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The Effects of Cigarette Smoking on the Cardiovascular System: Mechanisms of Damage, Risk Factors, and Prevention Strategies

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Abstract

Introduction: Cardiovascular diseases remain the leading cause of morbidity and premature mortality. Even though the prevalence of cigarette smoking has decreased over the last few decades, it is still one of the most important preventable risk factors for cardiovascular diseases. Moreover, recently, an increasing number of people have been transitioning to e-cigarettes, which also influence blood pressure and the cardiovascular system.

Purpose of the study: The following review analyzes the association between cigarette smoking and both prevalence and development of cardiovascular diseases. It also suggests the management of tobacco addiction.

Materials and methods: A literature review of English language papers was conducted to summarize the latest knowledge on the topic, focusing on the most recent papers. The review was conducted using the PubMed database, with 53 works used and accessed before December 2024.

Conclusions: Tobacco significantly affects the cardiovascular system, with numerous studies highlighting the negative impacts of both active and passive smoking. Although extensive knowledge exists about tobacco smoke's impact on the cardiovascular system, further research is still needed. A better understanding of the link between smoking and the development of cardiovascular diseases, as well as methods for the management of the addiction, is crucial to developing successful treatment and prevention strategies.

Keywords: cigarettes, tobacco, smoking, cardiovascular disease

Introduction to the Epidemiology of Smoking

Cigarette smoking remains a leading global cause of preventable morbidity and mortality, contributing to more than 8 million deaths annually, of which over 7 million are directly attributable to tobacco use and approximately 1.2 million result from exposure to secondhand smoke. Despite global public health efforts, smoking prevalence continues to exhibit significant variability across regions, with higher rates observed in low- and middle-income countries. These disparities are influenced by factors such as socioeconomic status, cultural norms, and aggressive marketing by tobacco companies [1,2].

The prevalence of smoking among adults globally has declined over recent decades, largely due to the implementation of effective tobacco control policies, including taxation, public smoking bans, and public health campaigns. For instance, the World Health Organization's (WHO) Framework Convention on Tobacco Control has guided countries in adopting evidence-based measures to reduce tobacco use. Nevertheless, challenges persist, particularly in curbing the increasing use of alternative nicotine delivery systems, such as e-cigarettes, and addressing tobacco use among adolescents and women in some regions [1,2].

Understanding the epidemiological trends of smoking is critical for identifying vulnerable populations and designing targeted interventions. The global decline in smoking prevalence is encouraging, yet the absolute number of tobacco-related deaths continues to rise due to population growth and aging [2].

Cardiovascular diseases and smoking

Cardiovascular disease is the leading cause of morbidity and premature mortality, causing 17.9 million deaths per year [3]. There is no doubt that cigarette smoking is a key modifiable risk factor for cardiovascular disease (CVD) and as much as 10% of CVD-related deaths are attributable to smoking [4]. Passive smoking also hurts health [5]. Smokers and passive smokers are at risk for reduced heart rate, hypertension, decreased exercise tolerance, and coronary artery disease [6]. Furthermore, a case-control study has shown that the offspring of pregnant women exposed to tobacco smoke during the first three months of pregnancy may have an increased risk of coronary artery disease [7].

Smoking-induced cardiac damage is associated with two main mechanisms: a direct adverse effect on the myocardium leading to smoking-related cardiomyopathy and an indirect effect on the myocardium by inducing complications: atherosclerosis and hypertension, which ultimately cause cardiac damage and remodeling [8]. Lifelong smokers lose at least 10 years of life [9]. Smoking increases the risk of hypertension, which is a major risk factor for stroke, myocardial infarction, heart failure, and sudden cardiac death [10]. The risk of these conditions and others such as atrial fibrillation, and aortic aneurysms increases about 2-4 times in smokers compared to non-smokers. This correlation is associated with a low capacity for detoxification of xenobiotic products by cardiovascular tissues [11]. However, the mechanisms affecting the cardiovascular system associated with cigarette smoking are complex. One of the first discoveries in this area was the harmful effect of tobacco smoke on

the vascular endothelium. Oxidizing compounds in cigarette smoke cause oxidative stress in the endothelium, which leads to the impairment of its structure and, consequently, dysfunction of vasodilation, and disturbances of homeostasis. Factors adversely affecting the endothelium include increased production and release of endothelin, higher levels of superoxide anions, and reduced NO bioavailability [3].

Tobacco smoke consists of over 7,000 different chemical compounds. It is difficult to indicate one direct component responsible for the association with cardiovascular diseases because probably no single component will be associated with endothelial dysfunction. Whereas the complex mixture of components that interact with each other participates in the initiation of atherosclerosis and negatively affects the cardiovascular system [12].

The most popular component of tobacco smoke is nicotine, which serves as the main addictive substance in tobacco products. This alkaloid acts on nicotinic acetylcholine receptors [13, 14]. Chronic smoking leads to desensitization of nicotinic receptors and consequently to stiffening and narrowing of blood vessels, increased blood pressure, decreased insulin sensitivity, and this may lead to diabetes or exacerbate existing diabetes [15]. Cigarette smoke consists of a gaseous and molecular phase [16]. The gaseous phase contains, among others, large amounts of reactive oxygen species, nitric oxide, reactive nitrogen species, and nitrosamines. Interestingly, unique tobacco-specific nitrosamines are also identified in e-cigarettes containing nicotine. Nitrosamines are carcinogenic factors [17]. Carcinogenic substances can damage DNA and accelerate aging while increasing the incidence of cardiovascular diseases in smokers [18]. The molecular phase of tobacco smoke contains quinones in high concentrations, which in biological systems undergo a redox reaction leading to the formation of O2-, which then reacts in the vascular endothelium with NO and the formation of the highly cytotoxic peroxynitrite anion ($ONOO^-$). This explains the decrease in vasodilation [19]. Flow-mediated dilatation (FMD) is a commonly used method to assess endothelial function in large vessels. FMD is reduced in smokers and passive smokers [20]. It usually returns to normal levels within a year of quitting smoking [21,22]. Another important element linking smoking with cardiovascular diseases is chronic inflammation of the vascular wall, which is the main pathogenic mechanism of smoking-induced atherosclerosis [4]. The detailed mechanism of inflammation is not fully clear, but it is associated with local and systemic activation of the immune system mediated by pattern recognition receptors (PRR) and damage-associated molecular patterns (DAMP). DAMPs are molecular structures released from damaged cells and tissues, as well as from necrotic cells involved in the induction of innate immunity and inflammation [23]. An increase in neutrophils, lymphocytes, and monocytes is observed in smokers [24]. The level of inflammatory cytokines, such as tumor necrosis factor-α increases. CRP levels also increase [25, 26]. All this leads to chronic vascular inflammation and the progression of atherosclerosis. In addition, cigarette smoke affects atherothrombosis by increasing platelet activation, adhesion, and aggregation. The coagulation cascade and fibrinolysis are impaired [27,28]. It is worth mentioning that long-term smoking impairs the release of NO from platelets [29]. Of smokers, an increase in von Willebrand factor has also been noted in endothelial cells [30]. A subendothelial matrix in contact with flowing blood promotes platelet activation and aggregation. This is due to the interaction between platelet surface glycoprotein receptors, subendothelial collagen, and von Willebrand factor. This process is the initial stage of pathological thrombus formation [31]. However, cigarette smoking affects all phases of atherosclerosis up to acute clinical events. Numerous studies confirm that tobacco smoke contributes to the formation of thrombi and the progression of atherosclerosis, which consequently increases the risk of acute coronary syndrome [32]. Among patients with acute coronary syndrome, smokers have a higher rate of thrombus formation in stents. Moreover, as

many as two-thirds of smokers die from sudden cardiac death caused by acute atherothrombosis [33]. Some biochemical markers of heart dysfunction show a correlation with cigarette smoking. For example, a marker associated with ventricular dysfunction and heart failure (natriuretic peptide) is increased in both smokers and passive smokers. However, a marker of acute myocardial infarction – troponin-I (cTnI) – is lower in smokers compared to nonsmokers [34]. In a study on the correlation between smoking and the risk of atherosclerotic cardiovascular disease (ASCVD) conducted by Jamal S Rana et al. and published in 2021, smokers had more than twice the risk of ASCVD than nonsmokers.
ASCVD has been defined as a composite of nonfatal MI, ischemic stroke, or coronary heart disease death by December 2015 [35]. The relationship between smoking and lipid abnormalities is also noteworthy. Recent studies have shown that this relationship is crucial for coronary artery disease. Smokers have increased triglyceride levels and decreased HDL–C levels, which are two key factors in the development of coronary artery disease [36]. Heart rate variability (HRV) is a technique that can predict cardiovascular health problems and can also be used to predict the health effects of smoking. Active and passive smoking disrupts the proper functioning of the autonomic nervous system, leading to increased sympathetic arousal. These disorders can lead to atrial fibrillation [37].

In recent years, e-cigarettes have become popular as alternatives to traditional cigarettes. Long-term studies on their cardiovascular effects are scarce, but early evidence suggests that they also have adverse cardiovascular effects. E-cigarette aerosol contains several potentially harmful chemicals that have been linked to critical pathophysiological pathways in cardiovascular disease. This can lead to endothelial dysfunction, oxidative stress, and vascular inflammation [38].

Despite the current extensive knowledge of the impact of tobacco smoke on the cardiovascular system, further research is still needed. Smoking significantly increases the risk of cardiovascular disease in active and passive smokers. This risk increases with the number of cigarettes smoked per day [39]. It is known that the most effective measure to prevent fatal cardiovascular consequences is to stop smoking. Unfortunately, the increased risk of cardiovascular disease may remain elevated for a decade or even longer after stopping smoking [40]. However, it is interesting that quitting smoking can reverse some of the endothelial damage and improve vascular function. Therefore, it is important to quit smoking as soon as possible, because some changes in the body may become irreversible over the years [41].

Quitting smoking and improving health

Active and also passive smoking is as proven deleterious effects on cardiovascular system [42,43]. However, the degree and speed at which it impacts current death rates from smoking-related diseases remain unclear [46]. In recent years, tobacco use among individuals aged 15 and older has shown a relative decline, with global trends indicating that countries are on course to achieve a 22% reduction in tobacco use by 2025. Nevertheless, despite the consistent decrease in the global number of smokers, tobacco continues to claim over seven million lives annually [45]. This applies to both regular and electronic cigarettes. With the growing popularity of e-cigarettes, their impact on health has also caught the attention of researchers. Especially since they were initially considered a healthier equivalent of traditional cigarettes. Changing classic cigarettes to e-cigarettes was considered an effective way to quit smoking, the so-called lesser evil [44].

However, the American Consensus Study Report on the public health consequences of e- cigarettes stated most e- cigaretts contain and emit toxic substances. E-cigarette use has been reported to cause an increase in heart rate and blood pressure. However, there is limited evidence linking e-cigarettes to long-term effects on heart rate, blood pressure, or changes in cardiac structure and function [44].

Non-pharmacological methods for smoking cessation are commonly used by smokers. However, current research on their effectiveness presents inconsistent findings and varies in quality [45].

Smoking is the main risk factor for atherosclerotic cardiovascular disease. It causes oxidative stress, raises the danger of sudden thrombotic events, inflammatory alterations and increased risk of stroke. Smoking is associated with an increase in cardiovascular diseases and a decrease in life quality [47]. Cigarette smoke contributes to the development of atherosclerosis by causing chronic inflammation of the blood vessel walls. Furthermore, cigarette smoke enhances platelet activation, increasing platelet aggregation and adhesion at sites of endothelial injury. These complex processes underscore the harmful effects of cigarette smoking on endothelial function, inflammation, and thrombosis, emphasizing the critical role of smoking cessation in maintaining cardiovascular health. Given the substantial public health burden of cardiovascular diseases, especially among smoking populations, emphasizing the critical importance of smoking cessation is imperative [48]. Quitting smoking at any age, is linked to reduced occurrence vascular diseases and mortality overall. Positive effects were noticeable as early as three years after quitting [46].

5. Prevention and treatment strategy

Article 14 of the Framework Convention on Tobacco Control stipulates that each country should provide support for smoking cessation, and implementing this approach is currently under consideration in many countries. Smoking cessation support should be a core component of tobacco control strategies in all European countries. [49]
Five strategies are recommended for addressing tobacco use in clinical settings. Known as the 5As (ask, advise, assess, assist, arrange), these strategies are:
• **Ask** all patients whether they smoke;
• **Advise** patients who smoke to quit;
• **Assess** their readiness to quit;
• **Assist** them in attempting to quit by providing behavioral counseling and prescribing smoking cessation medications; and
• **Arrange** follow-up support.

In current practice, there are two main types of smoking cessation interventions: minimal intervention (brief advice) and specialized smoking cessation treatment. Brief advice consists of "a summary of verbal guidance to quit smoking, presented in medical terms and including information on the harmful effects of smoking." Specialized smoking cessation treatment involves the administration of medications proven effective in treating nicotine addiction, along with a series of individual cognitive-behavioral counseling sessions. [49] There is high-quality evidence that individually-delivered smoking cessation counselling can assist smokers to quit. There is moderate-quality evidence of a smaller relative benefit when counselling is used in addition to pharmacotherapy, and of more intensive counselling compared to a brief counselling intervention. [50]

The standard way most people are advised to stop smoking is by quitting abruptly on a designated quit day. However, many people who smoke have tried to quit many times and may like to try an alternative method. In the study conducted by Lindson and colleagues, there was insufficient information to determine whether reducing smoking before quitting helped more people to stop smoking compared to no smoking cessation treatment. However, people who were asked to stop smoking all of their cigarettes at once were not more likely to quit than people who were asked to cut down their smoking before quitting. This suggests that asking people to cut down their smoking first may be a useful way to help people to stop smoking. People who cut down their smoking while using varenicline or a fast-acting form of nicotine replacement therapy (NRT), such as gum or lozenge, may be more likely to quit smoking than people who cut down their smoking without using a medicine to help them. Giving people face-to-face support to cut down their smoking may help more people to quit than if they are provided with self-help materials to cut down by themselves. [51]

Pharmacotherapy for smoking cessation is recommended for all smokers attempting to quit, unless contraindications are present. Although these medications work through different mechanisms of action, they can reduce the physical symptoms of nicotine withdrawal as well as the immediate, reinforcing effects of nicotine absorbed through tobacco if the person smokes. [52] Network meta-analyses have examined the absolute and relative efficacy, as well as the cardiovascular safety, of pharmacotherapy for smoking cessation. In a 2013 Cochrane network meta-analysis involving 267 studies with over 100,000 participants, nicotine replacement therapy (NRT), bupropion, varenicline, nortriptyline, and cytisine were all found to be more effective than placebo. Bupropion and NRT were comparable in terms of efficacy, while varenicline was more effective than single forms of NRT and bupropion. [53] Neither bupropion nor varenicline demonstrated an increased cardiovascular risk compared to placebo.

Combination pharmacotherapy involves the use of medications that work through different mechanisms and/or have different pharmacokinetics. [52] The combination of a slow-release nicotine patch with nicotine gum, lozenges, an inhaler, or a nasal spray (all with fast-release formulations) is more effective than using single NRT products and is equally effective as varenicline. Bupropion combined with a nicotine patch is more effective than bupropion alone, and adding bupropion to combined NRT (nicotine replacement therapy) improved efficacy compared to combined NRT alone. [53]

6. Conclusion

Smoking cigarettes has a significant impact on the cardiovascular system. Numerous studies have highlighted their negative effects on health and the reduction of life expectancy. Both active and passive smoking lead to changes in the body that can result in various diseases. An increasing number of individuals are transitioning from traditional cigarettes to e-cigarettes, which also adversely affect blood pressure and the cardiovascular system. Many people are now being encouraged to quit smoking altogether. We offer various methods to support patients in this effort, ranging from reducing the frequency of smoking to pharmacotherapy options. In summary, extensive research confirms the detrimental impact of tobacco on the cardiovascular system and its association with higher mortality rates. This growing awareness allows us to encourage patients to quit smoking through various approaches.

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