Rapid Communication

Effect of Smoking on Arterial Stiffness and Pulse Pressure Amplification

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Abstract—The brachial artery pressure waveform is abnormal in smokers, but the effect of smoking on the aortic pressure waveform in both smokers and nonsmokers, particularly in the younger population, is unknown. We compared the acute and chronic effects of smoking on large-artery properties in 185 healthy young smokers and nonsmokers (mean±SD, 22±5 years). We matched 41 chronic smokers for age, height, weight, and gender with 116 nonsmokers. The augmentation index, a measure of arterial wave reflection in the aorta, was measured by applanation tonometry (Sphygmocor). We also compared augmentation index, aortic pulse wave velocity (Complior), and blood pressure in 28 subjects (11 chronic smokers) before and for 15 minutes after smoking 1 cigarette (nicotine content, 1.2 mg). Although brachial blood pressure was not different, the aortic systolic blood pressure (101±8 versus 97±9 mm Hg) and augmentation index (0.7±13 versus −5.7±14) were higher (P<0.01) in chronic smokers than in nonsmokers, whereas aortic-brachial pulse pressure amplification was reduced (13.7±8 versus 17.7±5 mm Hg, P<0.01). These effects were seen in both male and female subjects. Acutely in both groups, smoking significantly increased (P<0.01) both brachial and aortic blood pressure, augmentation index, and pulse wave velocity. No changes were seen after sham smoking. This study shows an acute increase in arterial stiffness after smoking 1 cigarette in chronic smokers and nonsmokers. Higher aortic systolic blood pressure and greater arterial stiffness, in part due to reduced pulse pressure amplification and increased arterial wave reflection, suggest that the adverse hemodynamic effects have hitherto been underestimated in young chronic smokers. (Hypertension. 2003;41:183-187.)

Key Words: smoking ■ arterial stiffness ■ pulse pressure amplification

Smoking is a major risk factor in the development and progression of cardiovascular disease. Despite extensive research, the pathophysiological mechanisms that are responsible for smoking-related vascular damage have not been elucidated. In addition to alterations in hemostatic factors, endothelial function, and blood lipids, the dynamic properties of the arterial wall may play an important role. There is evidence that compliance of both large and medium-sized arteries decreases immediately after smoking 1 cigarette. 3–5

Arterial stiffness is increasingly being recognized as an important cardiovascular risk factor and an independent predictor of all-cause and cardiovascular death. 6–8 Stiffness may be assessed indirectly by measuring pulse wave velocity (PWV); the stiffer the artery, the faster a pressure wave travels through it and the extent to which the arterial wave is reflected from the periphery. Another indirect measure of arterial elasticity is aortic-brachial pulse pressure amplification, which is reduced with ageing. 9

McVeigh et al. 10 using invasive methods, demonstrated abnormalities in the brachial artery pressure waveforms of chronic smokers. In older subjects, smoking is associated with increased carotid artery stiffness, 11 even in the absence of atherosclerosis of the vessel. However, the effect of chronic smoking on an elastic artery such as the ascending aorta has not been fully characterized. We first studied the acute effects of cigarette smoking on the aortic pressure waveform by measuring the augmentation index (AIx) and PWV in healthy smokers and nonsmokers. Young subjects were chosen to minimize the compounding influence of age and disease states. We then studied the effects of chronic smoking on blood pressure (BP), the aortic pressure waveform, and pulse pressure amplification in healthy young subjects compared with nonsmokers.

Methods

Subjects

The study group comprised 185 (91 female) healthy volunteers, 52 chronic smokers with a mean (±SD) age of 22±5 years. None of the participants (university students) had systemic hypertension (BP >140/90 mm Hg), diabetes mellitus (fasting glucose, 4.9±0.3 mmol/L or 88±5 mg%), hypercholesterolemia (fasting total cholesterol, 5±0.2 mmol/L or 190±7 mg%), or cardiac disease or were taking any medications. The smoking habits and fitness levels were assessed from a questionnaire. The smokers smoked an average of 15 cigarettes per day for 6 to 10 years. The subjects were studied fasting, having abstained from caffeine, alcohol, or smoking in the previous 12 hours. Subjects rested in a supine position for 15 minutes.
in a quiet room at 22°C before the baseline hemodynamic measurements were obtained. Brachial BP and heart rate (mean, 3 readings) were measured in the left arm with an automated digital oscillometric sphygmomanometer (Omron, model 705-CP, Omron Corp). The subjects gave informed consent, and the study had institutional ethics committee permission.

**Acute Effects of Smoking**

Each subject (11 chronic smokers, 17 nonsmokers) smoked 1 cigarette (nicotine content, 1.2 mg) within 5 minutes, using a standardized protocol, and measurements of brachial and aortic BP, heart rate, AIx, and PWV were made at 5, 10, and 15 minutes after baseline. In addition, 8 of these subjects had the measurements performed after sham-smoking an unlit cigarette.

**Chronic Effects of Smoking**

Chronic smokers (n=41) were matched for age, height, weight, and gender with nonsmokers (n=116). Brachial and aortic BP, pulse pressure amplification, heart rate, and AIx were measured in both groups. Aortic-brachial pulse pressure amplification was calculated by subtracting aortic from brachial pulse pressure.

**Derivation of the Aortic Pressure Waveform**

The technique of pulse wave analysis was used. A high-fidelity micromanometer (SPC-301, Millar Instruments) was used to flatten the radial artery, and the radial pulse was continuously recorded. The aortic pressure waveform was derived from radial tonometry by using a previously validated transfer function relating radial to aortic pressure waveform within the system software of the Sphygmocor apparatus (Sphygmocor Atecor Medical, version 6.2), as previously described. Ascending aortic pressures and the AIx were derived from the aortic pressure waveform. The validity of the derived AIx has been confirmed by simultaneously recorded direct aortic measurements and is highly reproducible in both healthy and diseased populations.

**PWV Measurements**

Carotid-femoral PWV was determined according to the foot-to-foot method, using the Complior device (Complior, Dupont Medical) as previously validated.

**Statistical Analysis**

Results were analyzed with JMP (JMP IN, version 3.2.1 SAS Institute Inc), and a value of P<0.05 considered significant. The differences between the smokers and nonsmokers in both acute and chronic studies were analyzed by 1-way ANOVA and expressed as mean±SD. The acute changes in the hemodynamic parameters over time in the acute study were analyzed by repeated-measures ANOVA, testing for the effect of time and interaction between time and treatment. Because the AIx is heart-rate dependent, we also analyzed it over time corrected for the heart rate increase in the acute study.

**Results**

**Acute Effects of Smoking in Smokers and Nonsmokers**

At baseline, the AIx was significantly higher in smokers compared with nonsmokers (Table). Although the PWV was higher in smokers than nonsmokers (Figure), the difference was not statistically significant. No acute changes were seen in the hemodynamic parameters after sham smoking.

Short-term smoking caused a significant increase in brachial systolic and diastolic BP and heart rate, which was maximal at 5 minutes and returned to baseline 15 minutes after smoking (Figure). The aortic systolic and diastolic BP also increased significantly after smoking 1 cigarette both in smokers and nonsmokers, with the greatest changes seen in the first 5 minutes after smoking (Figure). Although AIx, which is heart rate–dependent, decreased in both smokers and nonsmokers after smoking, by applying a correction factor for changes in heart rate, the AIx increased significantly after smoking in both smokers and nonsmokers. PWV increased significantly both in smokers and nonsmokers from baseline and remained higher for the entire duration of the study for 15 minutes (Figure).

**Chronic Smoking, Aortic Pressure Waveform, and Pulse Pressure Amplification**

The demographic and hemodynamic profiles of the smokers and nonsmokers are shown in the Table. The aortic systolic BP was significantly higher in smokers than in nonsmokers, and pulse pressure amplification was significantly reduced compared with nonsmokers. The AIx was significantly higher in smokers (0.7±13 versus −5.7±14%, P<0.01) than in nonsmokers.

Because gender is such an important determinant of arterial stiffness, we analyzed the data for male and female subjects
separately. The male subjects in our study had higher (P<0.001) brachial systolic (120±11 versus 109 versus ±11), aortic systolic BP (101±9 versus 95±9), and pulse pressure amplification (19±6 versus 15±7, all in mm Hg) than female subjects. The AIx was significantly higher in female subjects (0.7±12 versus −8.7±14%, P<0.001) than in male subjects. There was no difference in brachial BP, aortic diastolic BP, and heart rate between male smokers and nonsmokers. However, as in the whole group, the aortic systolic BP was higher (105±6 versus 100±9 mm Hg, P<0.05) and pulse pressure amplification less (15±6 versus 20±5 mm Hg, P<0.01) in the male smokers than nonsmokers. Also, the AIx was higher (−4.4±14 versus −11±11%, P<0.05) in male smokers than nonsmokers. Results were the same for the female subjects with a higher aortic systolic BP (98±8 versus 93±9 mm Hg, P<0.05) and lower pulse pressure amplification (12±9 versus 16±5 mm Hg, P<0.05) in female smokers compared with female nonsmokers. Also, female smokers had stiffer arteries, as shown by a significantly higher AIx (5.4±10 versus −1.3±14%, P<0.05) than nonsmokers.

As the level of fitness may influence the results, we graded the smokers and nonsmokers into sedentary, moderately active, and actively involved in sports and analyzed the effects of smoking in each group separately. In the sedentary subjects (n=41), AIx was higher (6.35±7 versus 2.7±9, P<0.02) and pulse pressure amplification less (13±6 versus 17±6 mm Hg, P=0.09) in smokers than nonsmokers, but not statistically significant. In the moderately active group (n=77), the smokers had significantly higher aortic systolic BP (104±8 versus 94±9 mm Hg, P<0.05) and lower pulse pressure amplification (12±10 versus 17±5, P<0.01) than nonsmokers. The AIx was higher in the smokers (4±11 versus −3.3±11, P<0.05) than in nonsmokers. The subjects who were actively engaged in sports (n=39) also differed, depending on smoking habits, the smokers having higher AIx (−9±14 versus -17±12, P=0.1) and aortic systolic BP (104±9 versus 99±9, P=0.16) than nonsmokers, though it was not statistically significant. The pulse pressure amplification was, however, significantly reduced (14±6 versus 20±6 mm Hg, P<0.05) in smokers than in nonsmokers.

Discussion

We have shown a significant effect of smoking on large-artery properties. Acutely, cigarette smoking increased the AIx and PWV, suggesting an increase in arterial stiffness. Perhaps the most interesting finding was that young, otherwise healthy smokers have higher aortic systolic pressure and AIx compared with nonsmokers as the result of increased arterial wave reflection in the aorta, suggesting stiffer arteries. Decreased elasticity of such arteries is also suggested by the reduced pulse pressure amplification in chronic smokers.

The effect of acute cigarette smoking in healthy nonsmokers on forearm arterial hemodynamics showed an increase in BP, heart rate, and PWV.16 Acute cigarette smoking decreased arterial compliance in both large elastic and medium-sized muscular arteries.3,17 More recently, Stefanadis et al3 using invasive methods, showed decreased aortic compliance acutely after smoking 1 cigarette in middle-aged men with coronary artery disease.

In the current study, AIx was significantly higher at baseline in smokers than in nonsmokers. PWV was also higher, although not significantly, presumably because of the relatively small number of subjects in this part of our study. PWV increased immediately after smoking. Arterial wave reflection depends on the timing of ventricular ejection.
Because of the proportionality between ejection time and cardiac cycle duration, the peak of the forward traveling wave occurs earlier at faster heart rates. In such a setting, even with a fixed reflection site and PWV, there is an altered relation between forward and backward waves. AIx is therefore lower at higher heart rates and vice versa. Wilkinson et al. recently demonstrated a linear relation between AIx and heart rate in a pacing study, showing that AIx decreased by 4% for every 10-beat/min increment in heart rate. By applying this correction factor, the AIx increased in parallel with the PWV in our acute study (Figure). However, the correction may need to be interpreted with caution because there may be different mechanisms by which heart rate changes affect the AIx in different maneuvers, for example, smoking versus pacing. The mechanisms underlying the acute increase in BP and arterial stiffness may be several, including an increase in circulating and local catecholamines; nicotine stimulates sympathetic ganglia and increases the central nervous system sympathetic neural discharge—impaired nitric oxide production and endothelial dysfunction.

The chronic effects of smoking have been controversial. Wollersheim et al. described increased arterial stiffness of the popliteal artery and a tendency toward stiffening of the common femoral and carotid arteries in 13 habitual smokers measured ultrasonographically by the pressure-strain elastic modulus. Also, an invasive study showed abnormalities of the brachial artery pressure waveform in smokers, but others found no difference in regional arterial compliance between smokers and nonsmokers. In contrast, in the current study, we observed a much higher AIx in smokers compared with nonsmokers (Table) in a young homogenous group of healthy adults who were matched for age, height, weight, and hemodynamic status. In such a group, the confounding effects of age, hypertension, atherosclerosis, and so forth, are minimized. The earlier studies were carried out in a heterogeneous group of subjects; the age ranges were wide, and none of these measured aortic BP or pulse pressure amplification. Because pulse pressure amplification is age-dependent, decreasing markedly with age, the failure to measure it in the earlier studies may have led to underestimation of the chronic effects of smoking, particularly in the young. We were able to measure aortic systolic BP and pulse pressure amplification in our study and have clearly shown for the first time that the deleterious effects of chronic smoking would be overlooked if only peripheral BP and compliance measurements are made, as in the earlier studies. Furthermore, we have shown that the deleterious effects of smoking are seen in young people regardless of their gender and their level of fitness, although the extent of statistical significance here is less, partly as a result of the relatively lower numbers.

This study extends the earlier observations by McVeigh et al. that older smokers have abnormal brachial artery pressure waveforms compared with nonsmokers and the recent study showing increased stiffness index in the carotid artery in middle-aged and elderly smokers compared with nonsmokers. The additional finding of a higher aortic stiff BP, despite a similar or somewhat lower systolic BP in the brachial artery, is important and may be attributed to reduced pulse pressure amplification in the smokers. A number of epidemiological studies have reported either a similar or lower BP in smokers compared with nonsmokers, but this may be related to gender, alcohol intake, and body mass index. In a recent report on the Annual Health Survey for England, systolic BP was lower in women who smoked but higher in male smokers >60 years of age. Similarly, in 12,417 French men, current and former smokers were at greater risk of systolic hypertension, particularly over the age of 60 years. Our data may provide an insight into the mechanisms involved. In the ARIC study, lower arterial elasticity was independently related to the development of hypertension. With aging and reduced pulse pressure amplification, the brachial systolic BP equates more with the aortic systolic BP, and the higher aortic systolic BP in smokers may, with time, because of additional smoking-related reduced aortic brachial pulse pressure amplification, become evident as a higher brachial systolic BP.

**Perspectives**

These results suggest that the hemodynamic consequences of chronic smoking may have been underestimated. We believe that smoking reduces pulse pressure amplification largely as a consequence of increased arterial stiffness and increases arterial wave reflection, which leads to increased aortic systolic BP. The latter has not been suspected because peripheral BP and is usually deceptively lower in chronic smokers because of poor aortic brachial pressure amplification. Arterial stiffness is increasingly recognized as a more sensitive prognosticator of vascular events than either systolic or diastolic BP alone in populations with hypertensive and end-stage kidney disease. Smoking in the younger population, particularly women, is on the increase in many Western countries. We now provide evidence that smoking-related hemodynamic changes and increased stiffness may be evident in subjects as young as 22 years. Our ability to detect these changes may also provide an opportunity for intervention. Female gender and exercise are not protective from such vascular effects.

**References**
