Homocysteine is Associated with Exaggerated Morning Blood Pressure Surge in Patients with Acute Ischemic Stroke

Jun-Chao Xie, MD,[1] Ying-Ying Lin, MD,[1] Xiao-Hui Liu, MD, Yi-Chen Zhao, MD, Xiao-Ye Ma, MD, Jia Yu, MD, Xue-Yuan Liu, PhD, and Yan-Xin Zhao, PhD

Background: Considerable researches suggest that high level of homocysteine (Hcy) is associated with the risk of ischemic stroke. Ambulatory blood pressure monitoring (ABPM) parameters have also been confirmed associated with cardio-cerebrovascular events. However, the relationship between Hcy and ABPM parameters remains unclear in patients with acute ischemic stroke. In this study, we aim to investigate the association between Hcy level and ABPM parameters in patients with acute ischemic stroke. *Methods:* We enrolled 60 patients with acute ischemic stroke who received ABPM. We calculated ABPM parameters like morning blood pressure surge (MBPS), ambulatory arterial stiffness index, blood pressure variability, and night dipping patterns. *Results:* Multivariate logistic regression analysis indicated that patients in the top quartile of Hcy level tended to have a higher level of prewaking and sleep-trough MBPS compared with patients in the lower 3 quartiles after adjusted for age and gender ($P = .028$ and $P = .030$, respectively). When treating Hcy as a continuous variable, the linear regression showed the association between Hcy level and both MBPS parameters remained significant (prewaking MBPS, $r = .356$, $P = .022$; sleep-trough MBPS, $r = .365$, $P = .017$, respectively). However, there is no association between Hcy level and ambulatory arterial stiffness index, blood pressure variability or night dipping patterns ($P = .635$, $P = .348$ and $P = .127$ respectively). *Conclusions:* There is a relationship between the 2 major cerebrovascular risk factors: MBPS and Hcy.

Key Words: Morning blood pressure surge—Acute ischemic stroke—Homocysteine—Ambulatory blood pressure monitoring

Introduction

Homocysteine (Hcy), a sulfur-containing amino acid, is found associated with increased risk of cardio-cerebrovascular diseases and metabolic syndrome in hypertension patients.[1] The association between Hcy levels and first stroke risk was reported in the analysis of the China Stroke Primary Prevention Trial.[2] Studies also suggested that elevated Hcy levels in patients with acute ischemic stroke might predict mortality, especially in the large-vessel atherosclerosis subtype.[3] Hcy level was discovered positively associated with the presence of ischemic stroke in Chinese hypertensive patients.[4] Besides Hcy, The 24-hour ambulatory blood pressure monitoring (ABPM) parameters like morning blood pressure surge (MBPS), night dipping patterns, ambulatory arterial stiffness index (AASI), and blood pressure (BP) variability have also been confirmed as predictors for not only occurrence but also recurrence of cardio-cerebrovascular events.[5-12] The ABPM is considered as a gold standard for evaluating blood pressure (BP) condition especially in hypertension patients. In stroke patients, BP variability is associated with cardio-cerebrovascular outcomes.[13,14] AASI predicts future cardiovascular events, particularly

From the Department of Neurology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai 200072, China.

Received November 27, 2017; revision received May 17, 2018; accepted May 22, 2018.

Grant support: This project was supported by the National Natural Science Foundation of China (grant numbers 81571033 and 81371212), and the Science and Technology Commission of Shanghai Municipality [grant numbers 18140901900 and 17411950101].

Address correspondence to Xue-Yuan Liu, PhD or Yan-Xin Zhao, PhD, Department of Neurology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, 301 Middle Yanchang Road, Shanghai 200072, China. E-mailes: lxyshtj@163.com doctorx2017@126.com, zhao_yanxin@126.com

[1]These authors contributed equally to this work.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.05.032

stroke, and mortality of cardio-cerebrovascular events, and is associated with arterial function.[11,15,16] Thus, recording ABPM parameters is necessary for patients with cardio-cerebrovascular diseases and should be included in the secondary prevention scheme. Studies indicated that ABPM parameters may be associated with other cardio-cerebral vascular risk factors like total cholesterol, low-density lipoprotein and C-reactive protein values.[17,18] Since both Hcy level and ABPM parameters are risk factors and predictors of cardio-cerebrovascular events for individuals with or without cardio-cerebrovascular event,[14,19,20] we questioned whether there are some underlying specific links between them. However, few studies focused in this topic in acute ischemic stroke patients. Herein, we conducted this study to reveal the possible relationship between ABPM parameters (including MBPS, night dipping pattern, BP variability, and AASI) and plasma Hcy level in first-ever ischemic stroke patients.

Patients and Methods

Patients

This study was approved by the ethnic committee of Shanghai Tenth People's Hospital. We included consecutive cases with first-ever acute ischemic stroke that admitted to the Department of Neurology of Shanghai Tenth People's Hospital from March, 2014 to October, 2014. Acute ischemic stroke is defined as abrupt neurological dysfunction caused by focal brain ischemia leading to persistent neurologic deficit that accompanied by characteristic abnormalities on brain imaging. In our study, we enrolled patients who developed an acute ischemic stroke conformed by computed tomography or magnetic resonance imaging of the brain within 48 hours of symptom onset. Patients were diagnosed as ischemic stroke according to the World Health Organization criteria.[21] Patients with a history of chronic stroke or myocardial infarction were excluded. Blood samples were taken after the patients were hospitalized.

Ambulatory Blood Pressure Monitoring

ABPM was performed from the first 8:00 AM after the patients were admitted to our hospital to 8:00 AM the next day with a portable device (Welch Allyn ABPM 6100, Welch Allyn Inc, Skaneateles Falls, NY, USA). ABPM was performed with an adequate cuff on the patient's nondominant arm and automatic BP measurements were programmed to take place at 30-minute intervals while awake and 60-minute intervals while resting. Readings were excluded if less than 80% of the total measurements were obtained.

ABPM Parameters

In this study, we focused in 4 ABPM parameters: MBPS, AASI, BP variability, and night dipping patterns. For MBPS, we calculated both pre-awaking MBPS which calculated as the morning BP (the mean BP during 2 hours after wake-up) minus the pre-waking BP (2 hours average BP before wake-up) and sleep-trough MBPS which defined as the morning BP minus the lowest nighttime BP (average of 3 BP readings centered on the lowest nocturnal BP reading).

Night BP dipping was defined as ≥10% reduction in average systolic blood pressure (SBP) during sleep compared with average daytime SBP,[22] and nondipping as the reduction was less than 10%. The nocturnal SBP reduction (%) was calculated as 100 (1—night-time SBP/daytime SBP ratio).

BP variability was defined as standard deviation (SD) of SBP in 24 hours within a 24-hour period.

AASI was calculated as 1 minus the regression slope of diastolic over SBP values as recorded by the ABPM.[23]

Statistical Analysis

Normally distributed data was expressed as mean ± SD. For skewed distributed data, median and interquartile range was calculated. The baseline characteristics of patients in the top quartile and the lower 3 quartiles were compared with chi-square test or Mann−Whitney U test, as appropriate. Univariate and multivariate logistic regression analysis were applied to analyze dichotomies variables. For continuous variables univariate and multivariate linear regression analysis were conducted. Mann−Whitney U test was used to compare continuous variables between groups. All comparisons were 2-sided. Analysis of outcome variable was adjusted for age and gender. All analyses were performed using STATA software package (version 12.0; Stata Corp., College Station, TX). Statistical significance was considered when a P value less than .05.

Results

Baseline Characteristics

A total of 60 patients (mean age 63.85 ± 10.91; median age: 63, interquartile range: 56-74; male%: 60%) with first-ever acute ischemic stroke hospitalized in the Department of Neurology, Shanghai Tenth People's Hospital were consecutively enrolled according to our criteria. Baseline characteristics were shown in Table 1.

Analysis of the Dichotomised Hcy Level

Hcy level was ranged from 5.5 μmol/L to 19.9 μmol/L (mean ± SD: 11.64 ± 3.28 μmol/L). We dichotomized the Hcy level at the top quartile, and binary variables were created with 15 patients in the top quartile (Hcy level: 15.70 ± 2.87 μmol/L), and with 45 patients in the lower 3 quartiles (Hcy level: 10.29 ± 2.09 μmol/L). The baseline characteristics in the top quartile and the lower 3 quartiles were shown in Table 2. MBPS parameters (prewaking MBPS and sleep-trough MBPS) tended to be higher in the top quartile. Compared with patients in the lower 3