Review Article

Prediction Factors of Recurrent Stroke among Chinese Adults Using Retinal Vasculature Characteristics

Yuanyuan Zhuo, PhD,* Haibo Yu, PhD,* Zhuoxin Yang, PhD,* Benny Zee, PhD,†,‡ Jack Lee, PhD,† and Lei Kuang, PhD student†

Objective: To identify the characteristics of retinal vessels that are associated with recurrent cerebral infarction and to establish predictive model for recurrent cerebral infarction in further study. *Methods:* Up to 196 patients with cerebral infarction were included in our study, including 137 patients with new onset cerebral infarction and 59 patients with recurrent cerebral infarction. Retinal vessel characteristics of all patients were analyzed and reported by an automated retinal image analysis system. Retinal and clinical characteristics were compared between recurrent and new onset subjects. Multivariate logistic regression was used to identify risk factors associated with recurrent ischemic stroke within the year after an initial stroke onset. *Results:* Every unit increase in the vessel caliber measures of central retinal artery and vein equivalent was found to give coronary heart diseases an additional 4.28 times (95% confidence interval 1.204-15.215) the risk of stroke recurrent whereas every increased unit of arterial and venous angles would be associated with 3.9 and 13.7 times increase in such risk among atrial fibrillation subjects. Measures such as bifurcation coefficient of arterioles showed opposite effects when interacted with different clinical factors. Negative integrations were found between venous asymmetry index and various factors such as atrial fibrillation (odds ratio .73, 95% confidence interval .61-.88), coronary heart diseases (odds ratio .79, 95% confidence interval .70-.89), and bifurcation coefficient of arterioles (odds ratio .38, 95% confidence interval .21-.72), indicating a decreased recurrent risk among these subjects when venous asymmetry level increases. *Conclusions:* Retinal vessel characteristics interacted with each other as well as traditional clinical risk factors in affecting the risk of stroke recurrence. **Key Words:** Cerebral infarction—recurrent infarction—retinal vessels—risk prediction.

From the *Shenzhen Traditional Chinese Medicine Hospital, Shenzhen, China; †Division of Biostatistics, Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong SAR; and ‡Clinical Trials and Biostatistics Lab, Shenzhen Research Institute, The Chinese University of Hong Kong, Hong Kong SAR.

Received October 9, 2016; revision received January 3, 2017; accepted January 20, 2017.

This research was supported by the Shenzhen Science and Technology Project (No. JCYJ20140408152909288).

Address correspondence to Zhuoxin Yang, PhD, Acupuncture and Moxibustion Department, Shenzhen Traditional Chinese Medicine Hospital, 1st Fuhua Road, Futian District, 518033 Shenzhen, China. E-mail: 48132537@qq.com.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2017.01.020

Introduction

Stroke is one of the most important diseases that endanger human health in the world. The health burden of stroke, represented by increasing mortality and incidence rate, is more severe in some developing countries. In recent years, some emphasis has been put on recurrent stroke as it showed a higher death and disability rate as compared to that of initial onset. In addition, according to recent statistics, one third of the stroke was associated with recurrent attacks.[1] The death rate and disability rate of recurrent cerebral infarction are higher than that of the first time onset. After initial transient ischemic attack or minor stroke, there is an approximately 10% risk of subsequent stroke within 90 days, with 4%-5% of this risk occurring in the first 48 hours. Primary prevention targeting at high-risk patients is by far the most effective strategy to reduce the burden of stroke. Hence, identifying a patient at risk should be one of the major methods for recurrent stroke prevention.

Traditional risk factors for recurrent stroke have been well studied and accepted, which include existence of coronary heart disease (CHD), atrial fibrillation (AF), hyperlipidemia (HLM), hyperhomocysteinemia (Hhcy), improper diet, overwork, emotional excitement, and body mass index (BMI). However, it is still insufficient for us to use these factors to identify all recurrent strokes, thus, new tools should be used.

Retina vessel circulation shares similar morphology, function, and pathologic changes with cerebral vascular system. As retina is the only place throughout the body where a small part of the vascular system can be observed directly, cerebral vascular changes can be explored through retinal image to determine the risk of strokes. Previous studies have shown that a number of retinal characteristics were significantly associated with strokes.[2-6] However, none of the studies had investigated if and how retinal measures were related to recurrent stroke. In this paper, we extracted the retinal parameters from color fundus retinal images and identified the risk factors associated with recurrent stroke cases; we further explored the use of retinal characteristics in a multivariate model for a recurrent stroke risk assessment.

Methods

Ethics Statement

This study was approved by the Ethics Committee of the Shenzhen Traditional Chinese Medicine Hospital and was performed in accordance with the guidelines of the Helsinki Declaration. All patients or their legal representatives provide their written informed consent form.

Data Source

In the case–control study, a total of 328 ischemic stroke patients from Shenzhen Traditional Chinese Medicine Hospital were enrolled in the study. Baseline data, including age, gender, medical history, physical examination, laboratory tests, and electrocardiography, were collected. All patients underwent detailed computed tomography (CT) or cranial magnetic resonance (MR) scan.

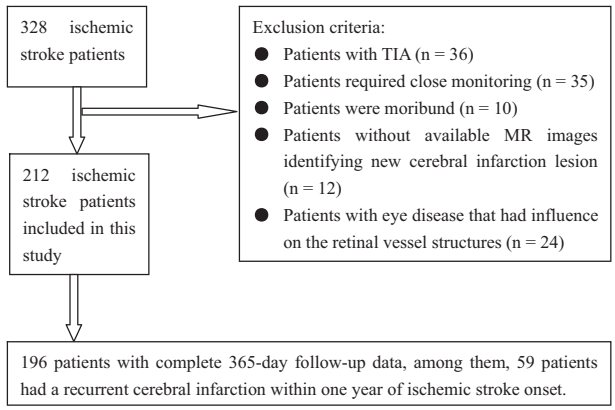

Figure 1. *Flow chart of enrollment of study population. Abbreviations: MR, magnetic resonance; TIA, transient ischemic attack.*

Inclusion criteria included onset of ischemic stroke over 1 year, age of 30-80 years, and adequate sitting balance to carry out the retinal photography. Subjects were excluded if any of the following conditions appeared: clinically unstable, required close monitoring, moribund, eye disease that had influence on the retinal vessel structures, or physically or subjectively unable to comply with MR examination. Patients suspected to suffer from cerebral diseases and those with diseases that influenced vessel morphology were also excluded in the study. In the end, 212 of the 328 patients who presented with ischemic stroke were included in our study (Fig 1).

The clinical and imaging information of these patients such as age, gender, past history, and stenotic degree of responsible cerebral artery was evaluated, and the associated risk factors for recurrent ischemic stroke within 1 year were analyzed.

Recurrent ischemic stroke was defined as a sudden focal neurological deficit sustained for a duration of more than 24 hours, suggesting a new ischemic event that was verified by cranial CT or magnetic resonance imaging (MRI).[7]

Study Design, Patient Population, and Observation Period

A retrospective case–control study was used to evaluate the risk for stroke patients. Stroke (clinical or baseline) risk factors including age, gender, hypertension, diabetes, HLM, CHD, AF, Hhcy, smoking status, drinking status, and BMI were recorded in the study. Hypertension was defined as systolic blood pressure greater than 140 mmHg, diastolic blood pressure above 90 mmHg, or use of antihypertensive medication during the previous 2 weeks. Diabetes mellitus was defined as a fasting blood glucose concentration above 7.0 mmol/L, a nonfasting value of