Association between Cerebral Arterial Stiffness and Large Artery Atherosclerosis in Acute Ischemic Stroke

Xian Fu, PhD, MD,* Qi Liu, MD,† Xianfan Zeng, MD,* Shiyan Huang, MD,* Ruxun Huang, MD,‡ and Qingchun Gao, PhD, MD*

Background and Purpose: Carotid–cerebral pulse wave velocity (ccPWV) reflects the segment (C-M segment) stiffness between common carotid artery and ipsilateral middle cerebral artery. The C-M segment atherosclerosis (CMSA) is regarded as a most frequent cause of anterior circulation ischemic stroke. We therefore, attempted to investigate the relationship between cerebral arterial stiffness and CMSA, and provide reliable data for the early diagnosis of CMSA. *Methods:* Between June 2012 and August 2016, 81 acute ischemic stroke (AIS) patients with 154 C-M segments successfully evaluated with digital subtraction angiography and ccPWV were enrolled into this study. Patient demographics and clinical data were retrieved from our AIS databases. *Results:* Multivariate analyses showed that ccPWV was independently associated with CMSA ($\beta = 39.6$, $P = .009$) and Systolic blood pressure ($\beta = 7.1$, $P < .001$) in AIS patients. The values of ccPWV had a trend to be higher in the groups with more lesions ($F = 45.9$, $P < .01$) and severer stenosis ($F = 102.6$, $P = .000$), and was positively correlated with the number of lesions ($r = .662$, $P = .000$), and degree of stenosis ($r = .858$, $P = .000$) of CMSA. The fractional polynomial plots with 95% CIs also describe the close relationship between ccPWV and the number of lesions and degree of stenosis in CMSA. *Conclusions:* Cerebral arterial stiffness is independently associated with the presence of CMSA, closely related to the vascular damage of C-M segment and reflects the vascular structure change of C-M segment in AIS patients. It may have the potential for assessment of CMSA in its initial stage.

Key Words: Cerebral large artery atherosclerosis—carotid–cerebral pulse wave velocity—cerebral arterial stiffness—acute ischemic stroke

From the *Department of Neurology and Institute of Neuroscience, the Second Affiliated Hospital of Guangzhou Medical University, Guangzhou; †New Era Stroke Care and Research Institute, General Hospital of the PLA Rocket Force, Beijing; and ‡Department of Neurology, the First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China.

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Address correspondence to Qingchun Gao, PhD, MD, Department of Neurology and Institute of Neuroscience, the Second Affiliated Hospital, Guangzhou Medical University, 250# Changgang East Road, Guangzhou 510260, China. E-mail: qcgao@263.net

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Introduction

Cerebral large artery atherosclerosis diseases are considered especially important causes of ischemic stroke (IS), which are responsible for about 15%-37% of all IS.[1–3] In anterior circulation, the segment (C-M segment) between common carotid artery (CCA) and the ipsilateral middle cerebral artery (MCA) is verified as the specific region more prone to atherosclerosis, and the C-M segment atherosclerosis (CMSA) is regarded as a most frequent cause of anterior circulation IS.[1,4–7] Therefore, early detection of CMSA may guide us for early therapeutic interventions in the hope of reducing the occurrence of IS, and is crucial for the primary prevention of IS in communities.[1,5,6]

Arterial stiffness is an important characteristic of the arteries and a direct reflection of the condition of these blood vessels, and reduced arterial elasticity is a sensitive marker that indicates damage to the blood vessel wall.[8]

Its assessment is becoming a focal point in the efforts of early detection and prevention of cardiovascular and cerebrovascular diseases.[9,10] At present, the most representative and noninvasive technique for assessing arterial stiffness is pulse wave velocity (PWV).[11−14]

Numerous studies have demonstrated independent associations between PWV with atherosclerosis of central or peripheral arteries.[15−21] However, few studies have considered the relationship between cerebral arterial stiffness and large artery atherosclerosis. The key reason is the absence of a suitable and accurate method to measure the cerebral arterial stiffness. Recently, carotid−cerebral PWV (ccPWV) measurement, which can be performed noninvasively and easily, has become available as a means of measuring cerebral arterial stiffness.[22] It mainly measures the cerebral arterial stiffness of C-M segment.

Therefore, the aim of the current study was to systematically examine the association between ccPWV and CMSA in acute ischemic stroke (AIS) patients, and provide reliable data for the early diagnosis of CMSA.

Materials and Methods

Patients

We collected database for consecutive patients with AIS within seven days of symptom onset who were admitted between June 2012 and August 2016. Among them, we enrolled anterior circulation AIS patients who underwent brain multimodal magnetic resonance (MR), digital subtraction DSA and ccPWV measurements during the admission period. We excluded patients with (1) arrhythmia that could influence the accurate assessment of PWV, (2) unsuitable temporal windows for conducting ccPWV measurements, (3) high or medium risk potential cardiac sources of embolism based on the Trial of Org10172 in Acute Stroke Treatment classification,[23] and (4) history of radiation therapy due to a head and neck cancer which may promote cerebral artery atherosclerosis. Written informed consent for this study was obtained from each patient or his or her family member. The ethics committee of our Institute approved the study protocol. Good Clinical Practice guidelines in accordance with the Declaration of Helsinki were used, and the privacy of patients was strictly protected.

Data Acquisition

All data were recorded in our AIS databases. Baseline characteristics included sociodemographic variables (age and gender) and cardiovascular risk factors (including hypertension, coronary heart disease, diabetes mellitus, hyperlipidemia, peripheral arterial disease, current smoking, systolic blood pressure [BP], and body mass index). Clinical features included results of DSA and ccPWV in the hospital. DSA was used to assess the CMSA. The degree of stenosis in the extracranial cerebral artery was measured using the method in the North American Symptomatic Carotid Endarterectomy Trial,[24] and that in the intracranial artery was measured using the method in the Warfarin versus Aspirin for Symptomatic Intracranial Disease.[25] CMSA was defined as an angiographically verified atherosclerotic stenosis within the C-M segment. Based on the results of DSA, all the segments were classified into different groups according to the number of lesions in CMSA [normal, one (one lesion), two (two lesions), and no less than three (≥three lesions) groups] and the stenosis of C-M segments [normal, mild stenosis (the severest stenosis <50%), and severe stenosis (≥50%) groups], respectively.

Measurement of ccPWV

As described previously,[22] ccPWV was measured with a special two-channels TCD (TCD-2000M; Beijing Chioy Medical Technology Co., Ltd., Beijing, China) using 2-MHz and 4-MHz ultrasound transducers in the supine position by two experienced operators. The TCD machine used in this study has a built-in program model called arterial pulse wave analysis system, which can store, derive, and process signals obtained from transducers on CCA and MCA sites and simultaneously display these signals with expanded waveforms. The 2-MHz probe was held in a temporal window for detecting the proximal part of MCA, and MCA was insonated at a depth of 50-55 mm using standard criteria.[26] The other 4-MHz transducer in the angle fixator of 30° was placed on the ipsilateral pulsation point of CCA beside the thyroid notch in the neck of the patient to detect CCA. The transit time (Δt, ms) of the pulse wave traveled between the two insonation sites was automatically measured by the arterial pulse wave analysis system based on the waveform analysis of CCA and MCA.[22] The mean transit time (Δmt) was then determined from 10 consecutive cardiac cycles. The distance (D, cm) traveled by the pulse wave was defined as the body surface distance (D_1, cm) between the two probes using a tape measure plus cosine 30° of detecting depth (D_2, cm) for CCA, namely, $D = D_1 + D_2 \times \text{cosine } 30°$.[22] Thus, ccPWVs on each side were calculated as ccPWV = D/Δmt (cm/s). All the above can be automatically completed by the arterial pulse wave analysis system except the measurement of body surface distance.

In all the studies, ccPWV was obtained after at least 5 minutes of rest. The validity and reproducibility of the measurement of ccPWV were previously reported elsewhere.[22]

Statistical Analysis

Values are reported as mean ± SD, or number (percentage) of subjects. To identify the factors associated with ccPWV, we performed multiple regression analysis with adjustments for sex, age, and variables that exhibited a P value < .05 in the