



Impact of Smoking on the Atrial Substrate Characteristics in Patients with Atrial Fibrillation

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Introduction

Cigarette smoking is a common health issue throughout the world. It can cause the development of various major diseases, such as chronic obstructive pulmonary disease (COPD),¹ most cardiovascular diseases and many types of cancer. Thus, people with a tobacco habit can produce devastating health consequences for themselves. At present, there are about five million people that die annually, which can be attributed to cigarette smoking, and half of those deaths, which are mortalities from smoking, always occur in middle age.² Therefore, how to reduce cigarette smoking remains the most important work to avoid the causes of health disabilities and premature death.

Cardiopulmonary Effect of Smoking

It is well known that smoking is an important risk factor for chronic bronchitis, COPD³ and can accelerate the decline in the pulmonary function.⁴ The incidence of atrial flutter (AFL) increased 1.9 times in those with COPD.⁵ On the other hand; many studies have well established the evidence of smoking's effect on coronary risk. Smoking, even at a light level, can have a major impact on coronary and peripheral vascular disease.⁶ Cigarette smoke is a complex mixture containing several ingredients that have the adverse effects of accelerating atherosclerotic progression and ath-

erothrombosis, by increasing the platelet adhesiveness⁷ and serum fibrinogen levels,⁸ and decreasing the high density lipoprotein cholesterol levels.⁹ It also increases the heart rate, blood pressure, sympathetic tone and consumption of oxygen by the heart muscle. When a healthy person smokes a cigarette, the coronary blood flow must increase to meet the increased demand.¹⁰ In the presence of coronary-artery stenosis, the coronary flow can not increase and ischemia may develop, with resultant angina pectoris or myocardial dysfunction.^{11,12} Recently, Barua RS, et al. demonstrated that smoking could cause dysfunction of the nitric oxide biosynthesis in endothelium cells by oxidative stress⁹ and that mechanism may further impair the endothelium-dependent coronary artery dilatation capability and reduce the myocardial oxygen supply.

Smoking and Cardiac Arrhythmias

Nicotine may be a precipitating factor of cardiac arrhythmias due to a marked elevation in the serum catecholamine concentration, heart rate, and blood pressure; production of coronary spasms; and increased myocardial oxygen consumption with a reduction in the myocardial oxygen supply.¹⁰⁻¹⁴ Cigarette consumption is directly related to increased rates of sudden cardiac death (SCD), mainly through its direct toxic effects. Recently, the impact of the smoking status on SCD was studied in patients with established coronary artery

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disease (CAD).¹⁵ In that study, current cigarette smoking was a powerful independent predictor of the SCD risk and those that quit smoking experienced a significant reduction in the SCD risk. Other studies, such as The CAST experience¹⁶ also had the same results, which showed a marked reduction in arrhythmic death and overall mortality with the cessation of smoking.

In 1997, Mehta et al. reported that high levels of serum nicotine may be a possible cause of cardiac arrhythmias in dogs with a dose-dependent arrhythmogenicity.¹⁷ There were only three sporadic case reports in humans¹⁹⁻²⁰ and suggested that high serum nicotine levels at the time the patient developed his first episode of atrial fibrillation may have had a causal relationship. Recently, one sub-study of the Multicenter Automatic Defibrillator Implantation Trial-II revealed continued cigarette smoking was associated with an increased risk of rapid supraventricular arrhythmias.²¹ Other studies have shown that nicotine administration could produce action potential alterations that could predispose to decremental conduction and hence, to a conduction disturbance.²² Nicotine administration, in addition, can also enhance the automaticity. A combination of enhanced automaticity with a simultaneous depression of the conduction favors the initiation of a number of arrhythmias. A previous study demonstrated that chronic exposure to nicotine promotes the occurrence of atrial flutter (AFL) in dogs with a myocardial infarction (MI).²³ They also found a nicotine-induced increase in the atrial interstitial fibrosis in dogs with an MI. The occurrence of increased atrial interstitial fibrosis and a flattened electrical restitution are important substrates for AFL.

Impact of Smoking on Atrial Substrates

Our previous study and other investigators have demonstrated a wide area of low voltage zones (LVZs) in patients with atrial fibrillation (AF) and AFL.^{24,25} Previous studies have found that the prolonged administration of nicotine was associated with a loss of intracellular K⁺ and the new appearance of cardiac necrosis.²⁶ So, smoking may theoretically change the substrate properties causing an attenuation of the atrial voltage and perpetuate the atrial tachycardia, especially in patients with typical AFL. This concept had been proven in animal study by Chen PS et al. who reported nico-

tine could increase the atrial interstitial fibrosis in dogs with a myocardial infarction.²³ In humans, one recent report had demonstrated that cigarette smoking contributed to the development of atrial fibrosis via nicotine in patients with CAD.²⁷ Previous studies had shown that atrial fibrosis can provide an arrhythmogenic substrate, which may increase the likelihood of the occurrence of atrial arrhythmias. Our group first reported the impact of smoking on the right and left atrial (RA, LA) substrates.²⁸ We found that the mean peak-to-peak bipolar voltage of the RA was lower in the patients with a previous history of smoking than in those without a history of smoking, but there was a similar mean peak-to-peak bipolar voltage in the LA. Further, the total activation time of the RA was longer in the patients with a previous history of smoking, than in those without a history of smoking, but that was not the case in the LA. Furthermore, the voltage reduction in the RA was related to the smoking intensity-duration in the patients with a history of smoking. In contrast to the mean peak-to-peak voltage, the voltage reduction in the LA was weakly correlated to the smoking intensity-duration.

Clinical Implications concerning the Management of AF

Several studies have clearly demonstrated that the atrial substrate is an important factor for perpetuating atrial arrhythmias.^{24,25,29} Substrate changes themselves may increase the difficulty in successfully terminating AF during radiofrequency catheter ablation. Thus, more delicate procedures during AF ablation may be needed in patients that smoke and have large substrate changes. Second, continuing smoking has been proven to be an important risk factor for increasing SCD^{15,16} and tachyarrhythmias in patients with implantable cardiovector defibrillators. Therefore, cessation of smoking should be encouraged in patient with AF, no matter whether they receive an invasive procedure to treat their AF or not.

Conclusion

Cigarette smoking can change the atrial substrate with a dose dependent effect, especially in the RA and that substrate change may perpetuate atrial tachyarrhythmias. However, the risk of smoking in patients with AF was low, as reported in the

Framingham Heart Study.³⁰ Thus, the causal relationship between smoking and AF still remains unclear. The mechanism involved in that deserves further study.

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