Vascular Abnormalities in Asymptomatic, Healthy Young Adult Smokers Without Other Major Cardiovascular Risk Factors: The Bogalusa Heart Study

Hong Li, Sathanur R. Srinivasan, Wei Chen,
Ji-Hua Xu, Shengxu Li, and Gerald S. Berenson

Cigarette smoking, an established cardiovascular (CV) disease risk factor, is known to impair pulsatile arterial function in middle-aged and older adults. However, information is scant in healthy young adults for whom smoking is the only CV risk factor, at current guidelines. Nonsmokers ($n = 145$) and smokers ($n = 142$) aged on average 36 years were selected for not having obesity, hypertension, dyslipidemia, diabetes, or clinically manifest CV disease. Pulsatile arterial function was measured in terms of large artery compliance (C1), small artery compliance (C2), and systemic vascular resistance (SVR) by noninvasively recorded radial artery waveforms. Smokers versus nonsmokers had significantly lower measures of adiposity and LDL-cholesterol; and higher systolic blood pressure and triglycerides. In addition, smokers versus nonsmokers had lower C2 (5.09 *v* 6.63 mL/mm Hg × 100, $P = .0009$) and higher SVR (1399.0 *v* 1325.5 dyn · sec · cm^{-5}, $P = .006$), after adjustment for race, sex, and age. Decreases in C2 (P for trend = .001) and increases in SVR (P for trend = .01) were noted with increasing years of smoking. Multivariate analysis revealed that duration of smoking was associated adversely with C2 ($P = .004$), independent of race, sex, age, systolic and diastolic blood pressures, HDL-cholesterol, triglycerides, glucose, and insulin. The odds of having adverse C2 (bottom 10 percentile) and SVR (top 10 percentile) were, respectively, 2.9 ($P = .01$) and 2.6 ($P = .07$) times higher in smokers versus nonsmokers. The observed deleterious effects of cigarette smoking on arterial wall dynamics in otherwise healthy young adults underscore the need for aggressive early prevention and intervention strategies to control smoking behavior.

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Cigarette smoking has been established as a major risk factor for cardiovascular (CV) disease, and it contributes to as much as 30% of all CV disease mortality in the US each year.[1,2] Risk factors for CV disease, including smoking, mediate their effects by adversely altering the structure, endothelial function, and dynamic properties of the arterial wall.[3] Smoking, either acute or chronic, is known to decrease vascular compliance.[4–10]

Recent studies have shown that alterations in the pulsatile behavior of the vasculature may be a sensitive marker to detect arterial injury related to CV risk factors.[11–13] In this regard, arterial pressure pulse contour, which can be obtained noninvasively, provides assessments of large artery (capacitive) compliance, small artery (oscillatory or reflective) compliance, and systemic vascular resistance.[11,14,15]

Most studies on the effect of smoking on the arterial wall properties were performed on heterogeneous groups of subjects with confounding factors such as varying ages, CV risk factors, and clinical manifestations of CV disease that could bias the outcome. Furthermore, information concerning the effect of smoking on the measures of pulsatile arterial function in otherwise healthy young adult smokers is sparse. As part of the Bogalusa Heart Study, a community-based investigation of early natural history of

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From the Tulane Center for Cardiovascular Health, Tulane School of Public Health and Tropical Medicine, New Orleans, Louisiana.

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Address correspondence and reprint requests to Dr. Gerald S. Berenson, Tulane Center for Cardiovascular Health, Tulane School of Public Health and Tropical Medicine, 1440 Canal St., Suite 1829, New Orleans, LA 70112-2824; e-mail: berenson@tulane.edu

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CV disease,[16] this study examines the effect of smoking on the compliance of large artery versus small artery and systemic vascular resistance in healthy young adults for whom smoking was the only major traditional CV risk factor.

Methods

Study Population

The screenings for the CV risk factors of the young adults, who participated earlier as children and remained accessible, were conducted periodically since 1979 as part of the longitudinal cohort survey in the biracial (65% white, 35% black), semirural community of Bogalusa, LA. During the 2000–2002 survey of young adults aged 18 to 45 years (n = 1203; mean age 36.3 years; 70% white, 43% men; 31.7% smokers), radial arterial pulse pressure waveforms were recorded on 815 participants (mean age 36.4 years; 70% white, 43% men; 33.9% smokers). Of these, 145 nonsmokers (mean age 35.4 years; 51% white, 45% men) and 142 smokers (mean age 35.6 years; 49% white, 55% men) without obesity (body mass index [BMI] $\geq$30 kg/m^2), hypertension ($\geq$140/90 mm Hg), diabetes (fasting glucose $>$125 mg/dL), dyslipidemia (total cholesterol/HDL-cholesterol ratio $>$5.8 for men and $>$5.3 for women), CV events (heart attack, bypass surgery, angioplasty, and angina), or on medication for these conditions, were selected for this study. Healthy (n = 114) former smokers and passive smokers without these conditions were not included for this study.

Written informed consent was obtained from the study precipitants, and study protocols were approved by the Institutional Review Board of the Tulane University Health Science Center.

Examinations

Data on risk factors were collected according to previously defined protocols.[17] Participants were instructed to fast 12 hours before screening with compliance ascertained by interview on the morning of the examination. All examinations were preformed after venipuncture and a light breakfast. Replicate measures of height, weight, subscapular and triceps skin fold thicknesses were made and the mean values used. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Systolic and diastolic blood pressures were measured three times by each of two randomly assigned trained observers on the right arm of participants in a relaxed, sitting position.

Information on health, medication history, and behavioral lifestyle were obtained by questionnaires. With respect to smoking behavior, subjects were asked about the age of initiation, the length (years) of use, the number of cigarettes smoked per week, and information on passive smoking (exposure to smoking in working and living environments).[18] The questionnaire on smoking was validated by measuring plasma thiocyanate as an independent measure of smoking.[19] Those subjects who never tried cigarettes and were not exposed to passive smoking were classified as nonsmokers. Current smokers were identified as smoking at least one cigarette per week during the past year.

Laboratory Analyses

Cholesterol and triglycerides levels in serum were determined by enzymatic procedures on the Hitachi 902 Automatic Analyzer (Roche Diagnostics, Indianapolis, IN). Serum very-low density lipoprotein (VLDL), LDL-, and HDL-cholesterol levels were analyzed using a combination of heparin–calcium precipitation and agar–agarose gel electrophoresis procedures.[20] The laboratory has been monitored for precision and accuracy of lipid measurements by the surveillance program of the Centers for Disease Control and Prevention (Atlanta, GA).

Plasma immunoreactive insulin levels were measured by a commercial radioimmunoassay kit (Phadebas, Pharmacia Diagnostics, Piscataway, NJ). Plasma glucose levels were measured by an enzymatic procedure as part of a multichemistry (SMA20) profile.

Arterial Compliance Measurements

Radial arterial pulse pressure waveforms were recorded by an acoustic transducer using the HDI/Pulsewave CR 2000 Research Cardiovascular Profiling System (Hypertension Diagnostic Inc., Egan, MN).[21] A wrist stabilizer was used to gently immobilize the right wrist and stabilize the radial artery during measurements. From each subject in the supine position, pressure waveforms were recorded for 30 sec, digitized at 200 samples per second, and stored in a computer. A modified Windkessel model of the circulation was used to match the diastolic pressure decay of the waveforms and to quantify changes in arterial waveform morphology in terms of large artery (capacitive) compliance, representative of the aorta and major branches, small artery (oscillatory) compliance, representative of the distal part of the circulation including small arteries and arterioles, and systemic vascular resistance (mean arterial pressure divided by cardiac output).[21–23]

Four measurements were taken for each subject: two continuous measurements followed by separation of sensor from the tonometer for 5 min of rest and then an additional two continuous measurements. The mean values of four measurements were used in the analyses. The reproducibility in terms of intraclass correlation coefficients between first two and second two measurements on 815 subjects was 0.74 for large artery compliance, 0.87 for small artery compliance, and 0.95 for systemic vascular resistance. To examine the reproducibility further, 60 randomly selected subjects were reexamined 1 to 3 h later, after the initial examination. The intraclass correlation coefficient between these two examinations was 0.63 for large artery compliance, 0.75 for small artery compliance,