

Serum Calcium and Phosphate Levels and Short- and Long-Term Outcomes in Acute Intracerebral Hemorrhage Patients

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Background: We investigated whether admission serum calcium and phosphate levels are associated with short- and long-term outcomes in patients with acute intracerebral hemorrhage. *Methods:* A total of 365 patients with acute intracerebral hemorrhage were enrolled in this study. Participants were classified into 4 subgroups according to serum calcium or phosphate quartiles. Demographic characteristics, lifestyle risk factors, medical history, and other clinical characteristics were recorded for all the participants. Excellent outcome was defined as discharge or 3-month modified Rankin scale scores of 0-1. *Results:* Univariate analysis comparing the highest and lowest quartiles indicated that an elevated calcium level was associated with 2.26- and 2.28-fold increases in the odds for discharge and 3-month excellent outcome, respectively. After adjustment for age, sex, and other potential risk factors, patients in the highest quartile still had significantly increased odds of discharge and 3-month excellent outcome; the corresponding odds ratios (ORs) were 3.43 (95% confidence interval [CI], 1.03-11.44) and 5.36 (95% CI, 1.69-16.98). When calcium was divided into two groups, the ORs of higher calcium were 2.9 (95% CI, 1.1-7.62) and 2.8 (95% CI, 1.15-6.82) for discharge and 3-month excellent outcome, respectively. However, no significant association was observed between serum phosphate and excellent outcome. *Conclusions:* Elevated admission serum calcium level but not phosphate level is positively associated with excellent outcome at discharge or 3 months in acute intracerebral hemorrhage patients. **Key Words:** Intracerebral hemorrhage—serum calcium—serum phosphate—prognosis.

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Introduction

Serum calcium and phosphate are essential nutrients for human life, and both play physiological roles in the multiple pathomechanisms underlying cerebral ischemia.^{1,2} Calcium influences the molecular pathways of ischemic neuronal death.³ The element has also been studied with regard to its relationship with stroke risk factors, and high dietary calcium intake has been associated with reduced stroke risk.⁴ Several studies have reported that higher serum calcium levels at admission are associated with better clinical outcomes after ischemic stroke.^{1,5} Other findings indicate that high serum phosphate is a risk factor of ischemic stroke, but this is contradicted in another report.⁶ Although the incidence of intracerebral hemorrhage is lower than that of ischemic stroke, the former remains a significant cause of morbidity and mortality throughout the world, especially in China. However, up to now, few studies have investigated the association between serum calcium or phosphate level and the prognosis of intracerebral hemorrhage, and have many controversies.^{7,8} In the present study, we aimed to investigate the relationship between admission serum calcium and phosphate levels and short- and long-term outcomes after intracerebral hemorrhage.

Patients and Methods

The study population comprised consecutive intracerebral hemorrhage patients admitted to our department within 7 days from symptom onset from November 2011 to March 2014. Intracerebral hemorrhage was confirmed by computed tomography scan. We excluded patients with trauma, brain tumor, hemorrhagic transformation of ischemic stroke, and vascular cerebral malformations; those who required neurosurgical procedures; and subjects with missing serum calcium and phosphate data. We analyzed the following variables: age, sex, hypertension, diabetes, hypercholesterolemia, current smoking status, systolic blood pressure (SBP) and diastolic blood pressure, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), blood glucose, uric acid hematoma volume, and National Institutes of Health Stroke Scale (NIHSS) score at admission. Serum calcium and phosphate levels were measured from blood samples taken from fasting patients within 24 hours after admission. Patients were classified into quartiles based on admission serum calcium levels (Q1 [≤ 2.14], Q2 [2.14-2.24], Q3 [2.24-2.32], Q4 [≥ 2.32] mmol/L) and serum phosphate levels (Q1 [$\leq .91$], Q2 [.91-1.04], Q3 [1.04-1.19], Q4 [≥ 1.19] mmol/L). Hematoma volumes were calculated by 2 neuroradiologists blinded to clinical data and follow-up CT scans using the formula $ABC/2$. The primary outcomes were discharge and 3-month modified Rankin scale (mRS) scores evaluated by telephone interviews. Excellent outcome was defined as discharge or 3-month mRS scores of 0-1.

Statistical Analysis

Study participants were classified into 4 subgroups according to serum calcium or phosphate quartiles. Continuous variables are expressed as mean \pm standard deviation or median (interquartile range), whereas categorical variables are expressed as frequency (percent). For group comparisons, analysis of variance was performed for continuous variables with a normal distribution, Wilcoxon rank-sum test was used for those with skewed distributions, and chi-square tests were applied for categorical variables. Uni- and multivariate nonconditional logistic regression models were used to assess the associations between serum calcium or phosphate levels and excellent outcome among acute intracerebral hemorrhage patients. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each group using the lowest quartile as a reference. Tests for linear trend in the ORs across serum calcium or phosphate quartiles were performed, modeling the calcium or phosphate category as an ordinal variable. Potential confounding factors such as age; sex; time from onset to admission; current smoking status; SBP/diastolic blood pressure; blood glucose; histories of hypertension, diabetes mellitus, and stroke; hematoma volume; levels of uric acid, creatinine, and lipids; and baseline NIHSS score were included in the multivariate model. All *P* values were 2-tailed, and a significance threshold of .05 was adopted. All statistical analyses were conducted using SAS statistical software (version 9.2; SAS Institute, Inc., Cary, NC).

Results

A total of 365 patients (243 males and 122 females) with acute intracerebral hemorrhage were enrolled. The mean participant age was 64.1 years (range: 21-96). At discharge, 140 patients (38.4%) had excellent outcome (mRS score of 0-1), and 165 patients (45.2%) had excellent outcomes at 3 months. The baseline characteristics of patients according to serum calcium and phosphate quartiles are shown in [Tables 1 and 2](#). Patients with a higher calcium level were more likely to be younger; have higher levels of TC, LDL-C, blood glucose, and uric acid; and have lower SBP. Patients with higher phosphate levels tended to be female and have higher levels of TC and LDL-C.

As shown in [Table 3](#), when the highest and lowest quartiles were compared in univariate models, an elevated serum calcium level was associated with a 2.26-fold increase in odds for excellent outcome at discharge (OR, 2.26; 95% CI, 1.22-4.16; *P* for trend = .013) and a 2.28-fold increase in odds for 3-month excellent outcome (OR, 2.28; 95% CI, 1.25-4.15; *P* for trend = .009). After multivariate adjustment, the patients in the highest quartile still had significantly increased odds of discharge and 3-month excellent outcome; 3.43 (95% confidence interval

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