



# Impact of Cigarette Smoking and Exercise on Arterial Stiffness: A Narrative Literature Review

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**PURPOSE:** Smoking often causes acute and chronic cardiovascular disorders. Cigarette smoking increases oxidative stress, reduces nitric oxide bioavailability, and changes the extracellular matrix, impairing arterial stiffness. However, regular physical activity and smoking cessation significantly and rapidly reverse the detrimental effects. This narrative review summarizes the relevant research that describes the impacts of cigarette smoking on the cardiovascular system and demonstrates the therapeutic or preventative roles of exercise and smoking cessation in smoking-associated arterial stiffness.

**METHODS:** We used scientific search engines, including PubMed, Web of Science, Google Scholar, and Wiley Online Library, to identify previous studies exploring the effects of smoking, exercise, and smoking cessation on arterial stiffness.

**RESULTS:** We discussed the most important therapeutic and/or preventive roles of exercise and smoking cessation in decreasing arterial stiffness. Most studies have demonstrated that acute and chronic smoking increase arterial stiffness. Smoking and physical activity were negatively associated. However, this relationship was often attenuated or reversed during adult exercise interventions. In addition, smoking cessation reversed the effects of smoking on arterial stiffness.

**CONCLUSIONS:** Smoking increases the risk of acute and chronic cardiovascular disease. Cigarette smoking deteriorates arterial stiffness by altering the vascular walls. However, regular exercise and smoking cessation can improve or prevent impaired arterial stiffness.

**Key words:** Arterial stiffness, Cardiovascular diseases, Exercise, Smoking cessation, Tobacco

## INTRODUCTION

Smoking causes a variety of diseases and reduces the quality of life and life expectancy [1]. The World Health Organization Framework Convention on Tobacco Control indicates that tobacco harms human health and should be avoided [2]. Cardiovascular disease is a leading cause of death in South Korea, and cardiovascular diseases (CVD)-related deaths increased from 112.3 to 122.7 per 100,000 individuals between 2008 and 2018 [3]. Over 480,000 people die from smoking cigarettes annually in the United States, where smoking is the leading cause of preventable death [1,4]. Worldwide, using tobacco results in approximately 6

million fatalities and more than \$500 billion in economic losses [2]. Smoking is the primary preventable risk factor for cardiovascular complications, including coronary artery disease, peripheral arterial disease, stroke, and hypertension [5].

Smoking causes approximately 30% of CVD-related deaths [6]. Active smokers reportedly have an average of 10 years lower life expectancy compared with non-smokers [7]. Smoking-induced CVD is attributed to endothelial dysfunction or harmful hemodynamic responses, including arterial stiffness [8]. A growing body of evidence suggests that smoking results in macro/microvascular stiffness and accelerates premature mortality independently [9-12]. Lifestyle modification and nursing interven-

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tions (e.g., exercise, smoking cessation therapies, counseling for behavior change) are strongly recommended for healthy or unhealthy smokers. Specifically, previous studies have demonstrated that smoking cessation is likely to restore cardiovascular dysfunction and attenuate CVD-mediated mortality [13,14]. In addition, regular exercise is the best evidence-based strategy for improving or ameliorating central/peripheral arterial stiffness in both non-smokers and smokers [15,16]. This mini review focuses on the harmful effects of cigarette smoking on cardiovascular complications and arterial stiffness. It also summarizes the relevant studies demonstrating that aerobic and resistance exercises mitigate cigarette smoking-associated arterial stiffness.

## METHODS

We collected and analyzed studies on the impact of smoking, exercise, and smoking cessation on arterial stiffness via scientific research engines including PubMed, Web of Science, Google Scholar, and Wiley Online Library.

## RESULTS

### 1. Cigarette smoking and cardiovascular disease

CVD has been the main cause of mortality and morbidity in the United States over the last 80 years, and it is responsible for more than 800,000 deaths annually in industrialized nations [1,2,17]. Cigarette smokers have an increased risk of CVD compared with nonsmokers [18]. Nearly one-fifth of deaths from CVD are caused by smoking [19], which is one of the main, preventable, and independent risk factors for CVD, including myocardial infarction, angina pectoris, stroke, heart failure, atrial fibrillation, and peripheral artery disease [20]. Approximately 25.9 million men (27.8%) and 23.5 million women (23.3%) in the United States are smokers [1]. Middle-aged male and female smokers have a four- and five-fold higher risk, respectively, of death from coronary heart disease.

Tobacco is a complex mixture of more than 9,000 substances such as oxidizing chemicals, carbon monoxide, volatile organic compounds, heavy metals, tar, and nicotine [19,21]. Tobacco's complexity makes it challenging to identify the pathophysiological mechanisms underlying the negative effects of smoking on the cardiovascular system. Therefore, further research is necessary to elucidate the cardiovascular adaptations to tobacco-related components and the ensuing health problems.

The impact of nicotine, a component of cigarettes, on systemic hemodynamics is closely linked to the activation of sympathetic nerves [22]. Nicotine enhances the release of epinephrine and norepinephrine from the adrenal glands and adrenergic neurons, respectively [19]. The activation of nicotinic cholinergic receptors (nAChRs) in the central and peripheral nervous systems (e.g., carotid chemoreceptor) stimulates the sympathetic nerves [22]. Cigarette smoking elevates plasma adrenaline by more than 150% and stimulates myocardial contractility, blood pressure, and heart rate (up to 10-15 beats per minute acutely) [19]. Nicotine-induced elevation of the heart rate, cardiac muscle contractility, and afterload (e.g., peripheral vascular resistance induced by vasoconstriction) may result in cardiovascular disorders.

The observation that smokers have chronically higher levels of muscle sympathetic activation—likely due to nicotine—supports smoking's long-lasting effect on blood pressure [23]. A recent study involving a large cohort of individuals aged 55 and older found significant associations between smoking and hypertensive heart disease and hypertensive renal disease [24]. While other chemicals in cigarettes may gradually damage blood vessels, nicotine may induce vasoconstriction and cause vascular damage [22]. Most of the previous studies on smokeless tobacco did not indicate that individuals exposed to nicotine are more likely to develop hypertension [25].

Smoking alters many blood constituents, including white blood cells and platelets [20]. It increases white blood cells by increasing the number of peripheral blood neutrophils [26], and even smoking just a few cigarettes activates leukocytes [27]. Neutrophil activation may increase the risk of cardiovascular disease development [20]. As neutrophils produce more oxygen-derived free radicals or elastases, the endothelium and arterial wall may degrade and/or accelerate atherosclerosis onset and progression [20]. Patients with and without coronary atherosclerosis may experience myocardial infarction due to these hematological alterations, which hastens thrombus formation.

Lipoproteins transport triglycerides and cholesterol in the bloodstream and help maintain the lipid balance in the body. Smoking leads to lipid and lipoprotein abnormalities, as smokers have increased low-density lipoprotein (LDL) and decreased high-density lipoprotein (HDL) compared with nonsmokers [17]. Increased cholesterol levels in smokers also indicate a higher risk of coronary heart disease [27]. Atherosclerosis onset and development are linked to higher LDL levels from cigarette smoking [20].

Cigarette smoking is a strong risk factor for cardiovascular disease.

Smoking-related vascular damage is caused by alterations in the pathophysiological processes that link smoking and cardiovascular disease, such as systemic hemodynamics, hemostatic factors, endothelial function, hematology, and dyslipidemia.

## 2. Cigarette smoking and arterial stiffness

Large and medium-sized arteries deliver blood to the peripheral arteries. Blood pressure (BP) oscillations are smoothed by these arteries' elastic characteristics, reduce the pulse pressure (PP), and perfuse the myocardium [28]. These characteristics rely on arterial stiffness, which controls the velocity of the incident and the reflected traveling pressure wave [29,30].

Applanation tonometry, Doppler, ultrasound, and echo-tracking are noninvasive methods that are frequently used to quantify arterial stiffness [31-33]. Until now, arterial stiffness has been measured easily, non-invasively, and consistently using pulse wave velocity (PWV), a measurement of how far a wave has traveled divided by the time it took to cover that distance [ $PWV = \text{distance (m)}/\text{transit time (s)}$ ] [30]. PWV, which indicates arterial stiffness in the vascular tree, can be measured between two sites located a specified distance apart. The pressure wave passes more quickly through a stiff artery and with more arterial waves applied from the periphery [29,31]. Normally, increased PWV can cause the reflected wave to reach the heart during late systole to diastole [31]. This quick return of the reflected wave raises systolic pressure and the heart after-load, which may impact left ventricular stiffness and hypertrophy. Previous studies have shown that PWV reflects age-related changes in vascular stiffness [30,31]. A functional change in the arterial response to pulsatile pressure associated with impaired vessel compliance can increase atherosclerosis risk and vascular damage.

Arterial stiffness is gaining recognition as a significant cardiovascular risk factor and independent predictor of all-cause and cardiovascular death [34]. Short- and long-term smoking cause an increase in arterial stiffness [30,31,35,36]. Acute smoking in healthy individuals changes arterial stiffness and blood pressure. Smokers have stiffer, more deteriorated arteries than non-smokers, and long-term smoking makes arteries stiffer [31]. Acute smoking significantly increased both blood pressure and carotid-femoral PWV (cfPWV), a "gold-standard measurement" of arterial stiffness [29]. cfPWV and brachial-ankle PWV (baPWV) are profoundly augmented in chronic smokers [29,31,36]. Smokers of all ages experience altered central and peripheral vascular function from cigarette use. Flow-mediated dilation (FMD) was impaired in subjects with systolic blood pressure (SBP) <120 mmHg due to cigarette smoking [37].

Smoking reportedly reduces arterial distensibility in both large and medium arteries [28].

Mechanisms underlying elevated arterial stiffness due to acute and chronic smoking may include endothelial dysfunction, enhanced platelets, insulin resistance, poor renal function, inflammation, diminished nitric oxide synthase (NOS) activity, and changes in prostacyclin and vasopressin levels [38]. Chronic smokers have decreased NOS activity and increased oxidative stress, which reduce NO bioavailability [13,31,32]. Endothelial cells produce and release NO, which relaxes blood vessels, reduces inflammation, and inhibits platelet activation [39]. The vasodilatory response, also known as FMD, which increases local blood flow, requires NO release. Both active and passive smokers exhibit endothelial dysfunction and FMD impairment [40]. NO inactivation and reduced bioavailability are thought to be the primary causes of endothelial dysfunction, which is also attributed to smoking-mediated oxidative stress and chronic inflammation. It is unclear how important nicotine is in the potent effects of oxidants and pro-inflammatory chemicals, although it might impair endothelial function whether administered locally or as a nasal spray. Increased calcification also contributes to chronic changes in arterial stiffness [30]. Smoking exacerbates arterial stiffness by reducing NO activity and stiffening vascular walls.

Although conventional cigarettes have a larger health impact than vape cigarettes, both immediately raise central PWV. Previous studies have shown that this may be due to an increase in blood pressure and/or heart rate [41,42]. The augmented PWV, however, remains substantial after adjusting for blood pressure and heart rate changes. Nicotine may also negatively alter arterial wall elasticity [43]. Therefore, smoking contributes to diverse mechanisms underlying the abnormal elevation of arterial stiffness and systolic blood pressure. Nicotine releases catecholamines that stimulate receptors in vascular smooth muscle cells and induce vascular contraction [43]. Nicotine diminishes NO bioavailability by generating oxygen free radicals, which worsens vascular distensibility [31,36]. These processes may explain why smoking's immediate influence on arterial stiffness resulted in functional rather than structural arterial changes.

## 3. Cigarette smoking and exercise

Smokers might exercise less frequently than non-smokers [44]. Smoking is associated with a decreased ability to perform vigorous exercise due to decreased lung function, increased carboxy-hemoglobin blood levels, a blunted heart rate exercise response, and decreased maximal ox-

oxygen consumption [45]. Smokers participate in less low-intensity or moderate-intensity vigorous activity than nonsmokers [46]. Numerous studies show that smoking reduces physical fitness, even in physically fit individuals and young members of the military [47-49]. Therefore, smokers' lower physical fitness levels are not attributable to less exercise, but rather to smoking's detrimental effect on physical fitness [49].

Although the relationship between smoking and physical inactivity has been studied [45,47-49], it is unclear how these risk factors are related at the individual level. Recent studies suggest that physical activity can reduce tobacco's harmful effects. Physically active people have better arterial compliance than their sedentary counterparts [50,51]. According to research from the Cooper Institute for Aerobics, smokers who maintain a rigorous level of physical fitness experience lower death rates overall than non-smokers [52]. This study specifically stated that high (most fit 40%) fitness level has a considerable protective impact on CVD-related mortality in both smokers and non-smokers [52].

Smoking impairs vascular function in healthy people, which reduces the vascular bed's capacity to respond to intense activity [32]. In healthy people, chronic smoking had a severe negative impact on vascular stiffness [28]. Particularly, light cigarette use can cause healthy young people to develop persistent vascular function impairment [53]. Another study demonstrated that aortic wave reflection was increased and microvascular function was hampered by ambient tobacco smoke exposure [54]. Regular aerobic exercise reduces the risk of cardiovascular disease in long-term smokers [32].

Physically active females have better arterial compliance than their fewer active peers. For instance, women who are healthy and inactive have age-related central arterial stiffness, but women who are physically active do not [55]. A cross-sectional study showed that regular aerobic exercise improves peripheral blood flow and lowers peripheral vascular resistance in smokers [56]. As regular exercise lessens the negative effects of chronic smoking on vascular structures, it is crucial to elucidate how exercise affects arterial stiffness to reduce the cardiovascular disease associated with smoking.

#### 4. Exercise and arterial stiffness

Aerobic activity and salt restriction are clinically effective lifestyle changes for avoiding and treating arterial stiffness [50]. Exercise lowers the age-related increase in arterial stiffness, which improves cardiovascular risk factors [57].

##### 1) Impact of resistance exercise interventions on arterial stiffness

Resistance and aerobic training help the body adapt to arterial stiffness. Although acute bouts of resistance training reportedly increase arterial stiffness [58], a four-week resistance training regimen consisting of two sessions a week did not adversely affect cardiovascular health [59]. Along with training duration and frequency, resistance exercise intensity is also significant for arterial stiffness. Specifically, various interventions ranging from 30-100% repetition maximum elicit different effects on arterial stiffness – while heavy-load resistance training tends to impair arterial stiffness, low-load resistance training contributes to reducing stiffness in young individuals [59]. These responses with different intensity protocols have also been observed in middle-aged and elderly individuals [60,61].

##### 2) Contribution of aerobic exercise interventions to arterial stiffness

One study found that a 16-week aerobic (e.g., brisk walking and running) intervention at a 60-75% heart rate reserve two to four days a week markedly ameliorated the central PWV, but not the femoral-ankle PWV in healthy and young untrained individuals [62]. In sedentary individuals, arterial stiffness was consistently reduced by a comparable aerobic exercise intervention that included continuous running for 30 minutes three times per week at a 60-70% heart rate reserve [63]. Hasegawa and colleagues used four distinct exercise regimens (low-intensity or moderate-intensity aerobic activities lasting 15 or 30 minutes) to investigate the effects of exercise intensity on arterial stiffness in elderly, inactive individuals [64]. Arterial stiffness was reduced in both the brachial-ankle and heart-brachial PWV, regardless of exercise duration and intensity. Therefore, exercise training reduces both central and peripheral arterial stiffness regardless of age or health conditions, even if it has heterogeneous impacts on arterial stiffness.

Acute exercise generally remodels blood flow to the working muscles caused by their vasodilation and organ vasoconstriction, such as the splanchnic circulation. Exercise can trigger increased endothelin-1 (ET-1) and nitric oxide (NO) release, which mediates blood flow redistribution during exercise [65]. In an animal study, local ET-1 increased in the splanchnic circulation and decreased in the coronary circulation, and NO production increased in the coronary circulation during exercise [31, 54]. A recent study demonstrated the beneficial effects of exercise on intima-media thickness, endothelial function, and arterial health, particularly arterial stiffness, in adults [66]. In numerous studies, physical activity lowered systemic blood pressure and improved arterial stiffness [67, 68]. Exercise training studies have demonstrated that physically active

individuals have reduced arterial stiffness compared to their sedentary counterparts [57,69]. Therefore, concurrent advancements may mediate exercise-related reductions in arterial stiffness, endothelial function, inflammation, and sympathetic activity. However, exercise's protective effect on arterial stiffness has been poorly studied in humans, and the mechanisms underlying the effect of regular exercise on arterial stiffness remain unclear.

### 5. Smoking cessation and arterial stiffness

Smoking cessation is one of the most important lifestyle modifications to improve health and well-being. Quitting smoking increases lifespan and lowers morbidity [19,70]. Smokers have a higher risk of developing cancer, heart disease, stroke, and premature death [37]. Those who stop smoking cigarettes have a lower risk of developing CVD and acute myocardial infarction [18] and may postpone the development of atherosclerosis by 10 years compared to those who continue to smoke [71]. The risk of death from smoking-related diseases is reduced by about 90% in those who quit before the age of 40 [1].

Smoking cessation has many physiologic benefits. However, its effect on arterial stiffness remains poorly established. Some studies indicated a reduction in arterial stiffness following both acute (e.g., 4 weeks) and long-term (e.g., 6 months) smoking cessation [38,72,73], but others revealed no difference in arterial stiffness after quitting smoking [30,74].

A previous meta-analysis demonstrated that, in the general population, quitting smoking (duration of smoking cessation was 6-12 months) results in a moderate reduction in arterial stiffness as evaluated by PWV (5.2%) [75]. In addition, the effect of smoking cessation (1 week vs. 4 years) on arterial stiffness is greater in healthy smokers compared with hypertensive smokers [76,77]. This apparent discrepancy between hypertensive smokers and healthy smokers may be explained by the fact that smoking has a less severe impact on the vascular wall in hypertensive individuals, and both smoking and high blood pressure share a comparable mechanism of action on the vascular wall [76,77]. Previous investigations demonstrated that improved arterial elasticity is sustained four weeks after quitting tobacco smoking for 4 weeks [38,78]. A meta-regression analysis study reported that arterial stiffness improves more once smoking has been discontinued for a longer period of time [75]. Inflammatory markers and endothelial dysfunction may be responsible for the improved arterial elasticity following smoking cessation [79]. Improvements after smoking cessation are associated with a lower risk of cardiovascular death [78,80].

## CONCLUSIONS

Smoking promotes cardiovascular diseases and increases mortality. Although the precise mechanisms underlying smoking-induced deterioration of the cardiovascular system are unclear, smoking negatively impacts arterial stiffness and endothelial function, the extracellular matrix, inflammation, vasomotor function, platelet function, fibrinolysis, and oxidative processes. Fortunately, lifestyle modifications, including exercise and quitting smoking, can effectively prevent or treat smoking-mediated cardiovascular dysfunction and disorders. However, how regular exercise and quitting smoking contribute to ameliorating arterial stiffness has not been completely explored. Thus, further investigations are needed to determine how these lifestyle modifications impact the vascular wall and arterial stiffness.

## CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest with the contents of this study.

## AUTHOR CONTRIBUTIONS

Conceptualization: W Park; Data curation: W Park, S Sung; Formal analysis: W Park, S Sung; Methodology: W Park, S Sung; Project administration: W Park; Visualization: W Park, S Sung; Writing - original draft: W Park; Writing - review & editing: W Park, S Sung.

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