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Research Article

Association of serum cotinine levels and the parameters of vascular structure and function in never-smoking adults

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Abstract

Passive smoking is now recognized to be associated with early arterial damage. The aim of this study was to assess the relationship between secondhand smoke (SHS) exposure, measured objectively by serum cotinine level, and the parameters used to assess vascular structure and function among never smokers in North China. From January 2008 to August 2008, 652 adults aged 20–70 years were enrolled. Brachial–ankle pulse wave velocity (baPWV), ankle–brachial index, and carotid intima-media thickness measurements were performed in all patients. All participants were required to respond to an interviewer-led questionnaire including medical histories and demographic data and to receive blood tests on biochemical indicators. We found that in nonsmokers, higher levels of serum cotinine were positively associated with higher baPWV and brachial pulse pressure after adjusting for heart rate, body mass index, and other confounders. Tests for linear trends for this association were statistically significant. In contrast, no association was present with ankle–brachial index and carotid intima-media thickness. In never smokers, higher SHS exposure measured objectively by serum cotinine levels was found to be associated with brachial pulse pressure and baPWV after adjusting for confounders. J Am Soc Hypertens 2015;9(12):918–924. © 2015 American Society of Hypertension. All rights reserved.

Keywords: Arterial stiffness; risk factor; secondhand smoke.

Introduction

Exposure to cigarette smoke is a leading preventable cause of cardiovascular disease (CVD) in China.[1] Despite efforts to adopt a stricter policy regulating smoking in public places, tobacco smoke remains a major indoor air pollutant in China, where only 45% of the population is actually covered by a complete smoke-free environment.[2] A consistent relationship has been demonstrated between active smoking and progression of atherosclerosis as well as increased arterial stiffness.[3] There is evidence that the ankle–brachial index (ABI) inversely and linearly correlates with cigarette smoking.[4] However, among never-smoking adults, it is not clear whether secondhand smoke (SHS) exposure is a risk for decreased ABI. Furthermore, there are only few studies investigating the relationship between SHS and carotid intima-media thickness (CIMT), as well as brachial–ankle pulse wave velocity (baPWV) in never-smoking adults, and all these studies used self-reported SHS exposure, which is prone to misclassification bias.[5,6] Cotinine is an alkaloid found in tobacco and is also a metabolite of nicotine. Cotinine has been effectively used as a biomarker for exposure to SHS.[7,8] In this context, we examined the relationship between SHS exposure, measured objectively by serum cotinine level, and the parameters used to assess vascular structure and function among never smokers in North China.

Conflict of interest: None.

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Methods

Participants

The cross-sectional survey was conducted between January and August 2008. Participants (n = 957), aged between 20 and 70 years, were invited to participate in this study in Beijing and Julu, a small town 400 km south of Beijing. These subjects included inpatients and outpatients as well as volunteers who underwent health-screening examinations in the medical examination centers.

The following exclusion criteria were applied: (1) former and current smokers (including cigarette smoking and smokeless tobacco use), (2) aortic valve diseases and/or aortic aneurysm, (3) history of percutaneous coronary intervention and/or coronary artery bypass grafting, (4) ABI of 0.9 or less, and (5) ejection fraction $<30\%$. We further excluded participants who were inpatients. This resulted in 652 participants included in the final analysis. Written informed consent was obtained for each participant, who was required to correspond to an interviewer-led questionnaire with questions on smoking habits, occupation, drinking habits, reproductive history, and medical histories. Approval of this study was granted by the Institutional Review Board, Capital Medical University.

Data Collection and Measurements

A team of trained research staff collected the anthropometric data. All instruments were standardized before the examination, and the balances were zero calibrated. Standing height without shoes was measured twice with a standard scale to the nearest 0.1 cm. Body weight was measured with the lightest clothing to the nearest 0.1 kg by an electronic weighting scale (Tanita BF-522, Japan). Waist circumference was measured midway between the lowest rib and the superior border of the iliac crest with an inelastic measuring tape at the end of normal expiration to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg)/height squared (m^2). Over weight/obesity was defined as ≥ 24 kg/m^2 according to Chinese guidelines for obesity.[9]

The participants rested for at least 5 minutes in seated position before blood pressure (BP) measurements. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the Chinese guidelines for the management of hypertension. Two measurements with 2-minute intervals were performed in the sitting position on the right arm with the supported arm elevated at heart level using a mercury sphygmomanometer. BP was calculated as the mean of two consecutive readings. A third measurement has been taken if the first 2 are quite different. Nine of the 652 participants have two of their BP measurements ≥ 5 mm Hg. Spaced 2 minutes apart, additional measurement has been taken and three measurements were averaged for SBP and DBP for them. Brachial pulse pressure was defined as the difference between SBP and DBP. Mean arterial pressure was calculated as DBP plus one-third brachial pulse pressure.

Carotid ultrasonography to assess CIMT was performed with the Sonosite Micromax ultrasound device (Sonosite Inc, Bothell, WA, USA) paired with a 5- to 10-MHz multifrequency high-resolution linear transducer. Sonocal software was used to perform automatic CIMT measurements. Six measurements were performed on each carotid artery using average values (average IMT) and maximum values (maximum IMT) automatically calculated by the software. The measurements were taken after the recommendations of the Manheim CIMT Consensus.[10]

An automatic device (ModelBP-203PRE, Colin Inc, Komaki, Japan) was used to perform baPWV and ABI measurements. Each participant was asked to take 5 minutes of rest and then to take examinations in the supine position with cuffs wrapped both on brachia and on ankles, electrocardiogram electrodes placed on both wrists, and a microphone for detecting heart sounds placed on the left edge of the sternum. The pulse volume waveforms were recorded via a plethysmographic sensor connected to the cuffs. Volume waveforms for the brachium and ankle were stored, then an automatic gain analysis with quality adjustment would be done after 10-second sampling. Interval between the brachial and ankle (Tba) was defined as time between the initial rise in the brachial and tibial pressure waveforms. The distance between two sampling points of baPWV could be calculated automatically based on the subject's body stature. Both length and height were measured to the nearest of 1 centimeter (cm). The length from aortic valve to ankle (La) was calculated via the following equation: La (cm) $= 0.8129 \times$ height (cm) $+ 12.328$, whereas that from the aortic valve to the brachia (Lb) was computed using another equation: Lb (cm) $= 0.2195 \times$ height (cm) $- 2.074$. Finally, based on the equation: baPWV $=$ (La $-$ Lb)/Tba, value of baPWV was obtained. In the meantime, bilateral baPWV, Tba BPs, electrocardiogram, and heart sounds were also obtained via automatically computation by this device. The ratio of ankle SBP to brachial SBP yields the ABI value. In this study, the mean value of the bilateral baPWV and left Tba BP was used.

Blood samples were collected from all the subjects after an overnight fast. Total cholesterol (TC), high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, and serum glucose were measured by using standard methods. Serum cotinine was measured using a commercial 96 well (STC Cotinine Micro-plate EIA, Cat.no.CT086D; Calbiotech Inc, Spring Valley, CA, USA). This technique is sensitive to 1 ng/mL.