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Neutrophil to lymphocyte ratio and the hematoma volume and stroke severity in acute intracerebral hemorrhage patients

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ABSTRACT

Background: Neutrophil to lymphocyte ratio (NLR) serves as a powerful inflammatory marker for predicting cardiovascular events. Here, we investigate whether admission NLR is associated with hematoma volume, stroke severity, and 3-month outcomes in patients with acute intracerebral hemorrhage (ICH).
Methods: 352 patients with acute ICH were prospectively identified in this study. Demographic characteristics, lifestyle risk factors, NIHSS score, hematoma volumes, and other clinical features were recorded for all participants. Patients was divided into quartiles based on the admission NLR levels (Q1: <2.78; Q2: 2.78–4.08; Q3: 4.08–7.85; Q4: ≥7.85). Multivariable linear regression models and logistic regression models were used to evaluate the association between NLR and hematoma volume, admission severity, or the outcomes after ICH.
Results: Median NIHSS scores for each quartile (Q1 to Q4) were 6.0, 6.0, 6.0, and 11.0 (P = .001), and median hematoma volumes were 9.5, 9.3, 9.1, and 15.0 ml (P = .005), respectively. After adjusting the age, sex, and other potential risk factors, the patients in Q4 had higher NIHSS scores (P = .042) and larger hematoma volume (P = .014). After 3-month follow-up, 148 poor outcomes (mRS, 3–6) and 47 all-cause deaths were documented. There were more patients with poor outcomes in Q4 than Q1. However, compared with the patients in Q1, those in Q4 were not associated with poor outcomes (*P*-trend = 0.379), and all-cause mortality (*P*-trend = 0.843) after adjust for other risk factors.
Conclusions: Higher admission NLR are associated with larger hematoma volume and more serious stroke, but not 3-month outcomes in patients with acute ICH.

1. Introduction

Intracerebral hemorrhage (ICH) accounts for 10–15% of all strokes. Although better treatments and nursing quality are applied, ICH still represents the most serious type of stroke with high morbidity and mortality [1,2]. Previous studies have been reported that the severe neurological deficit at presentation, large hematoma volume, hematoma growth, hematoma location and the presence of intraventricular bleeding are associated with poor outcomes of ICH patients [3-5].

Recently, a growing body of evidence supports that the inflammatory mechanisms were involved in the brain injury after ICH [6]. There were robust inflammatory responses, including peripheral leukocytes infiltration, microglia activation and subsequent release of various cytokines in ICH animal models [7,8]. A few clinical studies have demonstrated that the inflammatory markers were association with bad outcomes of ICH patients [9,10]. Compared to other inflammatory markers, leukocyte number is simpler and commonly used marker. Some studies indicated that elevated leukocyte level is associated with the large hematoma volume and bad outcomes in ICH patients [9-11].

Neutrophils and lymphocyte are the main components of the leukocytes. According to recent studies, the neutrophil to lymphocyte ratio (NLR) serves as a more powerful inflammatory marker than neutrophils or lymphocyte itself [12,13]. NLR has already been used to predict subclinical inflammation in patients with cancer [12] and also vascular disease (including coronary artery disease and stroke) [13,14]. And a study led by Wang et al. found that high NLR is associated with high 30-day mortality in ICH patients [15]. A study in a 177 ICH patients, reported that high NLR predictor the bad outcome in 3-month [16]. However, whether NLR is correlated with hematoma volume, baseline National

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Institute of Health Stroke Scale (NIHSS) remains unknown. And whether the relationship between NLR and 3-month outcomes and mortality of patients with ICH in china remains unclear. Thus, the aim of this study was to examine the associations between the NLR and hematoma volume, baseline NIHSS and outcomes in patients with acute ICH.

2. Methods

2.1. Study design and patients enrolment

From November 2011 to March 2014, we prospectively identified acute ICH patients from the Second Affiliated Hospital of Soochow University in China. The methods for recruiting study participants have been described elsewhere [17,18]. Briefly, all patients with computed tomography (CT) confirmed ICH was recruited. Patients with trauma, brain tumor, hemorrhagic transformation of IS, and vascular cerebral malformations were excluded, and a total of 413 potentially eligible patients were enrolled. Additional exclusion criteria were as follows: 1) requirement for neurosurgical procedures (n = 10); 2) time from onset to admission over 7 days (n = 11); 3) no modified Rankin Scale (mRS) score at 3-month (n = 27); and 4) no neutrophil and lymphocyte count (n = 13) measurements. 352 patients with available data for NLR were finally included in the analyses for this study (flowchart of participants selection; Fig. 1).

2.2. Ethics statement

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University, and informed consent was obtained from all the patients participating in this study.

2.3. Data collection

Demographic characteristics, lifestyle risk factors, medical history, clinical laboratory tests, imaging data (CT and magnetic resonance imaging) were collected at the time of enrollment. All information was obtained using a standard questionnaire that was administered by the trained staff blinded to the study objectives. Trained neurologists assessed the baseline stroke severity using the National Institutes of Health Stroke Scale (NIHSS) score. Cigarette smokers were defined as having smoked at least one cigarette per day for 1 year or more. Using a standard mercury sphygmomanometer, blood pressure (BP) measurements were performed in the supine position for admission. Blood samples were collected within 24 h of hospital admission. The WBC and differential counts were determined by the mindray, the NLR was calculated as the Neutrophil counts over Lymphocyte counts. All serum biochemical parameters were analyzed enzymatically on an Olympus Au5400 automatic biochemical analyzer (First Chemical Co., LTD, Japan) using the commercial reagents.

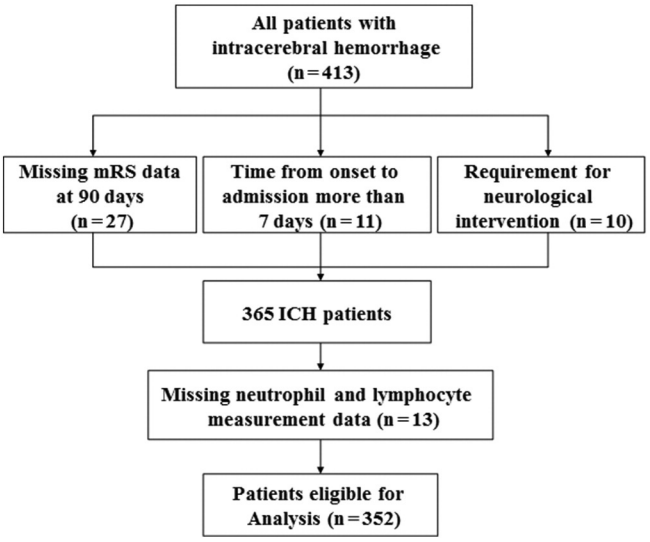

Fig. 1. Flowchart of participants' selection.

2.4. Outcomes assessment

Hematoma volumes were calculated by two neuroradiologists who were blinded to the clinical data and follow-up CT scans using the formula ABC/2 [19]. Stroke severity was assessed with the NIHSS by trained neurologists. Modified Rankin Scale (mRS) scores were evaluated at day 90 after onset, and poor outcomes were defined as mRS scores ≥3 or death. Deaths were reported by family members or work associates and/or obtained from death certificates and medical records.

2.5. Statistical analysis

Patients was divided into quartiles based on admission NLR levels (Q1: <2.78; Q2: 2.78–4.08; Q3: 4.08–7.85; Q4: ≥7.85). Continuous variables are expressed as mean ± standard deviation or median (interquartile range), whereas categorical variables are expressed as frequency (percent). For group comparisons, variance analysis was performed for continuous variables with a normal distribution. Wilcoxon rank-sum test was used for those with skewed distributions, and chi-square tests were applied for categorical variables. A Spearman correlation analysis was used to assess the correlation between admission NLR with hematoma volume and NIHSS score, as well as other related variables such as age, sex, time from onset to admission, cigarette smoking, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, total cholesterol, history of hypertension, history of diabetes mellitus, and history of stroke. In addition, multiple linear regression analyses were performed to evaluate the relationships between NLR and hematoma volume or NIHSS scores. The potential covariates such as age, sex, time from onset to admission, current smoking status, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, history of hypertension, history of diabetes mellitus, history of stroke, total cholesterol, and hematoma volume or baseline NIHSS score, were included in the multivariable model. Furthermore, multivariable non-conditional logistic regression models were used to assess the associations between NLR with 3-month poor outcomes and all-cause death among acute ICH patients. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each group, and the lowest quartile was used as the reference. Tests for linear trend in the ORs across admission NLR quartiles were performed with the modeling NLR category as an ordinal variable. All *P* values were 2-tailed, and a significance level of 0.05 was used. All analyses were conducted using the SAS statistical software (version 9.2, Cary, North Carolina, USA).

3. Results

3.1. Baseline characteristics of study participants

Complete data on conventional risk factors were available for 352 acute ICH patients (234 men and 118 women). The mean age of the participants was 64.2 ± 13.8 years (range: 21–96 years). The baseline characteristics were presented in Table 1. Patients with higher NLR have higher high density lipoprotein cholesterol, fasting plasma glucose, hematoma volume, and baseline NIHSS score, but have lower triglyceride levels. There were no significant differences in other baseline demographic and clinical parameters among the quartiles.

3.2. Correlation between NLR and hematoma volume or NIHSS scores

The spearman correlation analysis showed that the admission NLR positively correlated with the baseline NIHSS score (r = 0.125) and

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