Lymphocyte-to-Monocyte Ratio: A Novel Predictor of the Prognosis of Acute Ischemic Stroke

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Background: Lymphocyte-to-monocyte ratio (LMR) is associated with diverse malignancies and cardiovascular diseases. However, it has not yet been identified whether LMR is correlated with stroke severity and prognosis. We aimed to explore the relationship between LMR and stroke severity, prognosis, and the predictive value of LMR on a 3-month functional outcome in patients with acute ischemic stroke (AIS). *Materials and Methods:* A total of 512 patients were enrolled in this study. Baseline demographic and clinical data of all patients were collected. Based on the LMR value on admission (>4.83, 2.97-4.83, <2.97), patients were divided into 3 groups. Moderate to severe stroke was defined as a National Institutes of Health Stroke Scale score of 6 or higher. Poor outcome was defined as a modified Rankin Scale score of 3 or higher. We used the Spearman rank correlation to evaluate the relationship between LMR and stroke severity. Binary logistic regression analysis was used to assess risk factors of stroke severity and prognosis. The receiver operating characteristic (ROC) curve was used to estimate the predictive value of LMR on prognosis. *Results:* LMR was inversely correlated with stroke severity ($r = -.014$, $P = .019$). Moreover, LMR was an independent protective factor of stroke severity (odds ratio [OR] .891, 95% confidence interval [CI] .815-.973, $P = .010$) and prognosis (OR .507, 95% CI .437-.590, $P < .001$). ROC indicated that an LMR lower than 2.99 predicted a poor outcome, with a sensitivity of 69.3% and a specificity of 86.6%. *Conclusion:* A lower LMR on admission was independently associated with severe stroke and 3-month poor outcome in patients with AIS. **Key Words:** Lymphocyte-to-monocyte ratio—acute ischemic stroke—stroke severity—prognosis.

Introduction

Stroke is the second most common cause of mortality and becomes the third major cause of disability worldwide.[1] In China, new strokes are approximately 2.4 million annually, with a stroke mortality of 159 per 100,000 person-years, which results in stroke becoming the leading cause of death.[2] Ischemic stroke possesses nearly 87% of all cases, leading to severe neurological deficits.[3] However, the effective treatment for ischemic stroke is limited at present. Consequently, it is vital to understand the pathogenic mechanisms of stroke and to control risk factors as soon as possible, which is imperative for the prognosis of patients.

Inflammation response has been widely considered as a critical factor participating in the pathophysiology process of acute ischemic stroke (AIS).[4] Following an ischemic stroke, infiltration of immune cells and the release of proinflammatory cytokines are involved in secondary progression of neuronal injury, which exacerbates blood–brain

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barrier disruption, brain edema, and infarct volume.[5] Recent some studies have clarified that increased neutrophils is a poor prognostic biomarker in patients with AIS, which indicates that immunomodulatory therapy may be a potential treatment for AIS.[6-8] Nevertheless, a significant decrease in lymphocytes has been observed in patients with poor outcomes, confirming that low lymphocyte counts play a negative role in long-term functional outcome after AIS.[7,9] As another major trigger for the postischemic inflammatory process, monocytes are increased in the peripheral blood circulation after stroke onset, thus migrating into the infarct region and expanding brain lesion.[10]

Lately, the lymphocyte-to-monocyte ratio (LMR) has been reported to be associated with adverse prognosis in multiple malignancies.[11,12] Besides, as a novel marker of baseline inflammatory response, low LMR has been closely correlated with the severity of coronary artery disease and has been regarded as a risk factor for atherosclerosis.[13] Similarly, a decreased LMR has been independently linked to long-term mortality in patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention.[14]

However, the important role of LMR in a 3-month prognosis of patients with AIS is undefined. Therefore, we managed to investigate the relationship between LMR and stroke severity on a 3-month functional outcome in patients with AIS.

Materials and Methods

Patients

Patients with AIS admitted to the Department of Neurology at The Affiliated Hospital of Chengde Medical University were recruited retrospectively between January 2016 and December 2016. The patients were enrolled in the study if they met the following criteria: (1) the patients had AIS confirmed by magnetic resonance imaging; (2) the patients had neurological deficit symptoms and signs; (3) the patients were older than 18 years; and (4) the patients were admitted to the hospital 72 hours after stroke onset. The patients were excluded if they met the following criteria: (1) the patients had a stroke history and had a modified Rankin Scale (mRS) score higher than 2; (2) the patients had an infection history within 2 weeks before AIS; (3) with the patients took immunosuppressants or steroids; (4) the patients had malignancies or autoimmune diseases; (5) the patients had a severe liver or kidney dysfunction; and (6) the patients died or had respiratory infections during hospital admission. Ischemic stroke subtypes were classified according to the Trial of 10172 in Acute Stroke Treatment criteria.[15]

This study was approved by the Ethics Committee of The Affiliated Hospital of Chengde Medical University. All patients or proxies signed the informed consent.

Data Collection

We collected the baseline demographic and clinical information of patients, including age, gender, and risk factors such as hypertension, diabetes mellitus, coronary heart disease (CHD), hyperlipidemia, atrial fibrillation, stroke history, smoking, and alcohol drinking. Hypertension was defined as a systolic blood pressure of 140 mm Hg or higher and a diastolic blood pressure of 90 mm Hg or higher, or the current use of antihypertensive medication. Diabetes mellitus was defined as a fasting blood glucose (FBG) level of 7.0 mmol/L or higher, a casual blood plasma glucose level of 11.1 mmol/L or higher, or the use of diabetic medication. Hyperlipidemia was defined as meeting any of the following: a total cholesterol (TC) level higher than 5.72 mmol/L, a triglyceride (TG) level higher than 1.7 mmol/L, or a low-density lipoprotein cholesterol level higher than 3.12 mmol/L. CHD and atrial fibrillation were defined as a previous diagnosis or recording on electrocardiography.

Blood samples of all patients were measured within 24 hours after admission. The biochemical index was analyzed by biochemistry department, including lymphocyte count, monocyte count, FBG, TC, TG, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, serum creatinine, and serum uric acid. LMR was calculated based on the lymphocyte and monocyte counts on admission.

Assessment of Stroke Severity and 3-Month Outcome

Stroke severity on admission was evaluated according to the National Institutes of Health Stroke Scale (NIHSS). In terms of a previous study, moderate to severe stroke was defined as an NIHSS score of 6 or higher, whereas mild stroke was defined as an NIHSS score lower than 6.[16] We adopted telephone interview with patients to evaluate the functional outcome after 3 months. The 3-month outcome was measured according to the mRS score. We defined poor outcome as an mRS score of 3 or higher, whereas good outcome was defined as an mRS score lower than 3.[17]

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 19.0 software (SPSS Inc., Chicago, IL). Continuous variables were expressed as mean ± standard deviation or median (interquartile range). The Kolmogorov–Smirnov test was used to test the normality of distribution. Comparison among groups was analyzed with the Kruskal–Wallis and the Mann–Whitney *U*-tests. Categorical variables were expressed as frequency and percentage and differences among these variables were assessed by the chi-square test. If the expected frequency is 5 or less than 5, the Fischer exact test was used. According to their LMR values, the study population was divided into tertiles: