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The association between neutrophil-to-lymphocyte ratio and post-stroke depression

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ABSTRACTS

Background: Post-stroke depression (PSD) is the most common complication occurring among stroke survivors. It has been shown that increased neutrophil-to-lymphocyte ratio (NLR) is associated with depression. We explored the relationship between NLR and PSD.

Methods: In total, 299 ischemic stroke patients were consecutively enrolled in the study and received 1 month follow-up. The 17-Hamilton Rating Scale was used to measure depressive symptoms at 1 month after stroke. With the Hamilton Depression Scale score of > 7, parents were given the DSM-IV criteria for diagnosis of PSD. NLR was computered from the admission blood work. Meanwhile, the control group consisted of 180 healthy volunteers was also recruited.

Results: Seventy-eight patients (26.1%) were diagnosed with PSD at 1 month. PSD patients showed significantly higher levels of NLRs at admission as compared to non-PSD patients as well as normal controls ($P < .001$). In the logistic analysis, taking NLR values (< 3.701) a reference and PSD presence as a dependent variable, NLR values (≥3.70 l) were independently associated with the development of PSD (OR 4.038, 95% CI 2.174–7.500, $p < .001$).

Conclusions: Increased NLRs at admission are found to be correlated with PSD and may add prognostic information for the early discovery of PSD.

1. Introduction

Post-stroke depression (PSD), one of the most important and prevalent emotional disorders, afflicts approximately a third of individuals [1–3] who experience stroke [4]. The presence of PSD has been associated with reduced quality of life, negative impact on cognitive and functional performance [5], greater functional disability and increased mortality [2,6] so the recognition and early diagnosis of PSD is important to the functional recovery of stroke patients.

Extensive investigations suggested pro-inflammatory cytokines were involved both in the inflammatory response to acute ischemic stroke and depression [7], and might play a role in developing PSD [5]. Previous studies of PSD found a significant increase in inflammatory markers 1 y after stroke including interleukin-1, interleukin-18, interleukin-6 and tumor necrosis factor-α (TNF-α), interferon-γ (IFN- γ) [8,9]. Similarly, A longitudinal study found higher TNF-α levels and higher IL-1β were associated with PSD at 2 weeks after stroke [10]. And a recent study reported increased serum levels of high sensitivity C-reactive protein (hs-CRP) and homocysteine (HCY) were also associated with the development of PSD 1 year after the stroke onset [11]. These findings suggest that systemic inflammatory processes possibly play a role in the pathophysiology of PSD.

Neutrophil-to-lymphocyte ratio (NLR) is an easily available index of the inflammatory levels [12] linking to poor prognosis in patients with cardiovascular disease [13]. It was gradually used in patients with coronary atherosclerotic heart disease and stroke including ischemic stroke to predict the mortality [14–16]. Previous studies found increased NLR was associated with the prevalence of intracranial atherosclerosis and the number of carotid atherosclerotic plaques, and it was regarded to be an independent risk factor for ischemic stroke incidence [17–19]. Furthermore, several studies revealed that the NLR was associated with poorer prognosis of acute ischemic stroke [20,21] and

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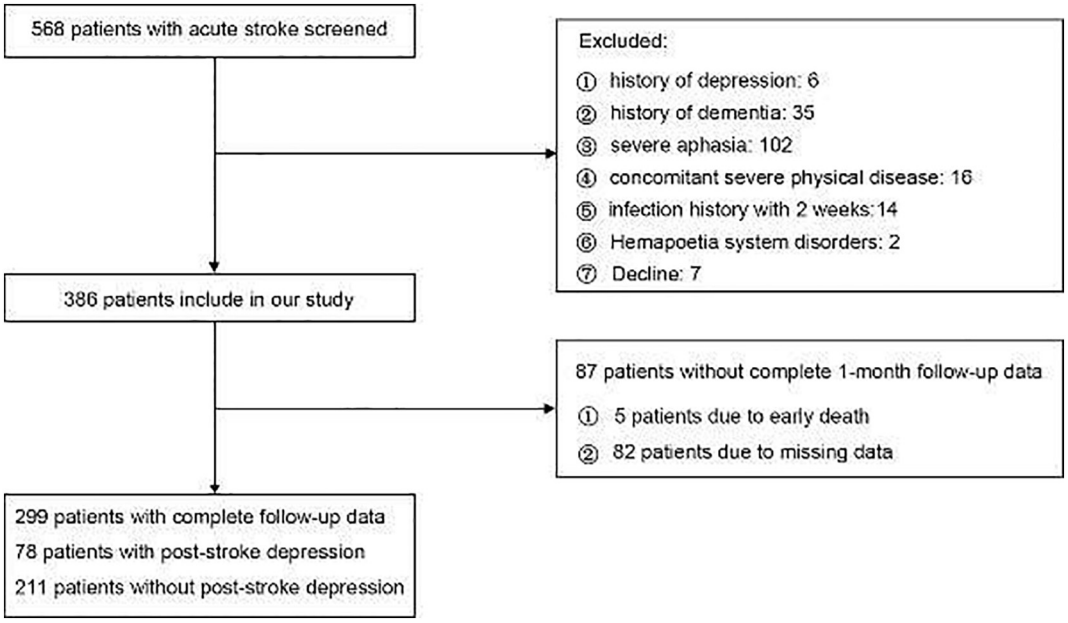

Fig. 1. Study recruitment profile.

predicted neurological deterioration after acute cerebral hemorrhage [12].

There have been several studies between NLR and psychiatric disorders, especially depression. Some studies observed the levels of NLRs as well as other anti-inflammatory cytokines(interleukin-10, C-reactive protein) in patients with major depression were increased comparing to normal subjects [22–24], and increased NLR also increased suicidal vulnerability in depressed patients [25]. However, to date, no study has explored the association between NLR and PSD.

2. Methods

2.1. Subjects

The study obtained the approval of the ethics committee of the First Affiliated Hospital of Wenzhou Medical University. Written informed consents were signed before included from all participants or their relatives. Between October 2013 and February 2015, acute ischemic stroke patients were consecutively admitted to the Stroke Ward of our hospital. All patients met the following inclusion criteria (i) age between 18 and 80 years; (ii) first-ever acute stroke occurring within 7 days after stroke onset; (iii) diagnosed with computerized tomography or magnetic resonance imaging; Patients met the following criteria were excluded (i) patients with any self-report psychiatric illness (previous treatment or clinical diagnose), especially a history of depression; (ii) patients with any central nervous system disease such as dementia or severe cognitive impairment, Parkinson's disease, tumor; (iii) severe aphasia or dysarthria, visual or auditory impairment and acute or chronic inflammatory disease; (iv) patients with hematologic disorders. Meanwhile, 180 healthy volunteers were recruited as controls.

2.2. Clinical measurement

Demographic data (age, gender, body mass index, education, etc.), vascular risk factor (hypertension, diabetes mellitus, hypercholesterolemia, etc.), and medical history were obtained at baseline. Stroke severity was assessed by experienced neurologists using the National Institutes of Health Stroke Scale (NIHSS) within 24 h of admission. Functional outcomes were evaluated by the modified Rankin Scale (mRS) and the Barthel Index (BI) at 1 month. Cognitive function was measured by the Mini Mental State Examination (MMSE) at 1 month follow-up.

2.3. Psychological measurement

All of the patients were interviewed for depressive symptoms by the 17-item Hamilton Depression Scale [26] at 1 month. Subjects with a HAMD score > 7 were considered to be diagnosed according to the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Evaluations were conducted by professional researchers who were unaware of the subjects' laboratories.

2.4. Laboratory tests

Blood samples were collected at admission in the Department of Emergency of our hospital and were obtained from the antecubital vein. NLRs were obtained by calculating the ratios of neutrophils and lymphocytes in peripheral blood samples. Determinations were performed in our hospital's laboratory by investigators blinded to the clinical outcomes as well as neuroimaging data.

2.5. Statistical analyses

Continuous variables were represented as means (SD) or medians (quartiles) depending on the normal or non-normal distribution of data, while categorical variables were expressed as percentages. Student's *t*-test was used for normal distribution test, while the asymmetrically distributed variables were compared using the Mann–Whitney *U* test, and χ^2 test was employed for proportions. Spearman's rank correlation was performed for bivariate correlations. In addition, binary logistic regression was employed to analyze the effect of NLR on PSD, which allows adjustment for potential confounding factors. All statistical analysis was performed with SPSS for Windows, vers 23.0. A $P < .05$ was considered statistically significant.

3. Results

3.1. Demographics and symptoms

A total of 568 patients with acute ischemic stroke were screened, 386 were eligible for the study, 299 completed the follow-up and were