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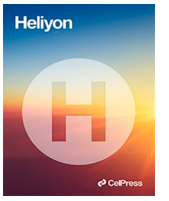

Risk factors for mortality in brain injury patients who have severe hypernatremia and received continuous venovenous hemofiltration

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ABSTRACT

Background and objectives: The mortality rate for people with brain injuries is increased when hypernatremia is present. Patients with severe hypernatremia, who have a significant short-term mortality rate, were shown to benefit from continuous venovenous hemofiltration (CVVH), which has been indicated to be successful. Exploring the risk factors for short-term mortality in brain injury patients who underwent CVVH and had severe hypernatremia was the aim of the current study.

Materials and methods: Retrospective screening was performed on patients with brain injuries who underwent CVVH at Xijing Hospital between 1 December 2010 and 31 December 2021 and who have a diagnosis of severe hypernatremia. The outcomes included 28-day patient mortality and hospital stay duration. The patient survival rate was examined using the Kaplan-Meier survival curve. To determine the risk factors for short-term death for patients, univariate and multivariate Cox regression analysis models were used.

Results: Our current study included a total of 83 individuals. The included patients had a median age of 49 (IQR 35–59) years. Of the included patients, 58 patients (69.9 %) died within 28 days. The median length of hospital stay for the patient was 13 (IQR 7–21) days. The APACHE II score, SOFA score, GCS, PLT count, INR, stroke, mechanical ventilation, and vasopressor reliance were related to 28-day mortality according to the univariate Cox analysis. INR (HR = 1.004, 95 % Cl: 1.001–1.006, P = 0.008), stroke (HR = 1.971, 95 % Cl: 1.031–3.768, P = 0.04), mechanical ventilation (HR = 3.948, 95 % Cl: 1.090–14.294, P = 0.036), and vasopressor dependency (HR = 2.262, 95 % Cl: 1.099–4.655, P = 0.027) were independently associated with the risk of 28-day death rates, according to multivariate Cox regression analysis.

Conclusions: Brain injuries who have severe hypernatremia requires CVVH, which has high short-term patient mortality. Mechanical ventilation, INR increase, stroke, and vasopressor dependence are independently associated with increased patient mortality risk.

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1. Introduction

At least 50 million patients suffer from brain injury every year worldwide, and more than 35 % of these patients experience hypernatremia [1–3]. Hypernatremia is a serious complication after brain injury, and it is also a risk factor for patient mortality. The blood sodium level had a substantial influence on the prognosis of patients with brain injury. The mortality rate increased with the increasing of serum sodium concentration [4]. Patients with hypernatremia with brain injury had a death rate of 20 %, while those with severe hypernatremia had a mortality rate as high as 80 % [5,6].

The relationship between hypernatremia and brain injury is complex. Several factors can trigger hypernatremia in patients with brain injury, such as central diabetes insipidus, the administration of hypertonic fluids (i.e., mannitol or hypertonic saline), iatrogenic sodium overload, inadequate water intake, and excessive water loss [7]. According to the etiology, the conventional therapy for hypernatremia in clinical practice is reducing the bloodstream levels of serum sodium, including fluid replacement, sodium intake limitation, and promotion of sodium excretion. However, these treatments are often insufficient to normalize serum sodium levels within 24–48 h for patients with acute severe hypernatremia or to achieve a correction rate of less than 20 % after 72 h for those with chronic severe hypernatremia [8]. Severe hypernatremia patients typically require continuous venovenous hemofiltration (CVVH). Many studies have focused on the effects of hypernatremia, blood sodium variability, and continuous infusion of hypertonic saline on the prognosis of brain injury patients [5,9–12]. Few studies have explored the influence of mortality and death risk factors on brain injury patients who also have severe hypernatremia treated by CVVH. Our previous study found that although the effect of CVVH in the treatment of severe hypernatremia was better than that of conventional treatment, the mortality rate was close to 60 % [13]. Our other study further explored the risk factors that impact mortality in individuals with serious conditions with significant hypernatremia treated by CVVH [14], but the inclusion of patients with multiple etiologies limited the expansion of the results. There is no research available right now on the risks of dying in CVVH-treated brain injury patients who have severe hypernatremia.

In this study, we evaluated the incidence of death in brain injury patients receiving CVVH treatment for severe hypernatremia, and we also identified the risk factors for patient mortality, which will aid clinicians in identifying patients at high risk and offering personalized treatment to enhance the quality of life for patients.

2. Materials and Methods

2.1. Population and setting

Retrospective screening was performed on patients with brain injuries who underwent CVVH at Xijing Hospital between 1 December 2010 and 31 December 2021 and who had a diagnosis of severe hypernatremia ($Na+ > 160$ mEq/L). Patients who met any of all of the following characteristics were disqualified: 1. age <18 years old; 2. severe infection; 3. the occurrence of severe hypernatremia before admission; and 4. chronic kidney disease in the past (eGFR$\leq$30 ml/min/1.73 m^2). The Declaration of Helsinki was followed when conducting the study. Our hospital's committee on ethics provided its approval to this present study, and considering that it is a retrospective, noninterventional study, official informed permission for participation was not needed.

2.2. Data collection

Data on the individuals undergoing treatment were obtained from the Xijing Hospital's digital medical records. Baseline characteristics consisted of patient demographics, vital signs, laboratory results, and admission diagnosis. The diagnosis on admission was recorded and included ischemic stroke, hemorrhagic stroke, encephalitis, and brain tumor after an operation. The Glasgow Coma Score (GCS), the Sequential Organ Failure Assessment (SOFA), and the Acute Physiology and Chronic Health Evaluation (APACHE) II scores were adopted to evaluate the degree of severity of the condition on the initial day of admission. The sodium-related characteristics listed below were recorded: timing of hypernatremia emergence, time from admittance to the beginning of hypernatremia, the blood sodium level just before discharge or death, and serum sodium concentration before starting CVVH. The start, stop, and treatment times of CRRT (continuous renal replacement therapy) were recorded. Other kinds of treatments include vasopressor, operation, and mechanical ventilation.

2.3. CRRT protocol

Detailed method descriptions for the treatment of CVVH have been published previously [15]. A Prismaflex twin lumen catheter was inserted into the vein in the femur to provide temporary vascular access. The Prismaflex HF 100 Set system (Gambro Hospal, Stockholm, Sweden), with a membrane area of 0.9 m^2 and 50 % predilution route, was used for the CVVH treatment. The replacement fluid rate was set at 2 L/h and the blood flow rate was 180 ml/min. The sodium concentration was controlled by adding 3 % sodium chloride, which was initially set to be 8 mmol/L lower than the serum level, and it was decreased by 2 mmol/L every 4 h. CVVH was continued until either the patient's hypernatremia was corrected or they passed away.

2.4. Definitions

A blood sodium level of more than 160 mEq/L has been deemed as severe hypernatremia [16]. For each study participant, we identified the serum sodium levels before and after CRRT treatment and the duration of CRRT treatment. Brain injury was categorized into stroke (ischemic or hemorrhagic) and no-stroke (brain tumor or encephalitis). The outcome was 28-day mortality and hospital stay. The patients who were still alive were followed-up over the phone when they were discharged.

2.5. Statistical analysis

Continuous variables were expressed differently based on their normality. The mean ± standard deviation (SD) was used to report normally distributed variables and were compared using a *t*-test. For nonnormally distributed variables, the median (interquartile range) was presented and compared using the Wilcoxon test. Categorical variables were compared using the chi-square or Fisher's exact test and presented as frequencies and percentages.

The cumulative survival of the patients was analyzed using the Kaplan–Meier survival curve, and log-rank tests were adopted to compare the survival variation across groups. The independent risk factors for 28-day mortality were identified using a multivariate Cox regression analysis model. The variables included in the multivariate Cox regression analysis model had statistical significance ($P < 0.05$) in the univariate analysis. Optimal cutoff values for continuous variables were evaluated by calculating the area under the receiver operating characteristic curve (AUC-ROC). Statistical significance was set at a two-tailed P value < 0.05. SPSS 20.0 (SPSS Inc, Chicago, IL) and R version 4.2.2 (The R Foundation for Statistical Computing, Austria, Vienna) were used to analyze the data in the present research.

3. Results

3.1. Patient characteristics

From 1 December 2010 to 31 December 2021, a total of 87 people with brain injuries who also had severe hypernatremia received CVVH. After the screening, in addition to 2 patients being excluded due to serious infections, 2 patients were excluded because they were below the age of 18. In the course of the research, 83 patients were included in the research (Fig. 1).

Table 1 displays the baseline characteristics and clinical outcomes of brain injury patients who also had hypernatremia. In the non-survival group, there were more patients with ischemic stroke, hemorrhagic stroke and brain tumor, and the APACHE II score, SOFA score, PLT and fibrinogen degradation product (FDP) were higher, while the GCS score and encephalitis were relatively less than those in the survival group. In the non-survival group, there were more stroke patients and more patients who needed vasopressor and mechanical ventilation. The patients had a median age of 49 (IQR 35–59) years. Forty-eight (57.8 %) and 35 (42.2 %) were male and female, respectively. Of the included patients, the median RRSeNa was 0.9 (IQR 0.6–1.2) mEq/L/hour, the median APACHE II score was 26 (IQR 20–30), the median SOFA score was 11 (IQR 8–15), the median GCS was 3 (IQR 3–6), and the median CVVH time was 28 (IQR 21–48) hours. Fifty-one (61.4 %) patients had an operation, 51 (61.4 %) patients had a vasopressor dependency, 66 (79.5 %) patients had mechanical ventilation, and 49 (59 %) patients had a stroke. The median sodium levels in the blood before CVVH, serum creatinine level at admission, 24-h liquid intake, and 24-h liquid output were 172.9 (IQR 165.5–179.6) mEq/L, 128 (IQR 94–199) μmol/L, 3925.0 (IQR 2464.0–5500.0) ml, and 3000.0 (IQR 1550.0–4500.0) ml, respectively.

3.2. Patient outcome

The clinical outcome of hypernatremia in patients with brain injury is also shown in Table 2. Fifty-eight patients (69.9 %) died within 28 days after the initiation of CVVH. No patient was lost to follow-up. The accumulated 28-day patient mortality proportion was 69.9 % (Fig. 2). The median patient survival time was 12 days. The median length of hospital stay for the patient was 13 (7–21) days.

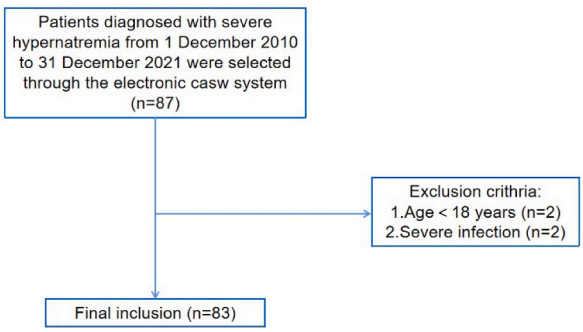

Fig. 1. Patient inclusion flow chart.

Table 1
Characteristics of patients.

Characteristic	All (n = 83)	Survival (n = 25)	Non-Survival (n = 58)	P Value
Age, years	49.0 (35.0–59.0)	45.0 (38.0–60.0)	50.5 (34.0–58.0)	0.721
APACHEII score	26.0 (20.0–30.0)	21.0 (18.0–26.0)	27.0 (23.0–30.0)	0.001
SOFA score	11.0 (8.0–15.0)	7.0 (5.0–10.0)	12.5 (9.0–16.0)	< 0.001
GCS	3.0 (3.0–6.0)	6.0 (3.0–10.0)	3.0 (3.0–5.0)	0.001
Body temperature, °C	37.8 (36.9–38.6)	37.8 (36.9–38.3)	37.9 (36.9–38.8)	0.717
Heart rate, bpm	101 (84–118)	101.0 (80.0–112.0)	101.0 (88.0–120.0)	0.335
MAP, mmHg	86.3 (79.3–95.3)	86.0 (80.0–95.3)	86.5 (78.7–94.7)	0.929
RRSeNa, mEq/L/hour	0.9 (0.6–1.2)	0.8 (0.5–1.1)	0.9 (0.5–1.2)	0.558
Serum sodium before CVVH, mEq/L	172.9 (165.5–179.6)	172.0 (166.7–177.5)	174.3 (165.0–179.6)	0.766
CVVH time, hours	28 (21–48)	40.0 (27.5–52.0)	24.0 (20.0–48.0)	0.07
24-h liquid intake, ml	3925.0 (2464.0–5500.0)	3697.0 (2500.0–4510.0)	4147.5 (2464.0–5804.0)	0.177
24-h liquid output, ml	3000.0 (1550.0–4500.0)	3000.0 (1800.0–3690.0)	3032.5 (1500.0–4820.0)	0.402
WBC,10^9/L	9.5 (14.1–18.6)	14.1 (8.9–17.8)	14.3 (10.3–18.6)	0.725
PLT,10^9/L	138 (83–243)	226.0 (123.0–268.0)	118.5 (79.0–210.0)	0.013
Hb, g/L	121 (105–143)	129.0 (113.0–145.0)	120.5 (101.0–136.0)	0.204
Serum creatinine, μmol/L	128 (94–209)	128.0 (89.0–209.0)	129.0 (104.0–185.0)	0.655
PH, mmol/L	7.3 (7.3–7.4)	7.3 (7.3–7.4)	7.3 (7.3–7.4)	0.605
PT, S	13.3 (12.1–14.7)	13.3 (12.1–14.9)	13.5 (12.1–14.5)	0.858
APTT, S	28.8 (23.8–33.7)	26.8 (22.7–32.8)	29.4 (24.4–33.7)	0.565
D-dimmer, mg/l	4.8 (1.9–26.4)	4.3 (1.6–20.3)	5.3 (2.2–27.5)	0.475
FDP, μg/ml	12.6 (5.8–46)	6.4 (4.3–14.0)	14.4 (7.1–56.7)	0.009
INR	1.2 (1.0–1.3)	1.1 (1.0–1.3)	1.2 (1.0–1.3)	0.299
Male, n (%)	48 (57.8)	14 (56.0)	34 (58.6)	0.824
Stroke, n (%)	49 (59.0)	7 (28.0)	42 (72.4)	< 0.001
Ischemic stroke, n (%)	26 (31.3)	5 (20.0)	21 (36.2)	0.001
Hemorrhagic stroke, n (%)	23 (27.7)	2 (8.0)	21 (36.2)	0.001
Brain tumor, n (%)	24 (28.9)	11 (44.0)	13 (22.4)	0.001
Encephalitis, n (%)	10 (12.0)	7 (28.0)	3 (5.2)	0.001
Operation, n (%)	51 (61.4)	14 (56.0)	37 (72.5)	0.503
Vasopressor dependency, n (%)	51 (61.4)	7 (28.0)	44 (86.3)	< 0.001
Mechanical ventilation, n (%)	66 (79.5)	12 (48.0)	54 (93.1)	< 0.001

APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Score; MAP, median arterial pressure; RRSeNa, reduction rate of serum sodium; SOFA, Sequential Organ Failure Assessment, CVVH, continuous venovenous hemofiltration; PLT, platelet; Fibrinogen Degradation Products, FDP.

Table 2
Outcomes of patients.

length of hospital stay, days	13.0 (7.0–21.0)
28-day mortality	58 (69.9)

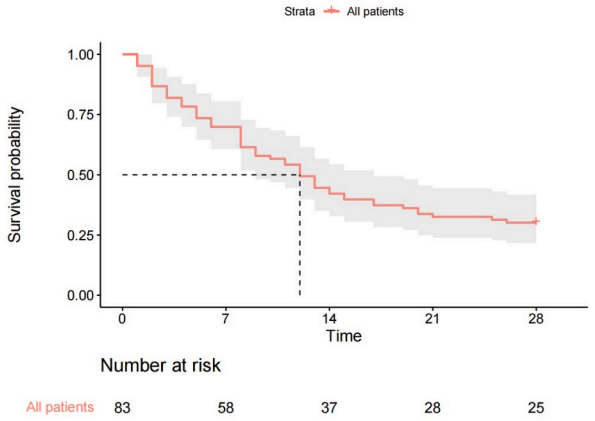

Fig. 2. Kaplan-Meier curve for 28-day mortality.

3.3. Risk factors for 28-day patient mortality

The following variables were found to be associated with 28-day mortality based on univariate analysis: APACHE II score (P = 0.001), SOFA score (P < 0.001), GCS (P = 0.005), PLT count (P = 0.02), INR (P = 0.046), stroke (P < 0.001), mechanical ventilation (P < 0.001), and vasopressor dependency (P = 0.001) (Table 2).

INR (hazard ratio [HR] = 1.004; 95 % confidence interval [CI]: 1.001–1.006; P = 0.008), stroke (HR = 1.971; 95 % CI: 1.031–3.768; P = 0.04), mechanical ventilation (HR = 3.948; 95 % CI: 1.090–14.294; P = 0.036), and vasopressor dependency (HR = 2.262; 95 % CI: 1.099–4.655; P = 0.027) were identified as independent risk factors for 28-day death in the multivariate Cox regression analysis (Table 3).

In accordance with the Youden index, the optimum INR cutoff value was 1.08. With the optimal cutoff value, 83 patients were classified into high and low groups. According to the Kaplan–Meier survival curve, patients with greater INR, stroke, mechanical ventilation, and vasopressor dependency were correlated with a higher risk of death at 28 days (Fig. 3).

4. Discussion

This is the first study to investigate the mortality and factors that increase the risk of death in brain injury patients with severe hypernatremia treated by CRRT. In this study, we found that mechanical ventilation, stroke, vasopressor dependency, and INR were recognized as independent risk factors for 28-day death.

The increase in risk of death was associated with hypernatremia. According to our research, patients experiencing brain injuries with severe hypernatremia had a significant short-term death rate. In our current study of patients with a brain injury who had severe hypernatremia, the death rate within 28 days was 69.9 %. Hypernatremia causes cellular dehydration in the brain, resulting in a rapid reduction in brain volume, which can increase the risk of focal intracranial hemorrhage, subarachnoid hemorrhage, myelin sheath injury, and even neuron death [16–18]. Previous studies found that the overall mortality rate for those with brain injuries who also have hypernatremia fluctuates from 30.7 % to 75 %, while the mortality rate of those with severe hypernatremia (Na^+ ≥160 mEq/L) was 86.8 % [5,19,20]. This was higher than our current research results. The difference may be partially attributed to the use of CVVH in our present cohort. Previous studies have shown that CRRT is beneficial for treating severe hypernatremia and improving the survival rate [13]. Yessayan et al. [21] recommended the initiation of CRRT in brain injury patients who also have severe hypernatremia (Na^+ >165 mEq/L).

The requirement for mechanical ventilation was an independent risk factor for death in our research. According to earlier research, the requirement for mechanical ventilation was a known independent risk factor for death in brain injury patients who also had

Table 3
Univariate and multivariable Cox regression analyses of patient 28-day mortality.

	Univariate analysis			Multivariate analysis		
	HR	95 % CI	P Value	HR	95 % CI	P Value
Age	1	0.985–1.015	0.969			
APACHEII score	1.072	1.029–1.117	0.001	0.99	0.937–1.045	0.712
SOFA score	1.15	1.087–1.218	<0.001	1.043	0.964–1.130	0.296
GCS	0.872	0.793–0.959	0.005	0.947	0.845–1.062	0.351
Body temperature	1.007	0.790–1.283	0.958			
Heart rate	1.007	0.996–1.018	0.244			
MAP	1.002	0.984–1.020	0.81			
RRSeNa	1.073	0.772–1.491	0.676			
CVVH time	0.993	0.982–1.004	0.193			
Serum sodium before CVVH treatment	0.993	0.967–1.020	0.632			
WBC	1.018	0.976–1.061	0.408			
PLT	0.996	0.993–0.999	0.02	1	0.996–1.003	0.978
Hb	0.994	0.984–1.003	0.19			
Serum creatinine at admission	1	0.999–1.002	0.81			
PH	0.567	0.016–20.209	0.756			
PT	1.011	0.959–1.067	0.675			
APTT	1.012	0.977–1.048	0.496			
D-dimmer	1	1.000–1.000	0.758			
FDP	1	0.998–1.001	0.676			
INR	1.002	1.000–1.005	0.046	1.004	1.001–1.006	0.008
Male	1.088	0.645–1.837	0.751			
Stroke (yes or no)	3.25	1.813–5.829	<0.001	1.971	1.031–3.768	0.04
Operation (yes or no)	0.867	0.507–1.485	0.604			
Vasopressor dependency (yes or no)	5.768	2.075–16.032	0.001	2.262	1.099–4.655	0.027
Mechanical ventilation (yes or no)	3.267	1.767–6.039	<0.001	3.948	1.090–14.294	0.036
RRSeNa≥1 mEq/L/hour	1.114	0.658–1.886	0.689			

APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Score; HR, hazard ratio; MAP, median arterial.
Pressure; RRSeNa, reduction rate of serum sodium; SOFA, Sequential Organ Failure Assessment; CVVH, continuous venovenous hemofiltration; PLT, platelet; Fibrinogen Degradation Products, FDP.

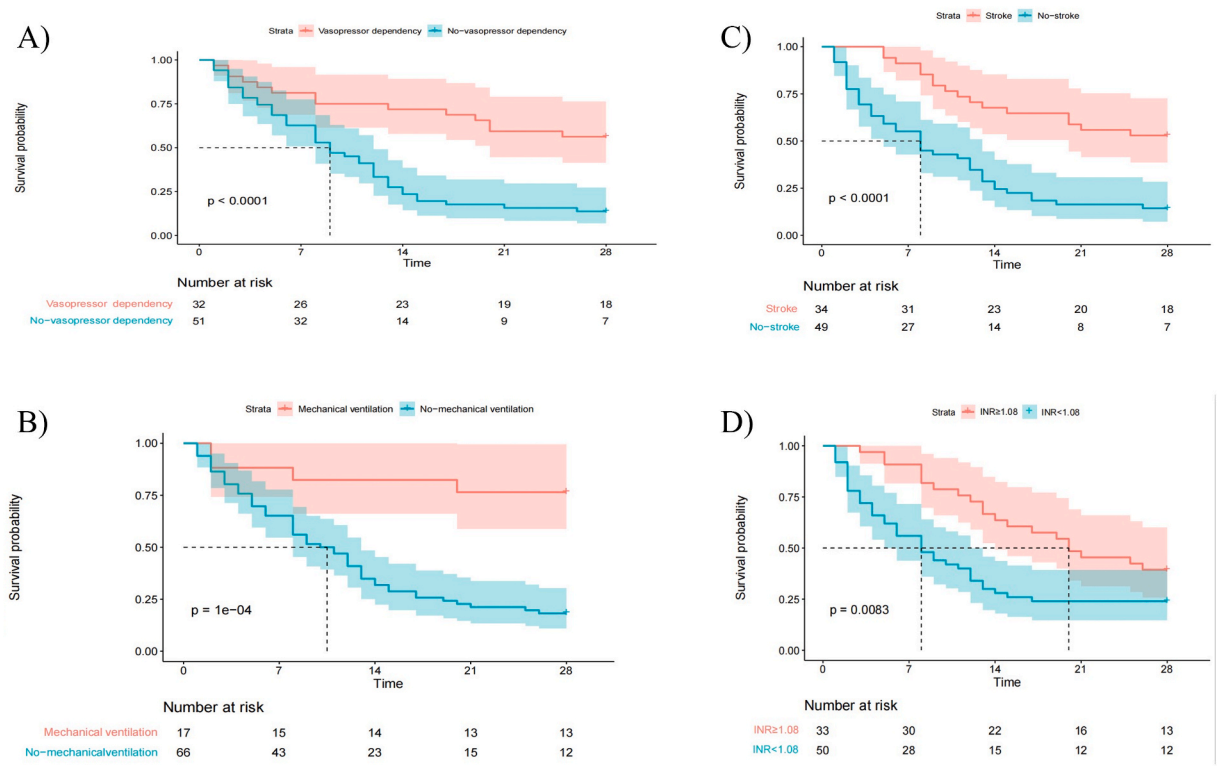

Fig. 3. Survival curve of brain injury patients who also have hypernatremia under different factors
3 A. Survival curve of brain injury patients who also have hypernatremia under vasopressor dependency
3 B. Survival curve of brain injury patients who also have hypernatremia under mechanical ventilation
3 C. Survival curve of brain injury patients who also have hypernatremia under stroke
3 D. Survival curve of brain injury patients who also have hypernatremia under INR≥1.08.

hypernatremia [22]. This corresponds to our current outcomes. Almeida KJ et al. [23] found that long-term mechanical ventilation was associated with higher rates of mortality, neurological complications, and infection. Patients with brain injuries often require ventilator-assisted breathing and sedation therapy as they may have an abnormal conscious state. However, the use of mechanical ventilation can cause dehydration or worsen hypernatremia, so we should always pay attention to electrolytes and replenish water in time, while long-term use may result in respiratory failure due to the loss of respiratory protective reflexes and a reduced respiratory drive. This might increase the risk of developing lung problems, including pneumonia and acute respiratory distress syndrome, which would raise mortality [24–26].

Additionally, stroke had a statistically significant impact on death in brain injury patients who had severe hypernatremia. The blood-brain barrier can be damaged by both ischemic and hemorrhagic stroke, which can result in brain edema and elevated intracranial pressure. The hypothalamus plays a critical role in regulating water and sodium balance is played by the hypothalamus, and when the hypothalamus-pituitary gland is affected by cerebral apoplexy, decreased secretion of antidiuretic hormone (ADH) as well as damage to the osmoreceptor or thirst center can occur. This can cause excessive excretion of low-sodium urine, aggravating hypernatremia in these patients (5). Hypertonic saline has been suggested as a potential treatment for acute intracranial hypertension. Although hyperosmolar therapy is commonly used in clinical practice to manage cerebral edema and increased intracranial pressure, hypernatremia can also be caused by it. There is currently inadequate evidence regarding the use of hypertonic saline in treating brain injury patients to improve neurological outcomes [10]. In our patient cohort, it remains uncertain whether the etiology of hypernatremia in all cases is related to hypertonic saline administration, and iatrogenic causes cannot be ruled out. Thus, careful consideration should be given to the benefits and risks of using hypertonic saline for the management of increased intracranial pressure and cerebral edema. Furthermore, frequent monitoring of serum sodium levels should be performed during treatment with hypertonic saline.

Our study, which was consistent with other research, established INR as an independent risk factor for death in brain injury patients who have severe hypernatremia [27,28]. A coagulation disorder is suspected if INR>1.2 and/or PLT<150 × 109/L and/or APTT>34.5 s [29]. In the presence of a coagulation disorder, patients with brain injury may be susceptible to progressive hemorrhagic injury [30]. Van Gent JAN et al. [29] demonstrated that patients with a coagulation disorder had a significantly higher mortality rate than those without, possibly due to platelet dysfunction, endothelial activation, fibrinogen modification, and inflammation. Therefore, early monitoring and correction of coagulation dysfunction may be crucial for improving patient outcomes.

In addition, we found that vasopressor dependency was an independent risk factor for death. This was consistent with our previous research conclusions [14]. The extensive use of vasopressor medications in patients with brain injury who have severe hypernatremia may be related to hemodynamic instability and insufficient tissue perfusion. As a result of our outcomes, the prognosis of patients with brain injury who have hypernatremia was associated with the degree of severity of the disease as well as the overall management of the condition.

5. Study limitations

The constraints of our present design studies are substantial. First, considering that it was a single-center trial, there could have been some bias, which will affect the universality of the results. However, we strictly followed the screening criteria, which will improve the repeatability of our research. Second, we collected data retrospectively through the electronic medical record system, and the results may be biased by unknown confounding factors. However, we performed multivariate analysis to adjust the important clinical parameters, lowering the possibility of bias. Third, the small number of participants limited the identification of risk factors with lower power. We need more multicenter research with a greater number of participants to provide us with stronger evidence.

6. Conclusion

The short-term death rate of individuals with brain injury who had severe hypernatremia was significant. Mechanical ventilation, INR increase, stroke, and vasopressor dependence were independently associated with the risk of 28-day mortality. Close monitoring of blood sodium concentration and coagulation function and timely treatment may be helpful to improve the prognosis of patients with brain injury.

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Data availability

The data related to my research is not stored in the publicly available repository, authors do not have permission to share data**.** The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Hao Wu: Writing – original draft. **Xiayin Li:** Methodology, Conceptualization. **Lijuan Zhao:** Data curation. **Jinguo Yuan:** Formal analysis. **Yan Xing:** Formal analysis. **Ming Bai:** Writing – review & editing. **Shiren Sun:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Neurol. 18 (1) (2019) 56–87.
[2] P. Pin-On, et al., Serum electrolyte imbalance and prognostic factors of postoperative death in adult traumatic brain injury patients: a prospective cohort study, Medicine (Baltim.) 97 (45) (2018), e13081.
[3] N. Deveduthras, et al., The prevalence of sodium abnormalities in moderate to severe traumatic brain injury patients in a level 1 Trauma unit in Durban, S. Afr. J. Surg. 57 (2) (2019) 62.
[4] M. Shehata, et al., Impact of hypernatremia on patients with severe traumatic brain injury (1) (2010).
[5] M. Li, Y.H. Hu, G. Chen, Hypernatremia severity and the risk of death after traumatic brain injury, Injury 44 (9) (2013) 1213–1218.
[6] A. Vedantam, C.S. Robertson, S.P. Gopinath, Morbidity and mortality associated with hypernatremia in patients with severe traumatic brain injury, Neurosurg. Focus 43 (5) (2017) E2.
[7] H. Wu, et al., Diagnosis and treatment of brain injury complicated by hypernatremia, Front. Neurol. 13 (2022), 1026540.
[8] H.M. Alshayeb, et al., Severe hypernatremia correction rate and mortality in hospitalized patients, Am. J. Med. Sci. 341 (5) (2011) 356–360.
[9] S.K. Tan, et al., The effect of continuous hypertonic saline infusion and hypernatremia on mortality in patients with severe traumatic brain injury: a retrospective cohort study, Can. J. Anaesth. 63 (6) (2016) 664–673.
[10] A. Roquilly, et al., Effect of continuous infusion of hypertonic saline vs standard care on 6-month neurological outcomes in patients with traumatic brain injury: the COBI randomized clinical trial, JAMA 325 (20) (2021) 2056–2066.
[11] J.H. Ryu, et al., Induced and sustained hypernatremia for the prevention and treatment of cerebral edema following brain injury, Neurocritical Care 19 (2) (2013) 222–231.

[12] M. Ziaeirad, et al., Association between outcome of severe traumatic brain injury and demographic, clinical, injury-related variables of patients, Iran. J. Nurs. Midwifery Res. 23 (3) (2018) 211–216.
[13] F. Ma, et al., Continuous venovenous hemofiltration (CVVH) versus conventional treatment for acute severe hypernatremia in critically ill patients: a retrospective study, Shock 44 (5) (2015) 445–451.
[14] F. Ma, et al., The reduction rate of serum sodium and mortality in patients undergoing continuous venovenous hemofiltration for acute severe hypernatremia, Am. J. Med. Sci. 352 (3) (2016) 272–279.
[15] C. Huang, et al., Treatment of acute hypernatremia in severely burned patients using continuous veno-venous hemofiltration with gradient sodium replacement fluid: a report of nine cases, Intensive Care Med. 39 (8) (2013) 1495–1496.
[16] R.H. Sterns, Disorders of plasma sodium–causes, consequences, and correction, N. Engl. J. Med. 372 (1) (2015) 55–65.
[17] R.H. Sterns, et al., Neurologic sequelae after treatment of severe hyponatremia: a multicenter perspective, J. Am. Soc. Nephrol. 4 (8) (1994) 1522–1530.
[18] H. Aegisdottir, et al., Incidence of osmotic demyelination syndrome in Sweden: a nationwide study, Acta Neurol. Scand. 140 (5) (2019) 342–349.
[19] W.J. Jung, et al., Severity of community acquired hypernatremia is an independent predictor of mortality, Intern Emerg Med 12 (7) (2017) 935–940.
[20] H. Hoffman, M.S. Jalal, L.S. Chin, Effect of hypernatremia on outcomes after severe traumatic brain injury: a nationwide inpatient sample analysis, World Neurosurg 118 (2018) e880–e886.
[21] L.T. Yessayan, B. Szamosfalvi, M.H. Rosner, Management of dysnatremias with continuous renal replacement therapy, Semin. Dial. 34 (6) (2021) 472–479.
[22] V. Krishnamoorthy, et al., Demographic and clinical risk factors associated with hospital mortality after isolated severe traumatic brain injury: a cohort study, J Intensive Care 3 (2015) 46.
[23] K.J. Almeida, et al., Hemotransfusion and mechanical ventilation time are associated with intra-hospital mortality in patients with traumatic brain injury admitted to intensive care unit, Arq Neuropsiquiatr 74 (8) (2016) 644–649.
[24] M.M. Braun, C.H. Barstow, N.J. Pyzocha, Diagnosis and management of sodium disorders: hyponatremia and hypernatremia, Am. Fam. Physician 91 (5) (2015) 299–307.
[25] J.F. Payen, et al., [Hypernatremia in head-injured patients: friend or foe?], Ann. Fr. Anesth. Reanim. 33 (6) (2014) 433–435.
[26] M. Oddo, et al., Fluid therapy in neurointensive care patients: ESICM consensus and clinical practice recommendations, Intensive Care Med. 44 (4) (2018) 449–463.
[27] Q. Yuan, et al., Prognostic value of coagulation tests for in-hospital mortality in patients with traumatic brain injury, Scand J Trauma Resusc Emerg Med 26 (1) (2018) 3.
[28] D.J.F. Solla, et al., Incremental prognostic value of coagulopathy in addition to the crash score in traumatic brain injury patients, Neurocritical Care 34 (1) (2021) 130–138.
[29] J.A.N. van Gent, et al., Coagulopathy after hemorrhagic traumatic brain injury, an observational study of the incidence and prognosis, Acta Neurochir. 162 (2) (2020) 329–336.
[30] T. Chang, et al., Risk factors and neurologic outcomes in patients with traumatic brain injury and coagulopathy within 72 h after surgery, Neuropsychiatr Dis Treat 17 (2021) 2905–2913.