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(REVIEW ARTICLE)

The impact of cigarette smoking on coronary artery disease: A comprehensive review

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Abstract

Coronary artery disease remains a leading cause of illness and death worldwide, with cigarette smoking being a significant modifiable risk factor for its onset and progression. This review examines the pathophysiological mechanisms by which smoking contributes to CAD, including endothelial dysfunction, chronic inflammation, and increased blood clotting tendencies. Epidemiological data emphasize the substantial burden of CAD among smokers and the direct link between smoking intensity and disease severity. Additionally, the review explores the harmful components of cigarette smoke and their specific effects on cardiovascular health. The paper highlights smoking cessation as a key strategy for preventing and managing CAD, addressing both its benefits and the challenges associated with quitting. It discusses various pharmacological and non-pharmacological interventions, underscoring the need for targeted smoking cessation programs to reduce CAD risk and enhance cardiovascular health.

Keywords: Smoking; Coronary Artery Disease; Lipid Levels

1. Introduction

An inadequate flow of blood and oxygen to the heart is known as coronary artery disease. This is brought on by coronary artery blockages, which cause an imbalance between the heart's supply and demand for oxygen. Plaque accumulation in the coronary artery lumen, which limits blood flow, is frequently the cause of the illness. [1]It is a multifactorial disease which is caused due to several factors that includes age, sex, family history, genetic factors, hypertension, diabetes mellitus, smoking, and high blood cholesterol. Smoking is a primary risk factor which accelerates plaque formation in coronary artery disease.[2]

The inhalation of cigarette smoke introduces a substantial number of oxidizing agents, which are linked to a reduction in the body's natural antioxidant levels. This depletion is associated with various mechanisms that may lead to cardiovascular disease. In smokers, modifications in blood coagulation, compromised arterial wall integrity, and alterations in blood lipid and lipoprotein levels increase the risk of developing CAD [3]

This review seeks to examine the impact of smoking on coronary artery disease (CAD), emphasizing the pathophysiological mechanisms, relevant epidemiological evidence, and the significance of smoking cessation in both prevention and treatment.

2. Epidemiology

Cardiovascular disease (CVD) ranks as a primary contributor to both death and illness, accounting for approximately 17.9 million fatalities globally each year. In 2022, there were 315 million cases of coronary artery disease (CAD) worldwide, with a prevalence rate of 3605 cases per 100,000 people, which marked an 18% decrease from 1990. The

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highest age- standardized prevalence of CAD in 2022 was found in Central Europe, Eastern Europe, and Central Asia (8019 cases per 100,000), while South Asia had the lowest prevalence (2393 cases per 100,000) [4][5] In 2019, over 1 billion individuals were identified as smokers, consuming in excess of 7 trillion cigarette-equivalents of tobacco. Since 1990, the rate of smoking has declined by 27–38% among both males and females; however, the overall number of smokers has risen due to the growth of the global population. Consequently, smoking was responsible for 7.7 million fatalities and 200 million disability-adjusted life-years, making it the primary risk factor for mortality among males, accounting for 20% of male deaths in 2019. [6]

In 1960, findings from the Framingham Heart Study demonstrated that smoking elevates the risk of heart disease. Consequently, smoking has been recognized as a significant risk factor for coronary artery disease (CAD). [2] Smoking is a significant factor in the development of coronary artery disease (CAD), accounting for around 17% of deaths in people over 65 and 23% of CAD cases in those under 45. [3]

2.1. Pathophysiology

The formation of atherosclerotic plaque is a defining feature of the pathophysiology of CAD. A fatty substance accumulation called plaque constricts the artery lumen and prevents blood flow. It begins with the development of a "fatty streak," where lipid- rich macrophages, known as foam cells, accumulate in the subendothelial space. In response to vascular injury, monocytes transform into macrophages, which absorb oxidized LDL particles, forming foam cells. Activated T cells release cytokines, further promoting this process. Growth factors stimulate smooth muscle cells to take up collagen and oxidized LDL, contributing to foam cell formation and plaque build-up. This results in subendothelial plaque formation. If the plaque remains stable, it may eventually become calcified and develop a fibrous cap. However, if the plaque enlarges or ruptures, it can lead to reduced blood flow, causing angina during periods of high demand. Resting symptoms may subside as oxygen demand decreases. A lesion must be at least 90% stenotic to cause angina at rest. In some cases, plaque rupture exposes tissue factors, leading to thrombosis, which can completely or partially occlude the artery [1]

2.2. Cigarette smoke

Approximately 7,357 distinct chemicals from various classes exist in either bound or free forms within aerosol or gas phases. Tar, or Total Aerosol Residue, refers to the mass of solid materials left after removing water and nicotine. This thick brown substance stains teeth and causes yellow-brown discoloration of fingers. It is effectively captured by the Cambridge glass-fiber filter, which retains 99% of particulate matter. The gaseous phase primarily contains nicotine, an addictive compound that, in small doses, is relatively harmless and serves as a mild stimulant and relaxant, along with carbon monoxide. Prolonged exposure to carbon monoxide can elevate carboxyhemoglobin levels by up to 10% in heavy smokers, leading to functional anemia and hypoxemia.[7]

This paper adheres to the criteria established by Fowles and Dybing, emphasizing chemical constituents with significant toxic potential, particularly those linked to cancer, respiratory, and cardiovascular diseases. For cardiovascular diseases, cyanide, arsenic, and cresols are identified as major hazards, while N-nitrosamines and polycyclic aromatic hydrocarbons also raise concerns. These elements, along with Hoffman's catalogue of biologically active chemicals, assist in identifying toxic substances in cigarette smoke.

The chemical makeup of cigarette smoke differs among types: mainstream smoke (MS), which is inhaled; side-stream smoke (SS), emitted from the burning end; and second-hand smoke (SHS), a mix of both. Side-stream smoke has higher concentrations of heavy metals and nitrosamines than other forms. Furthermore, the average concentration of polycyclic aromatic hydrocarbons (PAHs) is greater in both mainstream and side-stream smoke compared to cigarette butts, while phenol levels are also elevated in side-stream smoke. Mainstream smoke (MS) consists of 8% tar and 92% gases.

The tar contains over 10^17 free radicals per gram, which can last from hours to months, while the gas phase has more than 10^15 free radicals per puff, persisting only for seconds. Research mostly identifies carbon monoxide, reactive oxygen species, and nicotine as the main causes of smoking-related cardiovascular problems, despite the fact that cigarette smoke is complicated and contains approximately 4,000 chemicals associated with cardiovascular disease (CVD).[7]Earlier studies suggested a connection between carbon monoxide (CO) and cardiovascular changes from smoking, similar to hypoxic hypoxia. However, recent evidence indicates that CO is unlikely to play a significant role in atherosclerosis progression. Nicotine is the most studied component; it is known to increase cardiac output, heart rate, and blood pressure, yet its precise role in Atheros-thrombotic diseases remains unclear.

Currently, reactive oxygen species (ROS) are acknowledged as crucial factors in atherosclerosis development, originating from both the gas and tar phases of cigarette smoke, as well as from immune cells like monocytes, macrophages, and neutrophils, along with endogenous sources such as xanthine oxidase, endothelial nitric oxide synthase (eNOS), and the mitochondrial electron transport chain. [7]

3. Mechanisms of smoking-induced coronary artery disease

A number of clinical atherosclerotic illnesses, including acute coronary syndromes, aortic and peripheral artery diseases, cerebrovascular disorders, and sudden cardiac death, are associated with an increased risk of cigarette smoking. The processes of endothelial dysfunction, inflammation, and a hyper coagulable state play crucial roles in the onset and advancement of atherosclerosis.

3.1. Endothelial dysfunction

Numerous clinical and laboratory investigations have demonstrated that cigarette smoke induces endothelial dysfunction primarily through reduced bioavailability of nitric oxide (NO), heightened generation of superoxide anions, and increased synthesis and secretion of endothelin. The formation of reactive oxygen species (ROS) and the impairment of endothelial nitric oxide synthase (eNOS) are significant factors contributing to atherosclerosis associated with smoking. The gas phase of cigarette smoke is rich in free radicals and pro-oxidants, including NO, nitrogen dioxide (NO2), phenols, and nitrosamines. Conversely, the tar phase contains substantial amounts of quinones, which participate in redox cycles that generate superoxide (O2−), hydrogen peroxide (H2O2), and other oxidizing agents. Superoxide present in cigarette smoke is transported via the bloodstream to the vascular endothelium, where it interacts with nitric oxide to produce the highly cytotoxic peroxy nitrite anion (ONOO−). Additionally, the activation of nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) and xanthine oxidase has been found to enhance ROS production in endothelial cells. Water-soluble components of tobacco can induce mitochondrial outer membrane permeabilization (MOMP), which, while not directly causing cell death, leads to the leakage of mitochondrial contents, such as mitochondrial DNA and electrolytes, into the cytoplasm. This leakage can trigger ROS production and the release of damage-associated molecular patterns (DAMPs), which are inflammatory mediators.

3.2. Inflammation

Chronic inflammation within the vessel wall is a significant contributor to the development of atherosclerosis, with smoking identified as the primary initiating factor. At the cellular level, pattern recognition receptors of the innate immune system, notably Toll-like receptor 9 (TLR9), the NLRP3/AIM2 inflammasome, and cyclic GMP-AMP synthase (cGAS) in conjunction with the stimulator of interferon genes (STING), are integral to the formation of vascular lesions. cGAS is triggered by the release of free mitochondrial DNA (mtDNA) through minor mitochondrial outer membrane permeabilization (MOMP). Both the TLR9 and cGAS-STING pathways contribute to the upregulation of cytokine production, particularly interleukin-6 (IL-6) and interleukin-8 (IL-8). Additionally, cytosolic mtDNA released via minor MOMP activates the AIM2 inflammasome, while reactive oxygen species (ROS) typically stimulate the NLRP3 inflammasome. These inflammasomes promote pyroptosis mediated by gasdermin D (GSDMD) and the subsequent release of cytokines IL-1β and IL-18.

3.3. Hypercoagulable state

Cigarette smoke triggers the activation of endothelial cells, which results in heightened levels of ICAM-1, VCAM-1, and selectins (P and E). This process facilitates the attachment of monocytes/macrophages, lymphocytes, and platelets to the prothrombotic endothelium. Additionally, the presence of von Will brand factor (vWF) on the exposed sub endothelium induces platelet activation, adhesion, and aggregation, ultimately leading to thrombus formation. Prolonged smoking contributes to the development of atheromatous plaques, driven by an increased expression of matrix metalloproteinase (MMPs), specifically MMP-12 and MMP-9 in macrophages, MMP-8 and MMP-9 in endothelial cells, and MMP-2 and MMP-9 in vascular smooth muscle cells [7]

4. Clinical outcomes of smoking in cad patients

4.1. Early onset of CAD

Smoking's role in causing early atherosclerosis in young men between the ages of 30 and 40, so there is a direct correlation between increasing smoking severity and higher serum lipid profile levels and a higher risk of coronary

disease development. In order to protect young smokers' heart health, it is highly advised that they abstain from smoking [3].

4.2. Increased severity of CAD

The number of blocked coronary arteries can rise as a result of smoking duration, smoking dose, and disease duration. Smoking and the severity of CAD are related. The findings of the study also indicated that smoking was linked to LAD artery occlusion and that smokers might be at a higher risk of developing non-proximal coronary artery occlusion. One possible explanation for this link is the way that cigarettes and nicotine affect the vascular epithelium; nicotine can harm the coronary vascular epithelium. Additionally, smoking induces vasospasm and raises sympathetic tone. Nicotine's effects can result in myocardial necrosis. [2]

4.3. Impact on Post-Surgical Outcomes

There are drawbacks and consequences to both medicinal and surgical treatment for ischemic heart disease. Careful selection, medical knowledge, and patient education could all help to lessen these negative consequences. Arrhythmias, cardiac tamponade, post-operative hemorrhage, infection, renal impairment, and phrenic nerve injury are just a few of the risks that might arise with CABG. [1]

5. Smoking cessation and cardiovascular health

5.1. Benefits of Quitting Smoking

According to the study, people with CAD who quit smoking had a 20% lower chance of having a myocardial infarction the year after. According to a different study, quitting smoking decreased the quantity and severity of coronary artery alterations [2].

5.2. Challenges in Smoking Cessation

Smoking cessation is usually related with weight gain, with individuals typically seeing an increase of roughly 4–5 kg during the first year after stopping. Additionally, there may be a reduction in glucose and lipid metabolism, and weight gain can often cause persons to resume smoking In conclusion, weight gain frequently happens after Quitting smoking. [7]

5.3. Intervention Strategies

The three primary categories of non-pharmacologic smoking cessation therapies are clinical, public health, and alternative. Self-help programs, phone counselling, cognitive-behavioral therapy, and fitness regimens are examples of clinical treatments. Public health strategies include policy reforms as well as workplace, multimedia, and community interventions. Aversive therapy, acupressure, and hypnosis are further techniques.[7] All patients who want to quit smoking should have access to pharmacologic treatment, unless there are contraindications. The Food and Drug Administration (FDA) currently has seven medications approved for smoking cessation: varenicline, bupropion sustained-release (SR), transdermal nicotine patches, nicotine gum, nicotine lozenges, nicotine inhalers, and nicotine nasal spray [7].

6. Conclusion

Cigarette smoking plays a significant role in the development and progression of coronary artery disease (CAD) through various pathological mechanisms, including oxidative stress, endothelial dysfunction, chronic inflammation, and increased blood coagulability. Extensive epidemiological research has established a strong link between smoking and an elevated risk of CAD, particularly in younger individuals, highlighting its status as a major preventable cause of cardiovascular disease. Smoking cessation has been shown to lower CAD risk, enhance cardiovascular health, and reduce mortality rates. However, quitting smoking presents challenges, such as weight gain and metabolic changes, which can contribute to relapse. Therefore, a combination of pharmacological therapies and behavioural interventions is essential for achieving long-term smoking cessation and minimizing its harmful cardiovascular effects.

Future recommendations

- Future research should focus on developing more effective smoking cessation strategies that minimize side effects, particularly those related to weight gain and metabolic disturbances.
- Public health initiatives should strengthen awareness campaigns and enforce stricter regulations on tobacco advertising and sales to discourage smoking initiation.
- In order to develop targeted treatments, further research is required to examine the genetic and molecular processes through which smoking affects the course of CAD.
- Long-term cohort studies should evaluate the effects of smoking cessation on CAD progression and the efficacy of different intervention approaches.
- Smoking cessation programs should be fully integrated into routine cardiovascular care to ensure comprehensive management of CAD patients.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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