Thrombocytopenia and In-hospital Mortality Risk among Ischemic Stroke Patients

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Background: Thrombocytopenia has been associated with increased mortality in nonstroke conditions. Because its role in acute ischemic stroke is less well understood, we sought to determine whether thrombocytopenia at admission for acute ischemic stroke was associated with in-hospital mortality. *Methods:* We used data from a retrospective cohort of stroke patients (1998-2003) at 5 U.S. hospitals. Risk factors considered included conditions that can lead to thrombocytopenia (e.g., liver disease), increase bleeding risk (e.g., hemophilia), medications with antiplatelet effects (e.g., aspirin), and known predictors of mortality (e.g., National Institutes of Health Stroke Scale and Charlson Comorbidity Index scores). Logistic regression modeling evaluated the adjusted association between thrombocytopenia, defined as platelets <100,000/μL, and in-hospital mortality. *Results:* Among 1233 acute ischemic stroke patients, thrombocytopenia was present in 2.3% (n = 28). A total of 6.1% (n = 75) of patients died in the hospital. In unadjusted analyses, thrombocytopenia was associated with higher mortality (8/28 [28.6%] *v* 67/1205 [5.6%]; $P < .0001$). Thrombocytopenia was also independently associated with in-hospital mortality after adjustment for National Institutes of Health Stroke Scale score and comorbidities, with an odds ratio of 6.6 (95% confidence interval 2.3-18.6). *Conclusions:* Admission thrombocytopenia among patients presenting with acute ischemic stroke predicts in-hospital mortality. **Key Words:** Acute ischemic stroke—medical comorbidity—mortality—thrombocytopenia.
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Thrombocytopenia is associated with increased mortality among patients admitted with cirrhosis, pneumonia, and acute coronary syndrome (ACS).[1-3] Although the association between thrombocytopenia and hemorrhagic conversion of ischemic stroke has been studied, whether thrombocytopenia contributes to mortality among patients with acute ischemic stroke (AIS) is less well understood.[4] We examined the association between admission thrombocytopenia and in-hospital mortality among AIS patients. We also performed secondary analyses evaluating the association of thrombocytopenia with post-AIS intracerebral hemorrhage (ICH).

Methods

This study is a secondary analysis of a retrospective cohort study evaluating consecutive patients at 3 Veterans Health Administration (VA) and 2 non-VA hospitals with AIS and transient ischemic attack (TIA). Patients were included in the original study if they were ≥18 years of age, had symptom onset within 2 days of admission, and had a neurologic deficit present on admission (National Institutes of Health Stroke Scale [NIHSS] score ≥2).[5] We excluded patients with TIA or those receiving thrombolytic therapy because thrombocytopenia is an exclusion criteria for receiving thrombolytic therapy.[4] Institutional review board approval was obtained from all participating hospitals.

Measurements

Demographic information, medical history (Charlson Comorbidity Index [CCI] score), preadmission medications, vital signs, and radiographic and laboratory data were collected by chart review.[5] Thrombocytopenia was defined as an admission platelet count <100,000/μL, a threshold that has been studied in ACS and that clinically warrants additional investigation.[3] Stroke severity was obtained from neurology examinations documented in the medical record to construct a retrospective NIHSS score.[6]

Outcomes

The primary outcome was in-hospital mortality, representing a clinically important event that is reliably obtained from medical records,[5] and symptomatic post-AIS ICH, obtained through review of imaging results.

Statistical Analyses

Chi-square, Fisher exact, or *t* tests were used to compare baseline characteristics of patients with and without thrombocytopenia. We evaluated the association between thrombocytopenia and mortality using logistic regression modeling with backward stepwise elimination to obtain the most parsimonious adjusted model. A ratio of 10 outcome events per variable entered into the model was maintained.[7,8] $P < .05$ was considered statistically significant. Missing data were rare; imputations were not made for missing data. All statistical calculations were conducted with SAS software (version 9.2; SAS, Inc., Cary, NC).

Results

Among 1233 stroke patients, the mean age was 72 years; 42.3% were female and 78.7% were white (Table 1). Admission platelet values ranged from 10,000 to 780,000/μL; 2.3% (n = 28) of the cohort had thrombocytopenia; 75 patients (6.1%) died. As descriptive analyses, patients with thrombocytopenia were more likely to be younger, have liver disease, cancer, a higher CCI score, and were less likely to be taking an antiplatelet medication at the time of admission. Among patients with thrombocytopenia, 1 of 8 (12.5%) had liver disease, 4 of 8 (50%) had cancer, and 0 patients (0%) had both liver disease and cancer. Mortality rates were higher among patients with thrombocytopenia (8/28 [28.6%] *v* 67/1205 [5.6%]; $P < .0001$). Post-AIS ICH occurred more commonly among patients with thrombocytopenia (4/28 [14.3%] *v* 18/1205 [1.5%]; $P = .001$). Mean platelet count for patients with post-AIS ICH was 78,000/μL. Of the 4 patients with symptomatic post-AIS ICH, 75% died during the hospitalization.

In multivariable analyses, after backward stepwise elimination, variables associated with in-hospital mortality that remained significant included thrombocytopenia (adjusted odds ratio [OR] 6.6; 95% confidence interval [CI] 2.3-18.6), baseline NIHSS score (adjusted OR 1.2; 95% CI 1.1-1.2), and CCI score (adjusted OR 1.1; 95% CI 0.99-1.2). The C-statistic for the model was 0.852. When post-AIS ICH was added to the in-hospital mortality model, the results were as follows: thrombocytopenia (adjusted OR 5.2; 95% CI 1.7-15.7), symptomatic post-AIS ICH (adjusted OR 3.7; 95% CI 1.3-10.7), baseline NIHSS score (adjusted OR 1.2; 95% CI 1.1-1.2), and CCI score (adjusted OR 1.1; 95% CI 0.99-1.2). An interaction between thrombocytopenia and post-AIS ICH was not significant. Also in multivariable analyses, after backward stepwise elimination, variables associated with symptomatic post-AIS ICH included NIHSS score (adjusted OR 1.1; 95% CI 1.1-1.2), history of any cancer (adjusted OR 0.1; 95% CI 0.01-0.99), and thrombocytopenia (adjusted OR 17.6; 95% CI 4.6-67.0; Table 2).

Discussion

Although uncommon among all stroke admissions, admission thrombocytopenia was associated with greater in-hospital mortality and symptomatic post-AIS ICH. Thrombocytopenia has previously been associated with mortality in patients with cirrhosis, pneumonia, and ACS.[1,9,10]

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