Impaired Brachial Flow-Mediated Dilatation May Predict Symptomatic Intracranial Arterial Dissections

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Background and Purpose: Spontaneous intracranial arterial dissections are characterized by the sudden disruption of the internal elastic lamina in the intracranial arteries. The purpose of our retrospective study was to investigate whether patients with nontraumatic intracranial arterial dissections had normal endothelial function. *Methods:* The study included symptomatic patients with nontraumatic intracranial arterial dissections who underwent an endothelial function test. Controls were selected from headache patients matched for sex and age. Endothelial function was assessed using flow-mediated dilatation. We investigated patients' ankle brachial index and pulse wave velocity to determine the degree of atherosclerosis. Patient characteristics, brachial flow-mediated dilatation, ankle brachial index, and pulse wave velocity were compared between the 2 groups. *Results:* During the study period, there were 22 patients with nontraumatic intracranial arterial dissections matched with 22 controls. Clinical characteristics were compared between the groups. Although there were no significant differences in ankle brachial index or pulse wave velocity between the 2 groups, patients with intracranial arterial dissections had lower flow-mediated dilatation values than controls (median flow-mediated dilatation, 3.95% in dissection patients versus 7.3% in controls, $P = .0035$). Brachial flow-mediated dilatation was impaired in symptomatic patients with nontraumatic intracranial arterial dissections despite the normal ankle brachial index and pulse wave velocity. *Conclusions:* Impaired brachial flow-mediated dilatation is a probable predictor of intracranial arterial dissections.

Key Words: intracranial arterial dissections—flow mediated dilation

Introduction

Intracranial arterial dissections (IADs) are less common than cervical artery dissections in populations from Europe and North America. IADs are reportedly more common in Asian populations compared with Europe and North America,[1] and spontaneous IADs associated with stroke in young patients are attracting increasing attention.[2] Nontraumatic IADs are characterized by the sudden disruption of the internal elastic lamina in the intracranial arteries. Because IADs are rare, population-based incidence data are lacking.[3]

Intracranial arterial dissections cause arterial stenosis, occlusion, and aneurysm.[4] Intracranial arterial dissection is a clinical diagnosis based on a characteristic history and neuroradiological examination. IADs can be diagnosed using findings from magnetic resonance imaging, magnetic resonance angiography, 3-dimensional computed tomographic angiography, and cerebral angiography. However, the diagnosis of IAD is difficult in some cases. IADs may be an underdiagnosed cause of strokes defined by the occurrence of a hematoma in the wall of an intracranial artery.[1]

Endothelial dysfunction plays a pivotal role in the development, progression, and clinical manifestations of atherosclerosis.[5] The flow mediated dilation (FMD) test is

Abbreviations: IADs, Intracranial arterial dissections ICA, internal carotid artery; VA, vertebral artery; ABI, ankle brachial index; ECG, electrocardiogram; FMD, flow mediated dilation; PWV, pulse wave velocity; BD, baseline diameters; MD, maximum diameters

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the standard tool used to assess endothelial function.[6] Previous studies have reported that arterial endothelial function might be impaired in patients with extracranial arterial dissections.[7–9] However, no previous studies have addressed brachial FMD in patients with symptomatic nontraumatic intracranial internal carotid artery (ICA) or vertebral artery (VA) dissections.

The purpose of our retrospective study was to investigate whether patients with nontraumatic IADs had normal endothelial function.[10]

Methods

IAD Patients and Controls

Our retrospective analysis included patients with symptomatic nontraumatic IADs who were admitted to our institution from 2012 to 2015 and underwent an endothelial function test. Controls matched for sex and age were selected from headache patients without strokes admitted to the outpatient clinic. FMD can be easily achieved by inducing postischemic hyperemia in the brachial artery.[11]

Aortic Stiffness Expressed as Pulse Wave Velocity and Ankle Brachial Index

Ankle brachial index was measured using a blood pressure pulse wave inspection device (model BP-203RPE; Nihon Colin, Tokyo, Japan). Ankle brachial index (ABI) was estimated as ankle systolic blood pressure divided by brachial systolic blood pressure. The brachial−ankle pulse wave velocity (PWV) was determined using a noninvasive automatic waveform analyzer. PWV provides a noninvasive assessment of aortic stiffness.[12] A simple, new device that uses an oscillometric method for measuring PWV was recently developed.[13] In our study, the PWV was automatically calculated using a Colin Waveform Analyzer. This instrument simultaneously records PWV, blood pressure, an electrocardiogram, heart sounds, and ABI. The validity, reproducibility, and clinical significance of noninvasive PWV measurement have been reported elsewhere.

FMD Study Protocol

We measured vascular responses to reactive brachial artery hyperemia in all subjects. The subjects maintained a supine position in a quiet, dark, and air-conditioned room (constant temperature of 22°C-25°C) throughout the study. Basal brachial artery diameter and FMD were measured after 30 minutes in the supine position.

Measurement of FMD

Participants underwent brachial FMD examination after 15 minutes of rest in the fasting state. Prior to FMD measurement, baseline longitudinal ultrasonographic images of the brachial artery were obtained with a linear, phased-array high-frequency (10-MHz) transducer using an UNEXEF18G ultrasound unit (UNEX Co., Nagoya, Japan) and automatically stored on a hard disk. The vascular response to reactive hyperemia in the brachial artery was used to assess endothelium-dependent FMD. A high-resolution linear arterial transducer was coupled to computer-assisted analysis software (UNEXEF18G; UNEX Co.) that used an automated edge detection system to measure brachial artery diameter.

A blood pressure cuff was wrapped around the patient's elbow, 3 to 7 cm above the antecubital fossa, where it formed a straight segment, free of major branches. The baseline longitudinal ultrasonographic images of the brachial artery were obtained at the end of diastole from each of 10 cardiac cycles. The brachial artery diameters obtained from the 10 cardiac cycles were averaged, and this value represented the baseline brachial artery diameter. The blood pressure cuff was then inflated to 50 mm Hg above systolic pressure for 5 minutes. Pulsed Doppler velocity signals were obtained for 10 cardiac cycles at baseline and for 120 seconds immediately after cuff deflation. Images of the right brachial artery were captured continuously for 120 seconds after cuff deflation. Videotapes of the acquired images of the brachial artery were analyzed. The readings of these digitized images generated the baseline and maximum diameters (BD and MD) of the brachial artery from which the absolute change from baseline diameter and percentage (%) brachial FMD was computed. FMD% was computed with the formula: (MD − BD) multiply 100% divided by BD, ie, (MD − BD) × 100%/BD, and this value was used for analysis.

Evaluation

We compared patient characteristics (age and sex) between the groups. Ankle brachial index and PWV were evaluated to determine the degree of atherosclerosis. We obtained information regarding vascular risk factors in both IAD and control patients. Differences between the IAD and control groups were assessed using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Multivariate logistic regression analysis was used to determine independent predictors of IADs. *P* values less than .05 were considered statistically significant. All analyses were performed using JMP Pro version 11.0.

Results

During the study period, there were 22 patients with nontraumatic IADs. Twenty of these patients presented with headaches and/or altered neurologic status due to cerebral ischemia, and 2 patients presented with subarachnoid hemorrhage. The IADs were located in the VA (n = 15), the ICA (n = 4), the anterior cerebral