than hypercholesterolemia. On the other hand, high triglycerides raise the risk of cardiovascular disease overall [31].

4. Diagnosis and treatment

Ultrasound (US), magnetic resonance (MR), and computed tomography (CT) imaging are the primary methods used in atherosclerotic diagnosis; nevertheless, they are only able to detect advanced lesions, and the evaluation of plaque vulnerability is insufficiently precise [32]. Improved knowledge of the Macs' heterogeneity specific to atherosclerotic disease phases would aid in the development of diagnostic techniques and individualized therapies [10]. Imaging is used to diagnose left ventricular noncompaction (LVNC) cardiomyopathy; however, the existing criteria are not precise, and overdiagnosis is possible [33]. The transferability of the acquired results was hampered by the contrasts between the human scenario and the rodent models. In humans, 70–80% of individuals had autoantibodies when they were diagnosed [11]. To identify high-risk individuals and customize treatment, it is crucial to accurately and reliably diagnose susceptible atherosclerotic plaques before they show clinical symptoms [34]. Conventional imaging techniques like angiography and perfusion imaging have transformed the diagnosis and management of flow-limiting atherosclerotic plaques that cause chronic ischemia by assessing the degree of luminal stenosis and promised blood flow [35].

Significant progress has been made in the scientific study and therapeutic management of atherosclerosis in recent years. Although the objective of conventional treatment is to reduce low density lipoprotein (LDL) levels, many patients experience recurring clinical episodes even after reaching their "goal" LDL levels. "Residual risk" is the term used to describe this ongoing cardiovascular risk following effective medication [36]. Despite taking statins, individuals with dyslipidemia showed transcriptionally activated hyper-responsive monocytes, indicating that trained immunity persists in settings that lower cholesterol [24]. While age-standardized mortality rates for CVD have significantly decreased in high-income regions due to preventative efforts such lowering blood pressure, smoking, and atherogenic lipids, as well as advancements in therapy, the prevalence of CVD is increasing in developing nations [16]. According to some research, longer-term oral vitamin C administration can improve endothelial function by either boosting endothelial noproduction or lowering ROS levels in the arterial walls [37]. Researching the infarct repair process and finding novel therapeutic targets to use in the management of this disease are crucial [38]. Anmalignant statin treatment may prevent and encourage regression in established atherosclerotic lesions in both the carotids and the aorta, according to a recent meta-analysis comprising 51 studies that used either US or MRI. This confirms one of the main objectives for the management of atherosclerosis [39].

5. Conclusion and future direction

The future of "smart" atherosclerotic imaging will most likely involve overcoming this by creating molecular contrast agents that are selective, have greater payloads, have appropriate on/off kinetics, and may even have numerous targets. Focusing on (a) body composition and cardiorespiratory fitness instead of BMI, (b) food-based, calorie-unrestricted dietary recommendations instead of nutrient- and calorie-based ones, and (c) addressing exposure to new lifestyle risk factors through public health interventions may lead to more practical lifestyle guidance, enhance long-term adherence, and improve prognosis. When combined, these strategies may yield cumulative benefits. Recent advancements in the use of epigenetics to treat atherosclerosis, with particular attention to histone deacetylases (HDACs), BETs, and potential future targets for repressive histone changes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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