Decline in Hemoglobin during Hospitalization May Be Associated with Poor Outcome in Acute Stroke Patients

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Background and Purpose: Anemia upon hospital admission is a known predictor of poor functional outcomes in patients with acute cerebral infarction. However, it remains unclear whether reductions in hemoglobin levels during hospitalization influence stroke outcomes. We investigated the association between in-hospital decline in hemoglobin and poor outcomes. *Materials and Methods:* We retrospectively analyzed data from 480 consecutive patients who had experienced acute cerebral infarction and presented without anemia between January 2012 and March 2015. Decline in hemoglobin was taken as the difference between hemoglobin levels upon admission and nadir hemoglobin. Poor outcome was defined as a modified Rankin Scale score 3-6. A multivariate analysis of the relationship between decline in hemoglobin and poor outcome at discharge was conducted for various patient characteristics. *Results:* The mean hemoglobin level at admission was 14.3 ± 1.3 g/dL, whereas the mean nadir hemoglobin value was 13.1 ± 1.9 g/dL, with a mean decline in hemoglobin of 1.3 ± 1.5 g/dL. In patients with poor outcomes, mean decline in hemoglobin was significantly reduced to 3.1 g/dL ($P < .001$). The optimal cutoff decline in hemoglobin required to distinguish a poor outcome was 1.5 g/dL whereas the sensitivity and specificity were 62% and 82.3%, respectively, with an area under the curve of .77 ($P < .0001$). A decline in hemoglobin below 1.5 g/dL was found to be an independent predictor of poor outcome (odds ratio: 2.10; confidence interval: 1.10-3.99; $P = .023$). *Conclusion:* Decline in hemoglobin in patients hospitalized with acute stroke may be associated with poor outcome.
Key Words: Stroke—cerebral infarction—hemoglobin—anemia—functional outcome.

Factors associated with poor outcomes in patients with acute stroke include age,[1] severity at admission,[2] hyperglycemia,[3] and infarction volume.[4] In addition, hemoglobin levels play a key role in the transport of oxygen, and anemia is also associated with poor outcomes in this patient population.[5] Indeed, larger initial stroke volumes[6] as well as more rapid expansion of infarct volume have been noted[6-8] in patients with anemia following stroke. Furthermore, gastrointestinal[9] and urinary tract hemorrhage[10,11] during hospitalization also influences patient outcomes. We hypothesized that hemorrhage during hospitalization after the onset of acute stroke results in a significant decline in hemoglobin and that this reduction may be associated with functional outcome. Therefore, in the present study, we investigated the association between decline in hemoglobin and outcome at discharge in patients with acute stroke.

Materials and Methods

Patients

We retrospectively analyzed data from 480 consecutive patients with acute cerebral infarction admitted to

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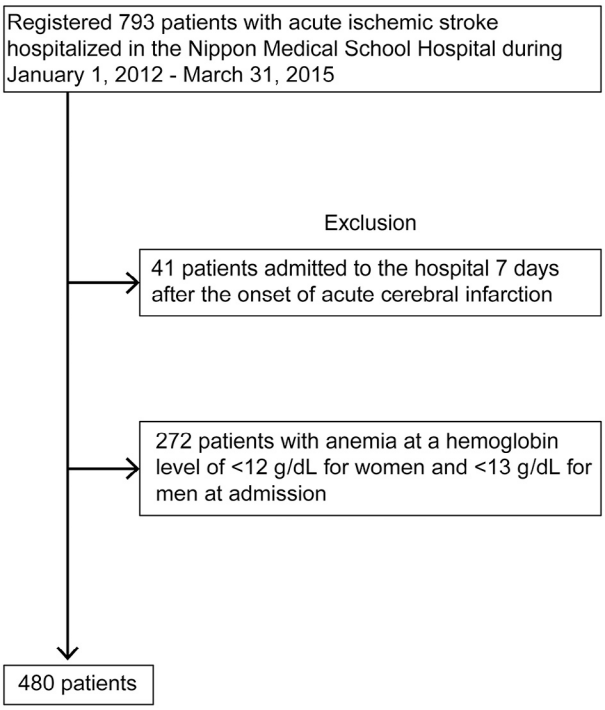

Figure 1. *Selection process for a group of patients with acute ischemic stroke admitted without anemia.*

the Nippon Medical School Hospital between January 1, 2012 and March 31, 2015 (Fig 1). Patients with modified Rankin Scale (mRS) scores higher than or equal to 2 before onset and those with anemia or active bleeding at admission were excluded from the present study. Anemia at admission was defined according to World Health Organization criteria as hemoglobin <12 g/dL in women and <13 g/dL in men. This study was approved by the institutional ethics committee of Nippon Medical School Hospital (28-10-653). We did not take informed consent from the patients due to the retrospective nature of this study.

Characteristics

Patients were evaluated with respect to age, sex, diabetes, hypertension, dyslipidemia, chronic kidney disease, smoking status, atrial fibrillation, history of stroke, National Institutes of Health Stroke Scale (NIHSS) score, stroke etiology, evolution of stroke, intravenous tissue plasminogen activator (t-PA) use, interventional radiology, in-hospital hemorrhage, use of antithrombotic drugs, and hemoglobin levels. Hemoglobin levels were measured within 1 hour of outpatient evaluation in the emergency room, as well as 24, 48, and 72 hours after evaluation. In addition to admission hemoglobin levels, the lowest level during hospitalization (nadir hemoglobin) and levels at discharge were also evaluated. Decline in hemoglobin was defined as the difference between hemoglobin level at admission and nadir hemoglobin. Blood transfusions were performed as determined by the attending physician in accordance with the Global Use of Strategies to Open Occluded Arteries guidelines.[12]

Hypertension was defined as systolic blood pressure higher than or equal to 140 mm Hg or diastolic blood pressure higher than or equal to 90 mm Hg before stroke onset or history of using antihypertensive agents. Diabetes was defined as random glucose level higher than or equal to 200 mg/dL and glycosylated hemoglobin higher than or equal to 6.5% or treatment with hypoglycemic agents. Dyslipidemia was defined as serum total cholesterol higher than or equal to 220 mg/dL or treatment with antihyperlipidemic agents. Patients or family members reported current smoking habits, and atrial fibrillation was diagnosed by electrocardiogram at admission or after 24-hour Holter electrocardiogram. Evolution of stroke was defined as a higher than or equal to 4-point increase in the total NIHSS score within 7 days from admission, as previously described.[13,14] Stroke severity was assessed using the NIHSS score.[15] Poor outcomes were defined as mRS scores higher than 2 at discharge, as previously described.[16,17]

Statistical Analysis

Participants were classified into 2 groups (poor and nonpoor) according to outcomes at discharge, and their clinical backgrounds were subsequently compared. Comparisons of baseline characteristics between poor and nonpoor outcome groups were performed using an analysis of variance for continuous variables. Student's *t*-test was used to detect differences in continuous variables, whereas Pearson's chi-square test was used to analyze categorical variables.

The optimal cutoff value of each continuous variable, including decline in hemoglobin, was obtained using receiver operating characteristics (ROC) curves to discriminate the poor outcome group from the nonpoor outcome group. In addition to the age and gender, factors with a probability of $P < .1$ in the univariate analysis were included in a multivariate logistic regression analysis to determine adjusted odds ratios. All data are presented as means ± standard deviation, unless otherwise specified. All statistical analyses were performed using JMP 12.2 software (SAS Institute Inc., Cary, NC).

Results

Table 1 lists the clinical characteristics of all 480 included patients (309 men, 171 women; mean age: 69 ± 13 years). A total of 332 patients (69.1%) had hypertension, 129 (26.8%) had diabetes, and 300 (62.5%) had dyslipidemia. Median NIHSS score on admission was 3 (range: 1-8). Mean hemoglobin levels were 14.3 ± 1.3 g/dL (admission), 14.0 ± 1.4 g/dL (24-hour), 13.8 ± 1.8 g/dL (48-hour), 13.7 ± 1.8 g/dL (72-hour), and 13.1 ± 1.9 (nadir,