

Current and Controversial Features of Cardiovascular Damage from Cigarette Smoking

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ABSTRACT

A great number of studies have undoubtedly demonstrated that cardiovascular damage from cigarette smoking cannot be denied, although some controversies on the topic still exist. The damage to the heart and blood vessels is initially characterized by transient functional alterations consisting of endothelial dysfunction, reduced exercise tolerance, increased systolic blood pressure and heart rate following acute exposure. On the contrary, chronic exposure to smoking develops, at the time, firstly reversible and, then, irreversible lesions mainly involving myocardium with an ischemic damage and smoke cardiomyopathy as well as coronary, carotid and cerebral arteries, which display atherosclerotic pathology. The analysis of the epidemiological studies on cardiovascular damage support the controversies on the effects of smoking, because not the same alterations are sometimes observed in different studies on the topic. However, when standardized experimental procedures are followed, the same alterations are clearly reproduced showing that cardiovascular damage from cigarette smoking cannot be denied.

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Key words: Smoking; Cardiovascular Damage; Myocardium; Endothelium; Type of Alterations

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INTRODUCTION

Despite of a great number of reports emphasizing that cardiovascular damage from cigarette smoking in both its forms, active and passive smoke, is an absolute certainty^[1-13], however debated opinions on the topic still exist primarily with regard to the type and reproducibility of damage, time of onset and progression of the lesions. In addition, a great question to be solved is whether once cardiovascular alterations begin are independent in their progression from smoking or, conversely, continue to need smoking compound effects.

The purpose of this review is to describe the characteristics of cardiovascular damage from smoking in an attempt to clarify the main controversial opinions, which exist on this topic.

ONSET AND TYPE OF CARDIOVASCULAR DAMAGE

It has been well recognized that the harm of the heart and blood vessels caused by cigarette smoking involves two main mechanisms (Table 1): an initially transient and functional mechanism involving the endothelium and heart muscle, and a final mechanism which lead to reversible, and then irreversible alterations of these structures. Both of them are under the adverse effects of nicotine and carbon monoxide, which are the main compounds that trigger the damage^[14-19].

The damage of the endothelium is probably the earliest event in the process of lesion formation, and, therefore, hence, the assessment of endothelial function may be a useful prognostic tool for artery disease. Endothelial dysfunction is usually observed and prevails on some vascular structures like coronary arteries, carotid and brachial arteries displaying more frequently alterations. When the endothelium loses its integrity becomes thrombogenic as this feature

is the promoter of all the following events, which precede anatomical alterations of atherosclerosis.

Exposure to environmental tobacco smoke is undoubtedly a strong factor of endothelial dysfunction following both acute and chronic exposure^[20-21], although different responses are the result of this factor. The alterations following acute exposure are, as aforesaid, transient, but repeatable with functional characteristics, particularly related to changes in vasodilator mechanisms, which depend on the reduced NO availability. In addition, increased systolic blood pressure is an easy parameter to be assessed during acute exposure since it occurs either while an individual smokes a cigarette or during passive acute exposure.

Hypoxia due to the increased concentrations of carboxyhemoglobin is responsible for heart alterations consisting of impaired exercise performance in both healthy individuals and individuals suffering from ischemic heart disease^[22-25] together with increased heart rate.

Both endothelial and myocardial changes occur as a direct and mediated effect of carbon monoxide and nicotine.

CHRONIC EXPOSURE AND TYPE OF DAMAGE

Cardiovascular damage as a result of chronic exposure to cigarette smoking recognizes two phases: chronic exposure characterized by structural, but reversible alterations of the heart and blood vessels, and chronic prolonged exposure with structural irreversible alterations.

The lesions documented consist of myocardial alterations primarily related to ischemic heart disease, development and progression of coronary atherosclerosis and its complications, intimal thickness of carotid and cerebral arteries and systolic hypertension. The table 2 summarizes the main cardiovascular pathology of chronic exposure to cigarette smoking.

All together these pathological alterations characterize the pattern of the experimental cardiomyopathy^[26-29]. There is a clear evidence that myocardial necrosis and vascular changes are the anatomical substrate of chronic damage from smoking.

Some of these characteristics of smoke cardiomyopathy, where carefully searched, permit to identify, at necropsy, an ischemic lesion from smoking also in smoker individuals and individuals passively exposed to smoking^[30].

Mechanisms of cardiovascular damage from smoking

Smoking compounds, primarily nicotine and carbon monoxide, cause cardiovascular damage by various mechanisms. Some of these are a consequence of a direct effect of the substances, while others recognize the activation and stimulation of anatomical and biochemical substrates strongly influenced by cigarette smoking.

The Table 3 describes the main mechanisms by which nicotine and carbon monoxide adversely influence cardiovascular system.

Nicotine entered the blood binds specific receptors and, so doing, activates its biochemical effects. It stimulates the sympathetic nervous system and similar structures like chromaffin tissue and, moderately, also the central nervous system. Initially, the action of the substance causes stimulant effects, which become in the time depressant.

The exact mechanisms by which nicotine triggers cardiovascular changes is still far to be completely clarified. However, the stimulation of sympathetic nervous system and consequent release of catecholamine undoubtedly play significant effects^[31-32].

As an effect of the nicotine, heart rate and systolic blood pressure

Table 1 Structures involved with cardiovascular damage from smoking.

Type of exposure	Structure involved	Responses triggered
Acute exposure	Endothelium	Impaired endothelium-dependent vasodilation (Transient) Systolic hypertension (transient)
	Heart	Transient impaired exercise tolerance Ventricular arrhythmias Increased heart rate (transient)
Initial chronic exposure	Endothelium	Reversible atherosclerotic lesions
Prolonged chronic exposure	Heart	Reversible myocardial cell lesions
	Endothelium	Irreversible vascular lesions
	Heart	Irreversible myocardial cell damage

Table 2 Main pathological and ultrastructural alterations of the heart and blood vessels due to chronic smoking and experimental observations.

- Changes in mitochondria function (respiratory chain impairment; cristae amputation)
- Focal areas of myocardial cell necrosis (with different stage of development)
- Perivascular infiltrates (intramural myocardial vessels)
- Punctate hemorrhage (between myocardial cells)
- Interstitial fibrosis
- Myocardial fiber swelling
- Lysosomal autophagocytosis

Table 3 Mechanisms by which nicotine and carbon monoxide alter cardiovascular system.

Chemicals	Structures involved	Responses triggered
Nicotine	Sympathetic nervous system	Increased arterial resistance
	Adrenergic system	Increased arterial resistance
Carbon monoxide	Arterial wall	Endothelial alterations
	Myocardium	Hypoxic alterations

increase, determining an increased demand in oxygen to the heart, which could be in relative hypoxia due to enhanced concentrations of carboxyhemoglobin due to carbon monoxide.

Carbon monoxide damages cardiovascular system through 4 phases: oxygen removing, its replacement by the gas, hypoxia due to the increased levels of carboxyhemoglobin, intracellular metabolism impairment^[33-35]. In addition, carbon monoxide plays a direct action on intracellular structure inhibiting respiratory metabolism of the cells. There is evidence that the percentage of carboxyhemoglobin in the blood determines the alterations observed as well as the time of appearance.

It is worth noting that chronic and prolonged exposure to carbon monoxide from smoking determines cardiovascular alterations, but is never responsible of acute poisoning from the gas.

Controversies on the topic

Epidemiological survey has been recognized as the factor to which ascribing the different opinions debated on the cardiovascular damage from smoking.

There is evidence that epidemiological studies rely on a statistical estimate and this pattern provides probabilistic percentages which give a different degree of the relationship between a factor and event to be assessed. Only when the 100% of the observations examined characterize the studied events, there exist a certainty of a cause-effect link.

Three types of epidemiological studies have been usually conducted^[36-39]: case-control, cohort, and metanalysis studies. Each of them may provide different responses unless similar experimental procedures are followed. However, all these findings displayed an impairment of cardiovascular function and structure

with a statistically mean of relative risk from 1 to 1.42 of the total observations with 95% confidence interval and a clear prevalence for meta-analysis studies. The statistical estimate is wide, so that different interpretations of the level and degree of cardiovascular damage may be conducted, but evidence indicates that cardiovascular damage, although variable in extent and significance, exists in all epidemiological studies and, therefore, it cannot be absolutely denied. It is worth noting that the Report ASH 2011^[40] referred to passive smoking establishes that whilst health risk from passive exposure to smoking is smaller than that due to active smoke, the overall health impact is large because of the diseases observed are common. In addition, this Report underlines that totally only domestic exposure to secondhand smoke in the United Kingdom causes around 2,700 deaths per year in individuals aged from 20 to 63 years and a further 8,000 deaths a year in older than 65 years.

These statistical reports undoubtedly support the true danger that exposure to smoking exerts and, consequently, to put an end to the controversies on the topic.

CONCLUSION

Consistent observations derived from clinical, pathological and epidemiological studies provide incontrovertible material to solve all the controversies existing on the fact that cardiovascular damage from smoking is still not documented.

With regard to the observations taken into account of a lack of similar, not always reproducible alterations due to smoking in different studies, there is evidence that these findings usually differ in methodological procedures and, therefore, the results obtained are not specifically comparable. In case of standardized experimental methods, the alterations of the cardiovascular system from cigarette smoking are exactly reproducible.

CONFLICT OF INTEREST

There are no conflicts of interest with regard to the present study.

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