Neutrophil Lymphocyte Ratio as a Predictor of Stroke

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Background: The aim of this study is to investigate the relationship of the neutrophil to lymphocyte ratio (NLR) with short-term mortality in acute stroke. *Methods:* This retrospective study included 255 patients with acute cerebral infarction who presented within 24 hours of symptom onset. A hemogram from peripheral venous blood samples was taken at the time of admission. The NLR was calculated as the ratio of neutrophils to lymphocytes. Duration of follow-up was defined as 60 days. *Results:* Seventy-one of 255 patients died during the follow-up period. The median NLR was significantly increased among the mortality group compared with the survival group (median 11.50, interquartile ratio [IQR] 10.40 vs median 3.79, IQR 4.72; $P = .001$). In our multivariate Cox regression model, NLR >5.0 (hazard ratio [HR] 3.30; 95% confidence interval [CI] 1.35-8.07), National Institutes of Health Stroke Scale score (HR 1.11; 95% CI 1.07-1.16), glucose values at admission (HR 1.007; 95% CI 1.002-1.011), and history of coronary artery disease (HR 2.49; 95% CI 1.26-4.92) were predictors of short-term mortality. The sensitivity for short-term mortality when the NLR was >5 was 83.10%, and the specificity was 62.00%. The positive predictive value of a NLR >5 was 45.7%, and negative predictive value was 90.50%. A strong linear association between NLR and National Institutes of Health Stroke Scale score was also observed ($r = 0.64$; $P = .001$). In addition, the NLR was higher in both the atherosclerotic and cardioembolic stroke subgroups than the lacunar infarct subgroup (6.5 [IQR 7.2], 7.5 [IQR 8.9], and 3.20 [IQR 3.50], respectively; $P = .001$). *Conclusions:* The NLR at the time of hospital admission may be a predictor of short-term mortality in acute stroke patients. Because of the routine use and inexpensive nature of hemogram analysis, the NLR should be investigated in future prospective, randomized controlled trials investigating acute stroke. **Key Words:** Mortality—National Institutes of Health Stroke Scale—neutrophil lymphocyte ratio—stroke.

Cerebrovascular ischemia has a high incidence of mortality and morbidity; many factors, such as acute phase reactants (C-reactive protein, etc.) and blood cell components (white blood cells [WBCs] and neutrophils, etc.) have been evaluated in acute ischemic events to predict infarct size, prognosis, and mortality.[1,2] The pathophysiology of acute ischemic stroke (AIS) is an inflammatory process that involves endothelial activation, blood–brain barrier disruption, oxidant and inflammatory mediator accumulation, and the mass infiltration of leukocytes and platelets.[3] This inflammatory process gradually develops within a few hours and plays an important role in ischemic damage.[4,5] In particular, the release of inflammatory cytokines and neurotoxins plays an important role in exacerbating damage,[6] but the prognostic impact of WBC subtype prevalence upon acute cerebral ischemia are unclear.[7]

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Received December 5, 2012; revision received January 14, 2013; accepted January 20, 2013.

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.01.011

Among patients with acute myocardial infarction (MI), it has been shown that an increased neutrophil to lymphocyte ratio (NLR) is a predictor of in-hospital mortality and morbidity,[8] and it has been shown that an increased NLR is related to impaired myocardial perfusion after percutaneous coronary angioplasty.[9] The effect of NLR on AIS severity and mortality is not known. Because of the similarity of risk factors and prognostic markers of acute MI with AIS, we examined the relationship between the NLR at the time of hospital admission and short-term mortality in patients with AIS.

Methods

Study Population

This study is a hospital-based retrospective investigation. Three hundred ninety-four patients with AIS who were >18 years of age and who were admitted to Meram Medical School Hospital were screened between January 2007 and June 2012. Patients with a diagnosis of AIS on the first day of admission were included in the study. The study was approved by the local ethics committee.

Exclusion criterion included patients who were admitted to the hospital >24 hours after AIS, patients with hematologic disorders, immunosuppressant drug users (steroids), those with an infection history within 2 weeks before the stroke, a stroke history within 6 months, and patients with a history of malignancy. Seventy patients with brainstem (infratentorial) infarct, which is known to have a direct effect on mortality, were also excluded. Two hundred ninety patients were included in the study protocol (Fig 1).

Study Protocol

AIS cases were screened using the *International Classification of Diseases, 10th revision* code (G 46.8) from the hospital's electronic record system. The demographic and clinical characteristics of 290 patients who met the criteria were obtained from the patient's archived records to evaluate Glasgow Coma Score (GCS), National Institutes of Health Stroke Scale (NIHSS) score, and mortality. Thirty-five patients were excluded from the study because of incomplete medical records (e.g., laboratory results and medical history). Supratentorial infarcts that were detected on cranial magnetic resonance imaging (MRI) and computed tomographic (CT) scans were divided into 2 groups: nonlacunar (>1.5 cm) infarcts and lacunar (≤1.5 cm) infarcts. In addition, the nonlacunar infarct group was further separated into 2 groups: (1) cardioembolic stroke (according to the presence of the history of atrial fibrillation, valvular heart disease, and congestive heart failure) or (2) atherosclerotic stroke (based on the documented carotid artery disease and/or aortic calcific plaque without overt heart disease). Hospital mortalities of patients were determined according to the records of epicrisis. The hospital's electronic medical record was searched for evaluation of nonhospital mortality within 60 days poststroke. Patients whose records continued after 60 days were considered alive. The families of patients with no records in the digital system after 60 days were contacted by telephone and were questioned about the mortality of the patient. Nonhospital mortality was found in 4 patients in total.

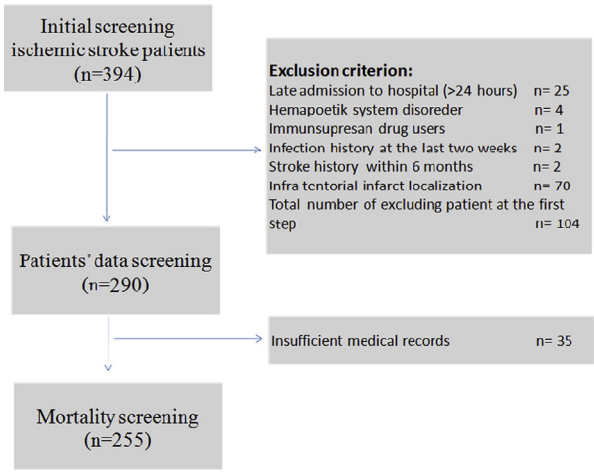

Figure 1. *Study flow chart.*

Blood Sample Analysis

A hemogram was evaluated using the peripheral venous blood samples taken on admission to the emergency department. The blood sample was collected in a calcium ethylenediaminetetra-acetic acid tube. Since 2007, blood counts have been evaluated in our hospital with an autoanalyzer (Cell-Dyn Ruby Hematology Analyzer; Abbott Laboratories, Abbott Park, IL). NLR was calculated as the ratio of neutrophils to lymphocytes in peripheral blood. In addition, other routine laboratory findings were examined using the digital record systems of the hospital.

Statistical Analysis

Data were analyzed using SPSS software (version 13.0; SPSS Inc, Chicago, IL) and presented as mean ± standard deviation or median (interquartile range [IQR]). Distribution normality was analyzed with the Kolmogorov–Smirnov test. Correlation analysis was carried out using the Spearman correlation test for nonparametrically distributed variables. The difference between 2 groups was tested using independent Student t tests for normally distributed variables; the Mann–Whitney U test was used for the comparison of nonparametrically distributed variables. The difference between categorical variables was determined using the Chi-square test. Kaplan–Meier survival analysis was performed to investigate the relationship between the median NLR value and death. Cox regression analysis was performed to determine predictors of 60-day mortality. GCS score, NIHSS score, age, sex,