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The relationship between hypomagnesemia and ICU mortality in severe hemorrhagic stroke patients: an observational multicentre study on eICU database

Xinzhao Jiang[1†], Faliang Gao[2†], Zongjie Shi[1], Fang Liu[1], Wenyan Zhao[3*†] and Guihong Gong[4*†]

Abstract

Background Hemorrhagic stroke is a potentially fatal condition with high mortality and morbidity. However, there is a lack of evidence for this relationship in critically ill patients with hemorrhagic stroke. This study aims to explore the relationship between hypomagnesemia and ICU mortality in severe hemorrhagic stroke patients.

Methods The study included 2,026 severe hemorrhagic stroke patients from the Electronic Intensive Care Unit Collaborative Study database, categorized into hypomagnesemia and non-hypomagnesemia groups based on serum magnesium levels. Primary outcome was ICU mortality. Secondary outcome was mechanical ventilation use. Multivariate Cox proportional hazards regression analyses were used to study the relationship between hypomagnesemia and the outcomes. We also performed a cumulative survival rate analysis by Kaplan–Meier curves.

Results A total of 2,026 severe hemorrhagic stroke patients, aged over 16 and hospitalized in the ICU for more than 24 h, were enrolled. Among them, 277 (13.7%) died in the ICU, and hypomagnesemia was observed in 489 patients. Multivariable Cox regression analyses demonstrated that hypomagnesemia was related to a 28% increased risk of ICU mortality (HR 1.28, 95% CI [1.02–1.68], $p=0.035$) and a 15% increased risk of mechanical ventilation use (HR 1.15, 95% CI [1.04—1.33], $p=0.010$) in severe hemorrhagic stroke patients.

Conclusions Our findings suggested that hypomagnesemia is associated with increased risks of ICU mortality and mechanical ventilation use in severe hemorrhagic stroke patients. Future randomized, prospective studies are needed to elucidate the role of hypomagnesemia and explore potential interventions.

Keywords Hemorrhagic stroke, Intracerebral hemorrhage, Subarachnoid hemorrhage, Hypomagnesaemia, Intensive Care Unit

[†]Xinzhao Jiang and Faliang Gao contributed equally to this work and share first authorship.

[†]Wenyan Zhao and Guihong Gong have contributed equally to this work and share correspondence.

*Correspondence:
Wenyan Zhao
zhaowenyan@hmc.edu.cn
Guihong Gong
guihong555@163.com
Full list of author information is available at the end of the article

Introduction

Hemorrhagic stroke (HS), comprising intracerebral hemorrhage (lCH) within the brain tissue and spontaneous subarachnoid hemorrhage (SAH) in the subarachnoid space, is a significant contributor to the global burden of stroke, accounting for approximately 10% of the estimated 15 million strokes worldwide each year [1–3]. This life-threatening condition often necessitates ICU admission due to brain vessel rupture, causing severe cerebral damage and potential organ dysfunction. The economic costs associated with HS treatment and post-HS care are substantial, and the mortality and morbidity rates remain high [4]. Understanding the factors that influence the prognosis of HS patients is crucial for improving their outcomes.

Magnesium (Mg), one of the most abundant intracellular cations, plays a crucial role in numerous vital physiological processes [5]. A prospective observational cohort study of 290 patients with spontaneous ICH showed that lower Mg levels were related to larger initial and final hematoma volumes and greater hematoma growth, as well as poorer 3-month prognosis [6]. Another study in 354 patients with spontaneous SAH indicated that lower Mg levels were associated with more hemorrhage volumes [7]. However, many of these previous studies were single-center studies with relatively small sample sizes, limiting the generalizability of their findings. Others lacked comprehensive data collection or did not account for potential confounding factors adequately. In contrast, our study is novel in two key aspects. Firstly, we specifically focus on severe ICH patients, a population of particular clinical importance due to the high morbidity and mortality associated with this condition. Secondly, we utilized the e-Intensive Care Unit Collaborative Research Database (eICU-CRD), a large multicenter dataset. This dataset includes data from over 200,000 patients admitted to 208 US hospitals between 2014 and 2015, providing a large and diverse sample. By overcoming prior study limitations, we can better understand hypomagnesemia and ICU mortality in severe HS patients.

The findings of our study strongly support the integration of routine Mg monitoring into the clinical management of severe HS patients. This would enable early detection of hypomagnesemia and potentially allow for timely interventions, such as Mg supplementation, after careful consideration of potential contraindications and risks.

Methods

Database

This research conducted a post-hoc analysis of the eICU Collaborative Research Database, a large multicenter critical care dataset provided by Philips Healthcare in partnership with the MIT Laboratory for Computational Physiology. The database encompasses data from multiple critical care units throughout the continental United States, focusing on patients admitted to these units in 2014 and 2015 [8]. All data were managed and accessed electronically through the eICU program provided by Philips Healthcare (Best, Netherlands). Before any analysis, the eICU program ensured that all data were anonymized. Detailed documentation of the database can be found at www.eicu-crd.mit.edu. Our independent analysis of the accessible eICU database did not require local ethics committee approval. However, it was reviewed and endorsed by the PhysioNet review board. An author (Wenyan Zhao) was approved by PhysioNet review boards and gained access and was responsible for using the data (certification number 42608104). The study was performed in accordance with the Declaration of Helsinki.

The eICU database has a relatively well-developed system for standardizing data and dealing with heterogeneity, and more details about the eICU database can be found on this website https://physionet.org/content/eicu-crd. In our study, after obtaining the necessary licenses, we used PostgreSQL (9.6 version) to retrieve relevant variables and results in Structured Query Language (SQL) format.

Study population

All included patients were discharged with a primary diagnosis of HS. The diagnosis of HS in this study specifically includes spontaneous ICH and spontaneous SAH, as designated by codes 430 to 432 in the 9th revision of the International Classification of Diseases (ICD).

Exposure variable and outcomes

The total Mg values used in our analysis were first detected from 12 h before admission to ICU to 24 h after admission to ICU. In this study, hypomagnesemia was identified as the exposure variable. In our research, hypomagnesemia was defined as a serum Mg concentration of $\leq$1.6 mg/dL. A recent review indicated that hypomagnesemia is defined as a serum Mg level below 0.7 mmol/L, which is approximately equivalent to $\leq$1.6 mg/dL after conversion [9]. This definition of hypomagnesemia is consistent with findings from several previous studies [10–12]. Serum Mg levels at or below 1.6 mg/dL may not present with overt clinical manifestations. However, when the levels drop to below 1.2 mg/dL, a spectrum of clinical symptoms, such as enhanced neuromuscular excitability, could emerge. Hypomagnesemia has been shown to be associated with an elevated risk of all-cause mortality and cardiovascular mortality [9]. In our analysis, the primary outcome was ICU mortality,

while mechanical ventilation use served as a secondary outcome.

Covariates

This study also collected additional data from the eICU-CRD. We obtained age, sex, ethnicity, height, and weight data from the patient table. The sequential organ failure assessment (SOFA) score evaluates the severity of a patient's condition upon ICU admission. The SOFA score is divided into two groups based on a cutoff value of 6. A score above 6 indicates more severe organ function impairment and poorer prognoses, including higher mortality rates and longer hospital stays. Conversely, a score of 6 or below suggests relatively milder impairment and better prognoses. Biological variables, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), were obtained from the Apache Aps Var table. Comorbidities were collected from the pastHistory table, including coronary artery disease, hypertension, congestive heart failure, diabetes, chronic pulmonary disease, ischemic stroke, and malignant cancer. The laboratory test data were extracted from the lab table, including white blood cell (WBC) count, platelet (PLT) count, hemoglobin, calcium and creatinine. All laboratory data were obtained as the average values of all the test results on the first day after ICU admission.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), while categorical variables are reported as counts and percentages. Two-sample t tests were used for continuous variable comparison between groups. For categorical variables, chi-square or Fisher's exact test was applied as appropriate. Multivariate Cox proportional hazards regression models were employed to assess the association between hypomagnesemia and the outcomes. We constructed three multivariate Cox models simultaneously. Model 1 did not adjust for any variables. In multivariate model 2, we adjusted for variables such as age, gender, and ethnicity. Multivariate model 3 included all variables from model 2, plus the SOFA score, comorbidities (hypertension, coronary artery disease, congestive heart failure, diabetes, chronic pulmonary disease, ischemic stroke, malignant cancer, renal disease), as well as SBP, DBP, WBC, hemoglobin, platelets, calcium, and creatinine. Three models estimated hazard ratios (HRs) and 95% confidence interval (CIs). We performed stratified analyses and examined interactions based on age, gender, SOFA score, subtypes of HS (ICH and SAH), and comorbidities such as hypertension, ischemic stroke, and diabetes. Kaplan–Meier curves were calculated to describe ICU mortality in hypomagnesemia and non-hypomagnesemia groups. Since the proportion of missing values for covariates was less than 5%, we employed dummy variables to indicate the missing covariate values. Model internal validation was conducted to obtain an unbiased assessment of model performance. We created a calibration plot and validated it by performing the bootstrap process 500 times to reduce bias. The discrimination was evaluated using the receiver operating characteristic curve (ROC). Additionally, the clinical applicability of the model was assessed using decision curve analysis (DCA), which computed the net benefits at various threshold probability levels. All analyses were performed using the R statistical software package (http://www.R-project.org, the R Foundation for Statistical Computing), Free Statistics software versions 2.0 and EmpowerStats (http://www.empowerstats.com, X&YSolution, Inc.) [13]. We defined statistical significance as $p < 0.05$.

Results

Patients' selection

The selection criteria and exclusions for patients are shown in Fig. S1. Exclusions included: (1) age ≤ 16 years (n = 200); (2) ICU stay < 24 h (n = 1,037); (3) missing ICU mortality data (n = 38); and (4) no magnesium measurement (n = 1,461). Consequently, we enrolled a total of 2,026 eligible patients.

Baseline characteristics

Table 1 presents the baseline characteristics of the patients. We classified the patients with HS into two groups based on total Mg levels: those with hypomagnesemia and those without. The average age of the patients was 61.8 years (female: 44.8%). Patients with hypomagnesemia had a higher SOFA score compared to those without. Additionally, they showed lower values for SBP, BMI, hemoglobin, PLT count, calcium, and creatinine. Moreover, the incidence of hypertension and renal disease was lower in the hypomagnesemia group. All differences were statistically significant.

The outcomes

Table 2 presents the primary and secondary outcomes for patients with severe HS, comparing the results between the hypomagnesemia group and the non-hypomagnesemia group. The ICU mortality rate was significantly higher in the hypomagnesemia group at 18.6% compared to 12.1% in the non-hypomagnesemia group ($p < 0.001$). In patients with hypomagnesemia, the risk of requiring mechanical ventilation was significantly higher compared to those without hypomagnesemia (59.9% vs 41.1%, $p < 0.001$).

Table 1 Baseline clinical and laboratory characteristics of the study patients

Characteristics	Total (n = 2,026)	Hypomagnesemia		*p* value
		No (n = 1,537)	Yes (n = 489)	
Age (years)	61.8 ± 17.3	62.5 ± 16.9	59.3 ± 18.3	< 0.001
Gender, n (%)				0.093
Female	906 (44.8)	671 (43.7)	235 (48.1)	
Male	1118 (55.2)	864 (56.3)	254 (51.9)	
Race/ethnicity, n (%)				0.756
Caucasian	1509 (74.5)	1140 (74.2)	369 (75.5)	
African American	222 (11.0)	175 (11.4)	47 (9.6)	
Hispanic	106 (5.2)	79 (5.1)	27 (5.5)	
Asian	46 (2.3)	37 (2.4)	9 (1.8)	
Native American	8 (0.4)	5 (0.3)	3 (0.6)	
Other/Unknown	135 (6.7)	101 (6.6)	34 (7.0)	
SOFA score				< 0.001
> 6	671 (33.1)	464 (30.2)	207 (42.3)	
≤ 6	1355 (66.9)	1073 (69.8)	282 (57.7)	
Comorbidities, n (%)				
Hypertension	1055 (52.1)	836 (54.4)	219 (44.8)	< 0.001
Coronary artery disease	162 (8.0)	123 (8.0)	39 (8.0)	0.985
Congestive heart failure	133 (6.6)	101 (6.6)	32 (6.5)	0.983
Diabetes	390 (19.2)	290 (18.9)	100 (20.4)	0.440
Chronic pulmonary disease	122 (6.0)	98 (6.4)	24 (4.9)	0.235
Ischemic stroke	250 (12.3)	198 (12.9)	52 (10.6)	0.188
Malignant cancer	146 (7.2)	117 (7.6)	29 (5.9)	0.210
Renal disease	110 (5.4)	94 (6.1)	16 (3.3)	0.016
Physical examination				
SBP (mmHg)	130.3 ± 15.8	131.2 ± 15.5	127.1 ± 16.4	< 0.001
DBP (mmHg)	69.1 ± 10.9	69.3 ± 10.9	68.3 ± 10.8	0.054
BMI (kg/m^2)	27.9 ± 6.7	28.1 ± 6.8	27.4 ± 6.4	0.050
Laboratory data				
WBC (× 10^3/μl)	11.9 ± 9.7	11.9 ± 10.8	11.9 ± 5.3	0.882
HB (g/mL)	12.5 ± 2.1	12.7 ± 2.1	11.9 ± 2.1	< 0.001
PLT (× 10^3/μl)	211.4 ± 79.3	214.9 ± 75.3	200.6 ± 89.7	< 0.001
Calcium (mg/dL)	8.6 ± 0.7	8.7 ± 0.6	8.3 ± 0.8	< 0.001
Creatinine (mg/dL)	1.1 ± 1.1	1.2 ± 1.2	1.0 ± 0.7	0.003

Note: Continuous variables were presented as mean ± SD. Categorical variables were presented as numbers (%). The SOFA score is divided into two groups with a cutoff value of 6

Abbreviations: *SD* Standard deviation, *SOFA* Sequential organ failure assessment, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *BMI* Body mass index, *WBC* White blood cell, *HB* Hemoglobin, *PLT* Platelet

Table 2 The outcomes in severe HS patients without and with hypomagnesemia

Outcomes	Total (n = 2,026)	Hypomagnesemia		*p* value
		No (n = 1,537)	Yes (n = 489)	
ICU mortality, n (%)	277 (13.7)	186 (12.1)	91 (18.6)	< 0.001
Mechanical ventilation use, n (%)	924 (45.6)	631 (41.1)	293 (59.9)	< 0.001

Abbreviations: *HS* Hemorrhagic stroke, *ICU* Intensive care unit

Association of hypomagnesemia with ICU mortality and mechanical ventilation use

Table 3 presents a comparison of ICU mortality and mechanical ventilation use among severe HS patients with and without hypomagnesemia. In model 1, patients with hypomagnesemia had a significantly higher risk of ICU mortality compared to those without hypomagnesemia (HR 1.36, 95% CI [1.06—1.75], $p = 0.017$). Hypomagnesemia was significantly linked to a higher use of mechanical ventilation (HR 1.22, 95% CI [1.06—1.40],

Table 3 Association of hypomagnesemia with ICU mortality and mechanical ventilation use in severe HS patients

Variables	Model 1		Model 2		Model 3	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
ICU mortality						
Non-hypomagnesemia	Ref		Ref		Ref	
Hypomagnesemia	1.36 (1.06, 1.75)	0.017	1.39 (1.08, 1.79)	0.011	1.28 (1.02, 1.68)	0.035
Mechanical ventilation use						
Non-hypomagnesemia	Ref		Ref		Ref	
Hypomagnesemia	1.22 (1.06, 1.40)	0.006	1.23 (1.06, 1.41)	0.005	1.15 (1.04, 1.33)	0.010

Note: This table shows hazard ratios (HRs) and 95% confidence intervals (95% CIs) for ICU mortality and mechanical ventilation use, comparing hypomagnesemia patients to those without hypomagnesemia across different models. 'Ref' represents the reference category, which is the non-hypomagnesemia group. Model 1: No covariates were adjusted. Model 2: Adjusted for age, gender, and ethnicity. Model 3: Adjusted for age, gender, ethnicity, SOFA score, comorbidities (hypertension, coronary artery disease, congestive heart failure, diabetes, chronic pulmonary disease, ischemic stroke, malignant cancer, renal disease), systolic blood pressure, diastolic blood pressure, white blood cell, hemoglobin, platelet, calcium, and creatinine

Abbreviations: *HS* hemorrhagic stroke, *ICU* intensive care units, *HR* hazard ratio, *95% CI* 95% confidence interval

$p=0.006$). Similarly, after adjusting for confounding factors in models 2 and 3, the trend remained consistent. In model 3, patients with hypomagnesemia also faced a significantly higher risk of ICU mortality compared to those without hypomagnesemia (HR 1.28, 95% CI [1.02—1.68], $p=0.035$). Hypomagnesemia was associated with a greater need for mechanical ventilation, with an HR of 1.15 (95% CI [1.04—1.33], $p=0.010$) for patients with hypomagnesemia compared to those without.

Subgroup analysis

To ensure the robustness of data analysis, we also conducted the sensitivity analyses. The subgroup and interaction analyses were performed to explore the role of other covariables on the association between hypomagnesemia and ICU mortality. As shown in Fig. 1, the results from the subgroup analyses supported the findings from the multivariate Cox regression analysis. Hypomagnesemia increased the risk of ICU mortality in patients with severe HS, regardless of the subgroup. Hypomagnesemia had a more significant effect on ICU mortality in males, all HS subtypes, non-diabetic patients, and individuals with a history of ischemic stroke. The interaction analysis indicated no significant interaction between hypomagnesemia and ICU mortality, except in patients with a history of ischemic stroke.

Kaplan–Meier survival curve

The Kaplan–Meier survival curve indicated that patients without hypomagnesemia had a higher survival probability during their ICU stays compared to those with hypomagnesemia. By the end of 30 days, the estimated survival probabilities for patients without hypomagnesemia and those with hypomagnesemia were approximately 63.9% and 60.3%, respectively. The log-rank test produced a significant *p*-value of 0.03, suggesting that hypomagnesemia is likely associated with poorer survival outcomes in the ICU (Fig. 2).

Additionally, the results of the ROC plot, calibration plot, and DCA plot for the model were illustrated in Fig. S2-4.

Discussion

This study used a large dataset from multiple centers to investigate the link between hypomagnesemia and ICU mortality in patients with severe HS. Our findings showed that hypomagnesemic patients had a 28% higher risk of ICU mortality and a 15% greater chance of needing mechanical ventilation compared to non-hypomagnesemic patients. These results were consistent in both multivariate Cox regression and stratified analyses. Additionally, we found that the relationship between hypomagnesemia and ICU mortality was stronger in males and in patients with a history of ischemic stroke.

Our finding that hypomagnesemia is associated with a worse prognosis in HS patients aligns with previous studies. Recent studies have shown that hypomagnesemia was independently associated with increased hematoma volumes and expansion [5, 7]. In a prospective observational cohort study of 290 patients with spontaneous ICH, those with lower Mg levels had significantly larger initial and final hematoma volumes, as well as greater hematoma growth, compared to those with higher Mg levels ($p=0.02$, 0.02, and 0.004, respectively). Furthermore, their results showed that lower admission Mg levels were associated with poorer prognosis at 3 months, after adjusting for other variables [14]. Another prospective observational cohort study of 354 patients with spontaneous SAH found that those with lower Mg levels had larger hemorrhage volumes compared to those with higher Mg levels ($p=0.022$) [7]. A Mendelian randomization study found a negative correlation between serum

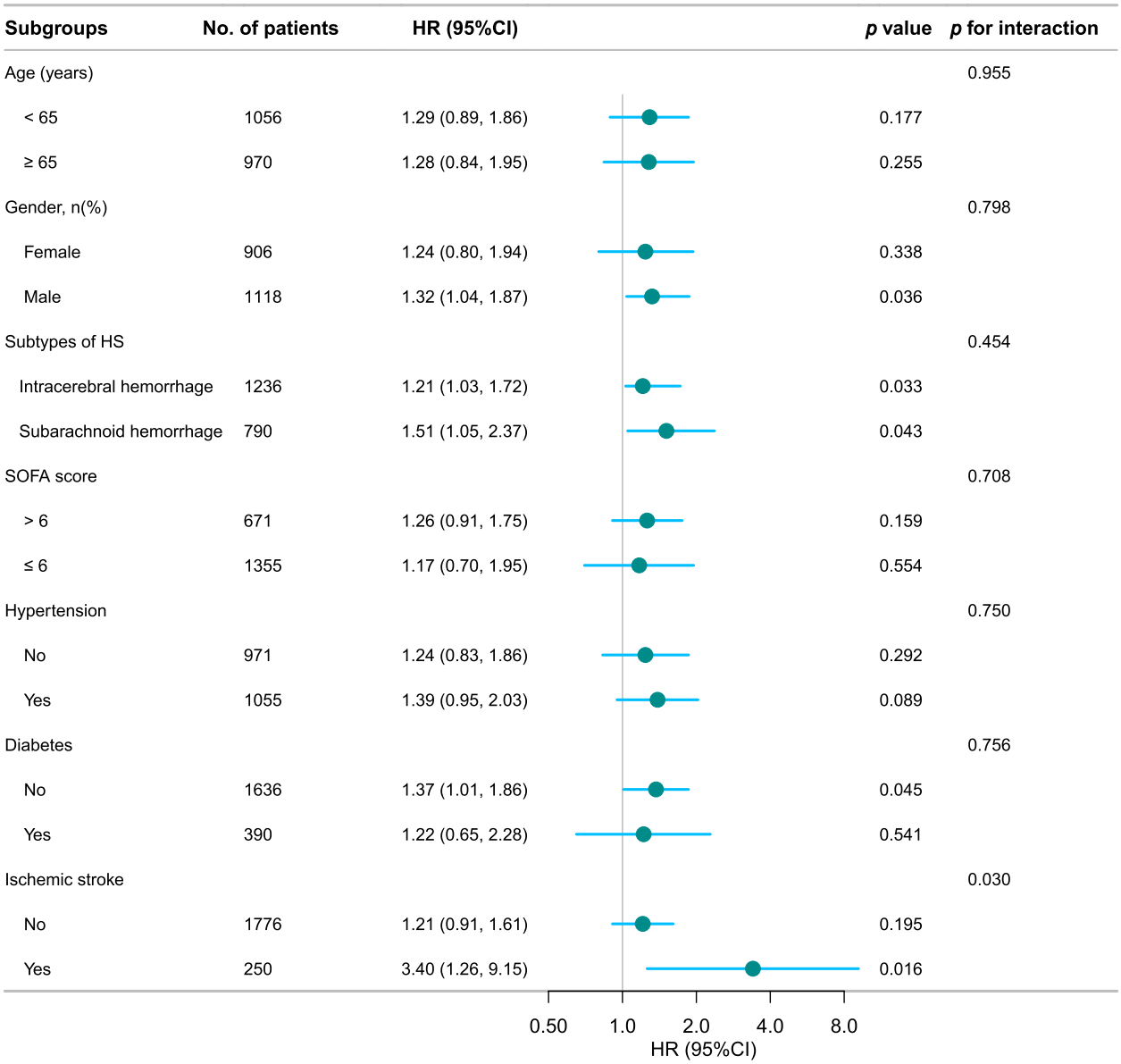

Fig. 1 Association between hypomagnesemia and ICU mortality according to subgroup. Each stratification adjusted for age, gender, race/ethnicity, SOFA score, comorbidities (hypertension, coronary artery disease, congestive heart failure, diabetes, chronic pulmonary disease, ischemic stroke, malignant cancer, renal disease), mean systolic blood pressure, mean diastolic blood pressure, white blood cell, hemoglobin, platelet, calcium, creatinine, except the stratification factor itself. Abbreviations: HS, hemorrhagic stroke; ICU, intensive care units; HR, hazard ratio; 95% CI, 95% confidence interval

Mg concentration and the risk of SAH, further supporting a causal relationship [15]. A population-based cohort study including 452 HS patients found that higher magnesium levels in drinking water was associated with a reduced risk of HS (HR 0.78, 95% CI [0.65—0.95]) [16].

The exact mechanism by which hypomagnesemia affects the prognosis of patients with severe cerebral hemorrhage is not yet fully understood. Previous studies suggest the following potential mechanisms: Firstly, at the molecular level, low serum Mg levels enhance N-methyl-D-aspartate (NMDA) receptor activity. This leads to increased glutamate and Ca^{2+} influx, potentially causing Ca^{2+} overload in neuronal cells. This may result in the production of toxic reactive oxygen species (ROS) and ultimately neuronal cell apoptosis [17–19]. Secondly, magnesium is crucial in the coagulation cascade [5, 20, 21]. Therefore, patients with hypomagnesemia and HS may experience larger initial and final hematoma

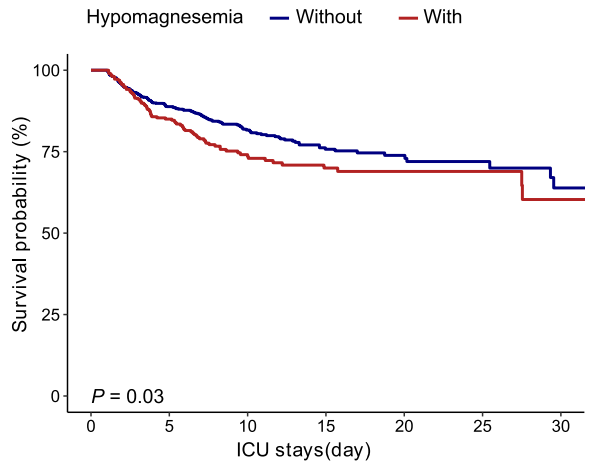

Fig. 2 Kaplan–Meier survival curves for severe HS patients with and without hypomagnesemia during 30-day ICU stays. The vertical axis is the survival probability, and the horizontal axis is ICU stays (day). The blue curve represents the survival probability for patients without hypomagnesemia, while the red curve represents the survival probability for those with hypomagnesemia. By the end of 30 days, the survival probabilities are approximately 63.9% and 60.3%, respectively ($p = 0.03$, log-rank test). Abbreviations: HS, hemorrhagic stroke; ICU, intensive care unit

volumes, increased hematoma growth, and a higher risk of mortality. Thirdly, magnesium, as the main effective divalent cation, influences the adhesion of platelets to the collagen matrix [22, 23]. This may explain the presence of platelet dysfunction and a poor prognosis in hypomagnesemia. Finally, magnesium plays a critical role in the systemic inflammatory response. Hypomagnesemia can trigger an inflammatory response, contributing to the cytokine storm associated with poor outcomes [24]. Additionally, magnesium significantly affects the inflammatory response, potentially damaging the blood–brain barrier (BBB) and increasing capillary permeability after HS [19, 25].

Our study revealed a stronger association between hypomagnesemia and ICU mortality in patients with ischemic stroke. This association may be explained by several factors: First, patients with a history of ischemic stroke often use antiplatelet or anticoagulant medications, which can lead to HS and early hemorrhage expansion [26]. Second, pericytes may be damaged after ischemic stroke, which is crucial for protecting cerebral tissue by maintaining the integrity of the BBB [27], performing immune cell functions [28], influencing cerebral blood flow, as well as vascular development [29].

Subgroup analyses revealed a stronger link between hypomagnesemia and ICU mortality in male patients. Several factors explain this result. First, previous studies have shown that men have higher blood pressure than women [30]. Similarly, in our study of 2,024 patients (906 females, 1,118 males), mean SBP was higher in males (130.97 ± 16.27 mmHg) than in females (129.38 ± 15.24 mmHg; $p = 0.028$). Males also had higher mean DBP (70.74 ± 10.80 mmHg) than females (66.97 ± 10.56 mmHg; $p < 0.001$) (Table S1). The INTERACT2 trial and AHA guidelines indicated that intensive blood pressure management (SBP < 140 mmHg) is safe and enhances functional outcomes in ICH patients [31]. Secondly, smoking, as an independent factor of atherosclerosis, is more common in male and increases the risk of HS in men [32, 33]. Finally, alcohol intake, similar to smoking, is more likely to be male. Previous studies showed that alcohol intake is associated with a higher risk of ICH [34, 35], perhaps due to the coagulopathy associated with alcoholic liver disease or the effect of alcohol on platelet aggregation [36, 37]. Furthermore, alcohol intake can increase the risk of hypomagnesemia. Some pathophysiological mechanisms can be explained as follows: Firstly, alcohol intake may cause reabsorption of Mg by renal tubules; Secondly, alcohol intake may affect the absorption of Mg ions in the gastrointestinal tract [36]. The combination of these factors may contribute to a higher ICU mortality rate for male patients with hypomagnesemia.

Clinical implications

Hemorrhagic stroke poses a significant threat to patient health due to its high morbidity and mortality rates. Given the established link between hypomagnesemia and poor outcomes in HS, routine Mg monitoring for ICU patients with HS is crucial. Once hypomagnesemia is diagnosed, evaluating the potential benefits of Mg supplementation becomes essential. However, clinical evidence supporting Mg supplementation in HS patients remains incomplete. One interventional study showed that daily supplementation with 64 mmol of magnesium sulfate could reduce the risk of delayed cerebral ischemia following SAH [38]. This finding provides theoretical support for Mg therapy. In contrast, a randomized controlled trial found no statistically significant difference in adverse outcome rates between patients receiving magnesium sulfate and those receiving a placebo over three months (risk ratio 1.03, 95% CI 0.85–1.25) [39]. Future research should include large-scale, well-designed randomized controlled trials to further investigate the role of Mg in HS treatment.

Limitations

Several limitations of this study must be acknowledged. Firstly, the retrospective design restricts causal inference and may introduce biases from confounding factors and historical data variability. Secondly, differences in ICU protocols, treatment approaches, and data collection

methods across institutions may have introduced heterogeneity and measurement bias, thereby affecting the reliability of the findings. Thirdly, relying solely on a single Mg measurement to evaluate the relationship between hypomagnesemia and prognosis may fail to account for the impact of Mg level trends on patient outcomes. Moreover, the study did not account for potential interactions such as lifestyle habits, therapeutic interventions, genetics, and individual differences.

To address the aforementioned limitations, we propose several directions for future research: First, we recommend conducting prospective multicenter randomized controlled trials (RCTs) to confirm the link between hypomagnesemia and ICU mortality. This approach will better account for confounding variables and strengthen clinical guidelines. Second, advanced statistical techniques, like machine learning models, should be explored to improve the predictive accuracy of Mg levels on ICU outcomes. Third, a controlled clinical trial should evaluate magnesium supplementation as a targeted intervention to improve outcomes for patients with HS. Finally, to address data heterogeneity, future studies should consider several strategies: i) Standardize data collection methods across centers to reduce measurement bias; ii) Use advanced statistical models, such as mixed-effects or Bayesian hierarchical models, to account for variations among different centers; iii) Collaborate with international centers to validate findings across diverse populations and healthcare settings, enhancing the generalizability of the results.

Conclusions

This study found that hypomagnesemia increases the risk of ICU mortality and mechanical ventilation use in severe HS patients. Therefore, in clinical practice, magnesium level monitoring should be incorporated into the routine ICU management of severe HS patients to enable early detection of hypomagnesemia. After confirming hypomagnesemia, clinicians should carefully assess the potential benefits of magnesium supplementation therapy. Further studies are needed to fully understand hypomagnesemia's role in severe HS patients and potential interventions.

Abbreviations

HS	Hemorrhagic Stroke
ICH	Intracerebral Hemorrhage
SAH	Subarachnoid Hemorrhage
ICU	Intensive Care Unit
eICU-CRD	E-Intensive Care Unit
Mg	Magnesium
SOFA	Sequential Organ Failure Assessment
BMI	Body Mass Index
PLT	Platelet
WBC	White Blood Cell
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04525-x.

Supplementary Material 1: Fig. S1 Flow chart of participants.

Supplementary Material 2: Fig. S2 Receiver operating characteristic curve of model for the internal validation with bootstrapping. The area under the receiver operating characteristic curve was 0.771.

Supplementary Material 3: Fig. S3 Calibration plot of predicted ICU mortality-probability against the observed ICU mortality-probability at 30 days. The red line shows the ideal calibration line, and the solid black line shows the actual performance of the predictive model. The yellow shadow represents a 95% confidence interval.

Supplementary Material 4: Fig. S4 Decision curve analysis of the predictive model. Net benefit was produced against the high-risk threshold. The blue solid line represents the predicted estimates. The straight red line represents the assumption that all patients will die at 30 days, and the green horizontal line represents the assumption that no patients will die at 30 days.

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Authors' contributions

XZJ wrote the original manuscript; FLG designed this study; ZJS was responsible for data download; FL verified the paper; WYZ contributed to the statistical analysis; GHG reviewed and edited the paper; and all authors read and approved the final manuscript.

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Data availability

The eICU datasets are publicly available at: https://physionet.org/content/eicu-crd.

Declarations

Ethics approval and consent to participate

This database was approved by the Massachusetts Institute of Technology (Cambridge, MA). It was a retrospective analysis of data from a publicly accessible data resource. Informed consent were waived for this manuscript.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Center for Rehabilitation Medicine, Department of Neurology, Zhejiang Provincial People's Hospital (Affiliated People's Hospital, Hangzhou Medical College), Hangzhou 310014, Zhejiang, China. [2]Center for Rehabilitation Medicine, Department of Neurosurgery, Zhejiang Provincial People's Hospital (Affiliated People's Hospital, Hangzhou Medical College), No.158, Shangtang Road, Hangzhou 310014, Zhejiang, China. [3]Center for General Practice Medicine, General Practice and Health Management Center, Zhejiang Provincial People's Hospital (Affiliated People's Hospital, Hangzhou Medical College), Hangzhou 310014, Zhejiang, China. [4]Department of General Practice Medicine, Xianju People's Hospital, Zhejiang Southeast Campus of Zhejiang Provincial People's Hospital, Affliated Xianju's Hospital, Hangzhou Medical College, 53 East Chengbei Road, Taizhou 317300, Zhejiang, China.

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