Association of Brachial-Ankle Pulse Wave Velocity with Asymptomatic Intracranial Arterial Stenosis in Hypertension Patients

Yan Wang, MD, PhD,* Jin Zhang, MD,* Yuesheng Qain, MD,* Xiaofeng Tang, MD,* Huawei Ling, MD,† Kemin Chen, MD,† Yan Li, MD,* Pingjin Gao, MD,* and Dingliang Zhu, MD, PhD*

Background: Intracranial arterial stenosis is a common cause of ischemic stroke in Asians. We therefore sought to explore the relationship of brachial-ankle pulse wave velocity and intracranial arterial stenosis in 834 stroke-free hypertensive patients. *Methods:* Intracranial arterial stenosis was evaluated through computerized tomographic angiography. Brachial-ankle pulse wave velocity was measured by an automated cuff device. *Results:* The top decile of brachial-ankle pulse wave velocity was significantly associated with intracranial arterial stenosis ($P = .027$, odds ratio = 1.82; 95% confidence interval: 1.07-3.10). The patients with the top decile of brachial-ankle pulse wave velocity showed 56% higher risk for the presence of intracranial arterial stenosis to the whole population, which was more significant in patients younger than 65 years old. We also found that brachial-ankle pulse wave velocity related to both intracranial arterial stenosis and homocysteine. *Conclusion:* Our study showed the association of brachial-ankle pulse wave velocity with asymptomatic intracranial arterial stenosis in hypertension patients, especially in relative younger subjects. Brachial-ankle pulse wave velocity might be a relatively simple and repeatable measurement to detect hypertension patients in high risk of intracranial arterial stenosis. **Key Words:** Intracranial arterial stenosis—brachial-ankle PWV—homocysteine—hypertension—Chinese population.

From the *Shanghai Key Laboratory of Hypertension, State Key Laboratory of Medical Genomics, Research Center for Hypertension Management and Prevention in Community, Shanghai Institute of Hypertension, Shanghai, China; and †Department of Radiology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

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Address correspondence to Dingliang Zhu, MD, PhD, Shanghai Key Laboratory of Hypertension, State Key Laboratory of Medical Genomics, Research Center for Hypertension Management and Prevention in Community, Shanghai Institute of Hypertension, 197 Ruijin 2nd Rd, Lu Wan Qu, Shanghai, China. E-mail: zhudingliang@sibs.ac.cn.

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Introduction

Stroke ranks the leading cause of death in China,[1] with ischemic stroke as the predominant subtype. In Chinese population, about 33%-50% of stroke and more than 50% of transient ischemic attack (TIA) relate to intracranial arterial stenosis (ICAS),[2-4] which is the most common cause of ischemic stroke.[5] Hypertension has been considered as a risk factor for both ischemic and hemorrhagic forms of stroke, as well as for ICAS.[6,7] However, there is little study focused on the significance of asymptotic ICAS in hypertension patients.

Arterial stiffness is a surrogate marker of atherosclerosis and carries a poor prognosis for cerebral outcomes independent of conventional risk factors.[8,9] It can be evaluated by measuring pulse wave velocity (PWV) between 2 sites in the arterial tree, with higher PWV indicating stiffer arteries. Carotid–femoral PWV is one of the popular indicators for estimating the level of arterial stiffness. Lots

of evidence have suggested that greater carotid–femoral PWV is associated with the increased risk of cardiovascular events and mortality[10-12]; therefore, it is recommended by several guidelines as a conservative estimate of alternation of aortic function.[13,14]

Brachial-ankle PWV is an alternatively developed technique to assess arterial stiffness, which is now widely used in clinical practice because it allows automatic detection of pulse waves using cuffs on the limbs and it is simpler to use compared with carotid–femoral PWV. Brachial-ankle PWV has been shown to be correlated with carotid–femoral PWV in several studies,[15,16] and proved to have a significant predictive value for cardiovascular mortality and events.[9,17,18] In our previous study, we have found that carotid–femoral PWV was associated with ICAS in a relative small untreated hypertensive population.[19] Brachial-ankle PWV reflects the mixed properties of both central and peripheral arterial stiffness, whereas carotid–femoral PWV mostly reflected properties of central arterial stiffness.[20] The difference in the source of arterial stiffness may have distinct impact on the ICAS. Therefore, we performed this study to investigate the relationship of brachial-ankle PWV with asymptotic ICAS in Chinese hypertension patients.

Method

Study Design

This study was undertaken within the framework of an ongoing cross section and prospective study in China, which was a computerized tomographic angiography (CTA)-based study of intracranial asymptomatic artery stenosis and stroke outcome in stroke-free hypertension patients. Subjects of this study were recruited from hypertension outpatients who were identified in Xinzhuang Community Hospital between May 2012 and December 2014, and then referred to Ruijin Hospital, a general hospital in Shanghai. Hypertensive status was defined as systolic blood pressure (SBP) greater than or equal to 140 mmHg and/or diastolic BP (DBP) greater than or equal to 90 mmHg, or individuals taking antihypertensive medication. All the participants were older than 50 years old. Those who had stroke, TIA, or atrial fibrillation identified from medical history were excluded. Those who were unfit for CTA examination because of iodine allergy were also excluded.

Ethics Statement

The study protocol was approved by the Ethics Committee of Ruijin Hospital and written informed consent was obtained from all participants.

Demographic and Clinical Measurements

After the subjects had rested for at least 5 minutes in the sitting position, SBP and DBP were measured using a verified electronic sphygmomanometer (HEM-907, Omron, Kyoto, Japan) by a trained physician or nurse. The average of 3 consecutive BP readings with 1 minute interval of each participant was used for the current analysis. Body weight and height were recorded with participants wearing light indoor clothing and no shoes. Clinical information was collected by interview, including smoking and drinking habits, current drug intake, personal history of diabetes, etc. Current smokers were defined as those who had smoked cigarettes on one or more days in the past 30 days. All the biochemical measurements including fasting plasma glucose, serum concentrations of total cholesterol (TC), triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein cholesterol were performed in the Central Laboratory of Ruijin Hospital (Shanghai, China) using the standard protocols.

Serum homocysteine was measured using automatic clinical analyzers (Beckman Coulter) at the core laboratory of the National Clinical Research Center for Kidney Disease, Nanfang Hospital, Guangzhou, China.

CTA Protocol

CTA was performed with a 64-section helical CT scanner (GE FX/I, General Electric, Fairfield, CT). CTA acquisitions were obtained after a single bolus intravenous injection of 70 mL Optiray (ioversol, Mallinckrodt Inc., MO) 320 into the antecubital vein at a rate of 3 mL/s. Scanning covered the whole brain down to the level of aortic arch with 5-mm slice thickness. Images were reformatted in axial, sagittal, and coronal planes with 1.25-mm slice thickness. All images were read independently at a workstation with the AW4.4 vessel analysis software (General Electric, Fairfield, CT) by 2 experienced radiologists who were blinded to clinical data of the patients. Stenosis was defined as a lesion that decreased the arterial internal diameter. The percentage of stenosis was calculated as the ratio of the diameter of the diseased artery at its most severe site divided by the diameter of a nearby normal segment. The intracranial arteries included intracranial segment of internal carotid artery and vertebral artery, basilar artery, anterior cerebral artery, middle cerebral artery, and posterior cerebral artery. The greatest stenosis at an intracranial artery was chosen as being representative for each subject. The number of arteries with stenosis for each patient was also counted. The 2 radiologists had good agreement in the designation of stenosis ($\kappa = .93$, $P < .001$). All disagreements were reviewed and adjudicated by a senior radiologist to reach a consensus.

Measurement of Brachial-Ankle PWV

Brachial-ankle PWV was measured by the use of the Vascular Profiler-1000 device (Omron, Kyoto, Japan) as previously described.[21,22] Briefly, trained technicians and physicians placed the pressure cuffs on both arms and both ankles and performed the measurement after the subject had rested for ≈10 minutes in the supine position. The device simultaneously measures pulse waves