Neutrophil-to-Lymphocyte Ratio and 30-Day Mortality in Patients with Acute Intracerebral Hemorrhage

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Background: Although a highly significant association has been described between neutrophil-to-lymphocyte ratio (NLR) and mortality in patients with various types of stroke, the association between NLR and mortality in intracerebral hemorrhage (ICH) patients remains unclear. *Methods:* In this observational study, we enrolled 224 ICH patients. They were divided into 2 groups based on their 30-day outcomes. Multivariate logistic regression was performed to identify independent risk factors of 30-day mortality. An optimal cutoff value for the continuous NLR was calculated by applying a receiver operating curve analysis to discriminate between the survival and death groups. *Results:* Among 224 patients, 26 died. No significant difference in NLR at admission was observed between the 2 groups (surviving: 2.39 ± 1.75 versus nonsurviving: 3.09 ± 2.16, $P = .065$), whereas NLR on the next morning following admission was significantly higher in the patients who died (12.53 ± 9.33) than in those who survived (5.53 ± 4.68) ($P < .001$). On multivariate logistic analysis, Glasgow Coma Scale score (odds ratio [OR] .805, 95% confidence interval [CI] .661-.979, $P = .030$), age (≥80 years; OR .203, CI .055-.750, $P = .017$), ICH volume (≥30 cm^3; OR .112, CI .108-.699, $P = .019$), and NLR on the next morning (OR 1.091, CI 1.002-1.188, $P = .044$) were independent risk factors of 30-day mortality. An NLR of 7.35 was identified as the optimal cutoff value. The area under the curve of NLR for 30-day mortality was .762 ($P < .001$). The mortality was significantly higher in patients with an NLR of 7.35 or higher than in those with an NLR less than 7.35 (31.6% versus 4.8%, $P < .001$). *Conclusions:* Higher NLR exhibited an increased mortality in ICH patients. NLR could be used to predict 30-day outcome in ICH patients. **Key Words:** Neutrophil-to-lymphocyte ratio—intracerebral hemorrhage—mortality—prognosis—risk factors.

Introduction

Intracerebral hemorrhage (ICH) is characterized by a high incidence rate, mutilation rate, and mortality. The ICH score, including age, Glasgow Coma Scale (GCS) score, ICH volume, intraventricular hemorrhage (IVH) and infratentorial origin of ICH, is validated for prediction of prognosis of ICH patients.[1] In addition to those risks, the inflammatory response plays a pivotal role in propagating injury due to ICH.[2] It can promote the formation of brain edema,[3,4] aggravate edema around hematoma, and may be associated with early hematoma enlargement.[5,6] These are likely to affect the prognosis. We conjectured

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that inflammation reaction may predict the prognosis of ICH patients through the above mechanisms.

The neutrophil-to-lymphocyte ratio (NLR), calculated by absolute neutrophil count divided by absolute lymphocyte count, is routinely performed on admission and is universally available. It conveys important information about the complex inflammatory activity in the vascular bed.[7] Highly significant associations have been described between NLR and mortality in patients with acute coronary syndrome, non-ST-segment elevation myocardial infarction, and every kind of strokes, including ischemic stroke, hemorrhagic stroke, and transient ischemic attack.[8-11] There have been no studies on the relation between NLR and mortality in ICH. Our anecdotal experience indicates that the majority of acute ICH patients have normal NLR at admission and those whose time to emergency care from ICH onset is delayed exhibit abnormal NLR, implying a possible correlation between time from onset of ICH to admission and NLR changes. These led us to examine NLR on the next morning following admission (defined as at least 8 hours of fasting following admission) and its correlation with the 30-day outcome of ICH patients.

Patients and Methods

Patient Population

In this observational study, we used residual blood samples of patients with spontaneous ICH who were hospitalized between January 2012 and January 2014 at the Emergency Department of Jiading District Center Hospital, Shanghai, China. The detailed inclusion and exclusion criteria are listed in Table 1. Blood samples were analyzed from 224 cases with acute ICH that were verified by computed tomography (CT) scans.

The study protocol was approved by Jiading District Center Hospital Medical Ethics Review Board and informed consent was not required of the participants because of the nature of the study. The study was performed in strict accordance with the Helsinki Declaration.

Data Collection

All patients who were enrolled in the study were observed until discharge from hospital or death in hospital. Data including age, gender, hypertension and diabetes history, GCS score at admission, ICH volume, presence of IVH, infratentorial origin, and mean arterial blood pressure (BP) on the next day after admission were recorded. Hypertension was diagnosed according to Mancia et al[12] and was established if systolic BP was 140 mmHg or higher, or diastolic BP was 90 mmHg or higher on 3 separate occasions in the rest state or the patient used antihypertension medication. Diabetes was confirmed by history of diabetes or antidiabetic medication use or clinical diagnosis upon admission.[13] Venous blood was collected at admission and the next morning in the fasting state. The blood samples were used for routine blood tests, and the residual blood samples were used to determine neutrophil and lymphocyte counts. The NLR was then calculated from the counts. NLR at admission was NLR0 and on the next morning was NLR. Pneumonia and stress ulcer bleeding, which were known to have a direct effect on mortality,[14,15] were in-hospital complications following acute ICH and were diagnosed by treating physicians in accordance with definitions used in other studies.[16-19] All patients received standardized treatment during hospitalization.[20]

Imaging Analysis

A blinded neurologist assessed CT scans obtained at admission in the following manner: on the CT slice with the largest area of ICH, the largest diameter (A) of the hematoma was measured in centimeter. The dimension of the hemorrhage perpendicular to the largest diameter represented the second diameter (B) in centimeter. The height of the hematoma was calculated by multiplying the number of slices involved by the slice thickness, providing the third diameter (C). The 3 diameters were multiplied and then divided by two (ABC/2) to yield the volume of ICH in cubic centimeters.[21] IVH was defined

Table 1. *Inclusion and exclusion criteria of the study subjects*

Inclusion criteria
Patients with a diagnosis of ICH verified by CT scans
Age 18 years or older
Exclusion criteria
Patients who were admitted to the hospital for more than 24 hours after ICH
Patients with hematologic disorders, who were immunosuppressant drug users (steroids), those with trauma, taking oral anticoagulation drugs, had a history of infection within 2 weeks before ICH, had a stroke history within 6 months, had a history of malignancy, and who were using anticoagulants
Patients who refused treatment

Abbreviations: CT, computed tomography; ICH, intracerebral hemorrhage.