Neutrophil-to-Lymphocyte Ratio Predicts Length of Stay and Acute Hospital Cost in Patients with Acute Ischemic Stroke

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Background: Although several risk factors for prolonged length of stay (LOS) and increased hospital cost have been identified, the association between LOS, hospital cost, and neutrophil-to-lymphocyte ratio (NLR) has not yet been investigated. We aimed to investigate the influence of NLR on LOS and hospital cost in patients with acute ischemic stroke. *Methods:* Patients with acute ischemic stroke diagnosed within 24 hours of symptom onset were included. Univariate analysis and stepwise multiple regression analysis were used to identify independent predictors of LOS and hospital cost. *Results:* A total of 346 patients were included in the final analysis. The median LOS was 11 days (range 8-13 days). The median acute hospital cost per patient was 19,030.6 RMB (U.S. $ 3065.8) (range 14,450.8 RMB-25,218.2 RMB). Neutrophil count to lymphocyte count (NLR) ($P < .001$), diabetes mellitus ($P = .034$), stroke subtype ($P = .005$), and initial stroke severity ($P < .001$) were significantly associated with prolonged LOS in the univariate analysis. NLR ($P < .001$), smoking ($P = .04$), stroke subtype ($P < .001$), initial stroke severity ($P < .001$), and LOS ($P < .001$) were significantly associated with increased hospital cost in the univariate analysis. Multivariate regression analysis showed that NLR was an independent predictor of both LOS and acute hospital cost. In addition, high NLR was significantly correlated with poor outcome at discharge, prolonged LOS, and increased hospital cost. *Conclusions:* NLR is significantly associated with LOS and acute hospital cost in patients presenting with acute ischemic stroke. It is a simple, inexpensive, and readily available biomarker and may serve as a clinically practical indicator for assessing the economic burden of stroke. **Key Words:** NLR—LOS—hospital cost—acute ischemic stroke.

Introduction

Stroke is the second highest cause of morbidity and mortality worldwide. In China, the annual mortality rate of stroke is approximately 157 per 100,000, which makes it the leading cause of death and adult disability followed by coronary artery disease.[1,2] Stroke is a considerable economic burden on healthcare services with associated direct and indirect medical costs. Direct costs include acute hospitalization, rehabilitation, and subsequent medical complications, and indirect costs include lost productivity and caregiver burden.[3] In 2003, the direct medical cost for stroke is 37.452 billion RMB, and from 1993 to 2003, the average annual growth rate of the direct medical cost of stroke was 18.04% in China.[4] The greatest direct economic cost,

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involving 70% of the total stroke cost, can be attributed to the patients' length of stay (LOS) in the hospital.[5] With already strained medical budgets, lack of healthcare resources and pressure from the private sector, accurate estimates of LOS and hospital cost are urgently needed. Hospital cost and LOS are associated with stroke severity, complications during hospital stay, stroke subtype, stroke risk factors (atrial fibrillation, hypertension, diabetes mellitus, and smoking), and age.[6-10] The inflammatory response is thought to be implicated in all stages of ischemic stroke, from brain cell necrosis of the early stage triggered by the interruption of blood supply to the recovery and repair of postischemic tissue of the late stage. The inflammatory response to cerebral injury region resulted in the evolution of ischemic brain injury and the deterioration of neurological function.[11] It has been demonstrated that there is a causal relationship between the inflammatory response and stroke-induced brain dysfunction and tissue injury.[12] As system inflammatory markers, neutrophil-to-lymphocyte ratio (NLR) was related to infarct volume and might be a predictor of short-term mortality in acute ischemic stroke.[13] Whether a high NLR is independently associated with LOS and acute hospital cost is unknown. Therefore, the objective of this present study is to identify the relationship between acute hospital cost, LOS, and NLR in patients with acute ischemic stroke.

Methods

Patients

Consecutive patients with acute ischemic stroke who were admitted to Jinling Hospital within 24 hours of symptom onset were retrospectively analyzed. Acute ischemic stroke was diagnosed if there were new focal neurological deficits explained by relevant lesions detected on diffusion-weighted imaging or computed tomography. The exclusion criteria included patients who (1) were diagnosed with infection within 72 hours pre- or postadmission, (2) were presently using corticosteroids or other immunosuppressive drugs, (3) were diagnosed with cancer or immune system disease, (4) had incomplete medical records, or (5) died during their hospital admission. This study was approved by the local committee of Jinling Hospital.

Demographic and Clinical Data Collection

The baseline data that were collected from medical records included demographic data (age and sex); vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, smoking, alcohol drinking, coronary heart disease, and myocardial infarction); time from stroke onset to admission; LOS; hospital cost, laboratory parameters (NLR, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides). Laboratory parameters were analyzed from fasting blood samples obtained during the first 24 hours after admission. NLR was calculated as the ratio of neutrophil count to lymphocyte count. Etiological classification of stroke was determined according to the Trial of Org 10172 in Acute Stroke Treatment criteria.[14] Stroke subtype was dichotomized as small-vessel occlusion or not in our study. NIHSS scores were evaluated by experienced neurologists immediately after admission and at discharge. Poor functional outcome was defined as a modified Rankin Scale score of 2 or higher at discharge.

Treatment and Neurological Assessment

During hospital admission, patients treated with tissue plasminogen activator or endovascular therapy were excluded. Guideline-based treatments[15] were managed in the enrolled subjects. Other treatments such as management of cardiovascular risk factors were implemented, as appropriate.

Statistical Analysis

Stata software (SPSS 17.0, SPSS Inc, Chicago, IL) was used for statistical analysis. Continuous data were presented as mean ± standard deviation or median values with interquartile ranges, and were evaluated using Student's *t*-test or the Mann–Whitney *U*-test. Categorical data were expressed as frequencies and percentage, and were assessed using chi-square test or Fisher's exact test, as appropriate. Age, sex, and variables that were statistically significant ($P < .05$) in univariate analyses were included in the multivariate liner regression analysis. Stepwise forward conditional process was applied in the multiple linear regression model to analyze the correlation between LOS, acute hospital cost, and other covariates, using acute hospital cost or LOS as the dependent variable. A 2-sided *P* value less than .05 was considered statistically significant.

Results

Four hundred eighteen subjects were screened, of which 72 patients were excluded: 51 subjects were diagnosed with infection within 72 hours pre- or postadmission; 6 subjects were presently using corticosteroids or other immunosuppressive drug; 8 subjects were diagnosed with cancer or immune system disease; 5 subjects had incomplete medical records (one lost the NIHSS score and four had incomplete laboratory data); and 2 subjects died during their hospital admission (both died from severe stroke that led to respiratory failure and circulatory failure). The remaining 346 patients were included in the final analysis.

The mean age was 60.8 ± 12.5 years, of whom 70.2% were male. The prevailing cerebrovascular risk factors and comorbidities were hypertension (65.0%), diabetes mellitus (23.1%), smokers (32.9%), alcohol drinking (21.1%), coronary heart disease (5.5%), myocardial infarction (.9%),