Original Article

Impaired Kidney Function Portended a Bleak Prognosis for Surgically Treated Hypertensive Intracerebral Hemorrhage Patients

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Abstract

Purpose: Spontaneous intracerebral hemorrhage (ICH) cases caused by hypertension often have poor prognoses. The use of dehydrant agents, such as mannitol, is common to reduce intracranial pressure and alleviate cerebral edema, but they may also pose a risk of worsening kidney function. This study aimed to investigate the impact of impaired kidney function on the outcomes of surgically treated hypertensive ICH patients. **Methods:** We conducted a retrospective analysis of a consecutive cohort of patients who underwent surgical intervention due to hypertension-related ICH at our institute between December 1, 2017, and January 31, 2022. Demographic, clinical, radiological, and prognostic data were collected. Patients were categorized into two groups based on 90-day mortality: group A [overall survival (OS) ≤3 months] and group B (OS >3 months). Survival analysis was performed to identify factors associated with poor outcomes. **Results:** Among the 232 eligible patients, group A exhibited significantly impaired kidney function, as indicated by mean estimated glomerular filtration rate (eGFR) at admission, postoperative, 3-day postoperative, and 7-day postoperative time points (91.9, 82.5, 73.5, 75.2 ml/min/1.73 m²). In contrast, group B did not show significant changes in kidney function (mean eGFR for the corresponding time points: 108.1, 106.5, 111.5, 109.6 ml/min/1.73 m²). The 3-day postoperative eGFR showed the strongest predictive ability for assessing prognosis [areas under the curve (AUC): 0.617, 0.675, 0.737, 0.730]. Univariate and multivariate analyses identified low Glasgow Coma Scale (GCS) score (3–8), ventricle intrusion of hematomas, cardiac failure, larger hematoma volume, infection, and lower 3-day postoperative eGFR as adverse factors for survival. **Conclusions:** Preserving kidney function is crucial for achieving favorable outcomes in hypertensive ICH cases. Impaired 3-day postoperative eGFR emerged as an independent risk factor for overall survival. Patients with cardiac failure, infection, and larger hematoma volume should receive careful management to improve outcomes.

Keywords: Hypertension, intracerebral hemorrhage, kidney function, prognosis

Introduction

Spontaneous intracerebral hemorrhage (ICH) is a highly acute and often fatal type of stroke that poses a significant threat to the quality of life and life expectancy, particularly among aging individuals.[1] The increasing elderly population has led to a substantial rise in the incidence of ICH, with an annual rate of 12–15 cases per 100,000 individuals.[2-6] The high morbidity, disability, and mortality associated with ICH present a formidable challenge for physicians and families alike.

Hypertension is closely linked to more than 50–70% of spontaneous ICH cases.[7] Prolonged hypertension can cause structural changes in small arteries and perforator vessels, resulting in irreversible degeneration. These abnormal vessels are often implicated in ICH occurrences, affecting regions such as the basal ganglia, thalamus, brainstem, and cerebellum. Factors such as aging, alcohol consumption, smoking, and drug use can directly contribute to uncontrolled hypertension, ultimately leading to ICH.[8,9] Critical treatment modalities for ICH include hematoma removal through surgical intervention, blood pressure reduction, and cerebral edema alleviation, which are vital for saving lives and improving outcomes.[2,4] However, controversies exist regarding blood pressure reduction and the use of dehydration therapy with mannitol due to potential kidney damage.[10] Rapid blood pressure reduction may result in inadequate blood supply to the peripheral circulation, while long-term use of dehydrating agents can impose an additional burden on the kidneys,

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exacerbating compromised kidney function in advanced patients.[11] Preserving optimal kidney function may help patients navigate the most critical period and achieve more favorable prognoses.[12] Nonetheless, the precise impact of kidney function on the prognosis of ICH patients remains insufficiently explored.

Therefore, in this retrospective study, we conducted a comprehensive evaluation of ICH patients treated in the intensive care unit (ICU) to investigate the relationship between kidney function and prognosis. By elucidating this association, our findings may contribute to the development of tailored therapeutic protocols that strike a balance between kidney function and the prognosis of ICH patients.

Methods and Materials

Study design and patient selection

This study retrospectively included a consecutive cohort of patients who experienced ICH due to hypertension and were admitted to the Trauma ICU at the First Affiliated Hospital, Xinjiang Medical University, between December 1, 2017, and January 31, 2022. Specifically, all patients in our study presented with intracranial hematoma and met the surgical intervention criteria as follows: 1) for supratentorial hematoma: hematoma volume >20 m, evidence of increased intracranial pressure on imaging, such as midline structure displacement >5 mm, obstruction of more than 1/2 of the ipsilateral lateral ventricle, and blurring or disappearance of the ipsilateral cisterns and sulci, or intracranial pressure (ICP) >25 mmHg; 2) for cerebroventricular hemorrhage: large hematoma volume exceeding 50% of the lateral ventricle, Glasgow Coma Scale (GCS) <8 points, obstructive hydrocephalus, or significant intracranial hypertension; 3) for infratentorial hematoma: hematoma diameter >3 cm or volume >10 ml, fourth ventricle compression or complete occlusion, significant space-occupying effect and intracranial hypertension, evidence of brain herniation (occipital foramen herniation is the main type, or significant obstructive hydrocephalus; 4) for brainstem hemorrhage: hematoma volume >5 ml and relatively concentrated, GCS score <8, accompanied by progressive deterioration of neurological function, unstable vital signs, especially significant central blood pressure, body temperature, and breathing abnormalities appearing early in bleeding, or strong willingness from family members to undergo surgery. Patients with the following criteria were excluded from the study: [1] (1) subarachnoid hemorrhage or aneurysm (27 cases), (2) ICH due to moyamoya disease (2 cases), amyloidosis (1 case), or arteriovenous malformation (7 cases), (3) recent history of trauma (1 case), and (4) patients with malignancies or other terminal diseases (3 cases) or loss of follow-up (5 cases). Demographic, clinical, radiological, and prognostic information of the finally qualified 232 cases was collected for further analysis. The study protocol was approved by the Institutional Review Board of Xinjiang Medical University, in accordance with the principles of the Declaration of Helsinki, and written informed consent was waived by the Institutional Review Board.

Radiological data

For patients suspected of having ICH, head non-contrast computerized tomography (CT) scans were performed in the emergency room using a GE Discovery CT750HD machine (USA) with the following parameters: 120 kV, 400 mA, slice thickness of 5 mm, and a gap of 2.5 mm. These scans were used to determine the location and volume of the hematomas. The location of the hematoma was categorized into the cerebral hemisphere, basal ganglia/thalamus, ventricle, or infratentorial structures (brainstem or cerebellum) based on the geographic epicenter of the hemorrhage. Hemorrhage volumes were measured using a computerized planimetric method and the simplified formula for the volume of an ellipsoid, ABC/2, where A represents the largest diameter of the hemorrhage, B represents the largest diameter 90° to A on the same slice, and C represents the approximate number of 2-mm slices.[13]

Estimated glomerular filtration rate (eGFR) tests

The serum creatinine level was measured at the time of hospital admission, postoperative, 3-day postoperative, and 7-day postoperative to determine the estimated glomerular filtration rate (GFR). The estimated GFR was calculated using the abbreviated Modification of Diet in Kidney Disease formula proposed by the Modification of Diet in Kidney Disease Study Group: eGFR (ml/minute per 1.73 m^2) =186 × [serum creatinine] - 1.154 × age - 0.203× [0.742 if female]. Patients without chronic kidney disease (CKD) from the Get with the Guidelines Intracerebral Hemorrhage (GWTG-ICH) database, with an eGFR >90, were used as the referent group for comparison. Patients were then categorized according to the degree of kidney dysfunction (eGFR in ml/minute per 1.73 m^2) using modified definitions from the National Kidney Foundation—Kidney Disease Outcomes Quality Initiative clinical practice guidelines: normal (eGFR ≥90), mild (60 ≤ eGFR <90), moderate (30 ≤ eGFR < 60), (15 ≤ eGFR <30), and kidney failure (eGFR <15).[14,15]

Treatment protocol and follow-up

The decision-making process for ICH management was outlined in detail [Figure 1a].[16,17] All patients underwent surgical intervention to remove the intracranial hematoma timely. Eligible patients received dehydrant agents such as mannitol, furosemide, and glycerin fructose to alleviate cerebral edema. The highest permissible creatinine level for administering mannitol in our study group was <133 umol/ml (or eGFR >80 ml/min). For patients with creatinine levels ranging between 133 and 177 umol/l (or eGFR 50–80 ml/min), a reduced dose of mannitol was administered. Mannitol was contraindicated for patients with creatinine levels >177 umol/l (or eGFR <50 ml/min). Additionally, it is important to note that the treatment protocol for anti-edema measures, including mannitol, furosemide, glycerin fructose, and 3% NaCl, was dynamic and adjusted based on the individual patient's condition and creatinine levels. The dosages and combinations of these medications were tailored to the specific needs of each patient. The administration

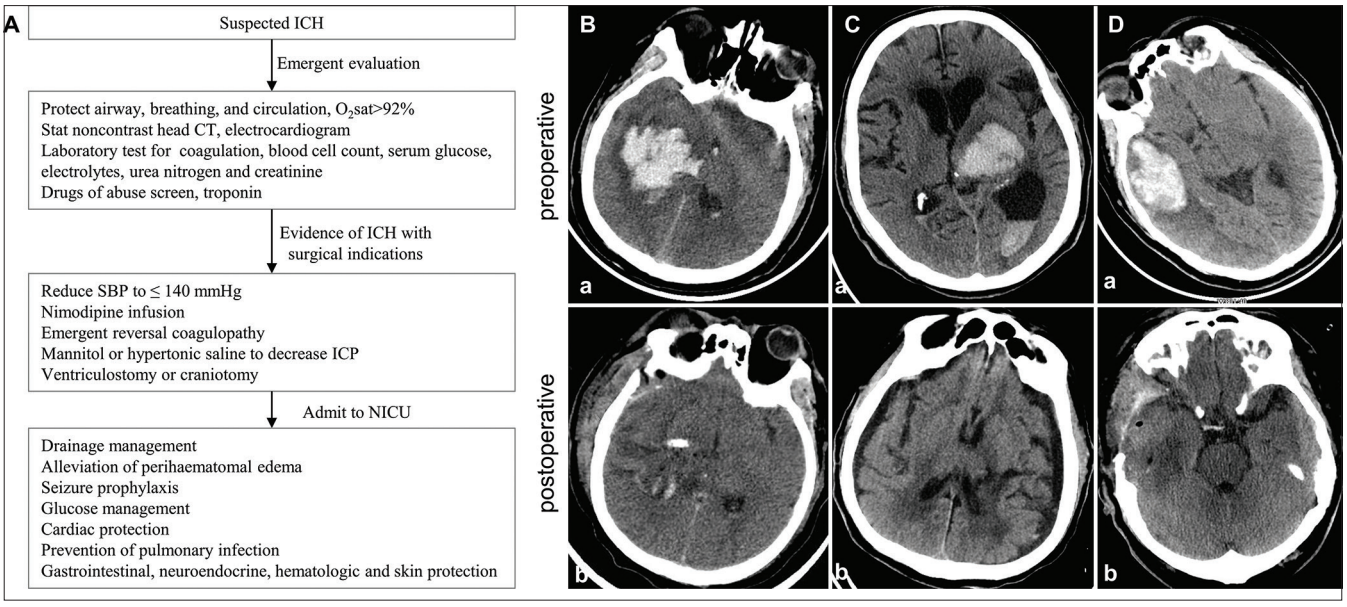

Figure 1: Treatment of ICH patients and outcomes. (A) the decision-making procedure in ICH management. (B-D) three representative hypertensive ICH cases who received evacuation of hematoma, a for preoperative and b for postoperative CT images

of these agents was carried out under the guidance of two senior physicians. Ventilatory support was performed for sedated patients by volume-synchronized intermittent mandatory ventilation (V-SIMV) or pressure-synchronized intermittent mandatory ventilation (P-SIMV). For patients who were spontaneously breathing, we employed continuous positive airway pressure (CPAP) or pressure support ventilation (PSV). Antiepileptic drugs (such as midazolam, sodium valproate, phenobarbital sodium) and anti-infective agents (like cephalosporin, vancomycin, meropenem) were prescribed to eligible patients. Any other complications that arose during the treatment were duly managed by the medical team.

Follow-up and outcome assessment

For patients who passed away during their hospital stay, the cause of death was determined based on clinical documentation, including medical records, physician notes, and autopsy reports, if available. Secondly, for patients who died after discharge, the cause of death was obtained through a thorough review of their medical records, including follow-up information, death certificates, and relevant clinical information from primary care providers or other healthcare facilities. Telephone follow-up was conducted every 3–4 months or as clinically indicated to monitor the patients' progress. The overall survival (OS) was defined as the duration between admission and either the date of death or the last follow-up.

Statistical analysis

Statistical analysis was performed using appropriate methods. Continuous variables were analyzed using the student's *t*-test, while nonparametric data were analyzed using the Mann–Whitney U-test. Categorical variables were compared using the Chi-square test or Fisher's exact test. Receiver operating characteristic (ROC) curves were constructed to determine the AUC and the optimal cutoff value using the Youden index (sensitivity + specificity − 1) with the pROC package in R. GraphPad Prism (Version 8.0.1, GraphPad Software, USA), R (version 4.0.3, USA), and R Studio (Version 1.2.5033, USA) were used for statistical analyses. The survival rate of patients was estimated using Kaplan–Meier plots, and differences between survival curves were compared using the log-rank test. Patients who underwent surgical intervention due to hypertension-related ICH group were further divided into subgroups based on the prognosis: inferior and favorable, with a cutoff of 3 months for overall survival. Cox proportional hazard regression models were constructed to estimate the hazard ratio (HR) for each potential prognostic factor. A nomogram incorporating the most important features was generated, and calibration curves were used to reduce overfitting bias. Decision curve analysis (DCA) was also applied to assess the value of the model, including the most important features. Two-sided tests were used to calculate probability values, and statistical significance was defined as $P < 0.05$.

Results

Demographic, clinical, and radiological information of patients who underwent surgical intervention due to hypertension-related ICH cases

A total of 232 qualified patients who underwent surgical intervention due to hypertension-related ICH cases were included in our study. Among them, 97 (41.8%) patients passed away within 3 months and were categorized as group A, while the remaining 135 (58.2%) cases showed relatively favorable prognoses and were assigned to group B. The distribution of gender and age between the deceased and surviving subgroups was comparable (all $P > 0.05$, Table 1).

Table 1: Clinical and radiological characteristics of patients who underwent surgical intervention due to hypertension-related ICH

Characteristics	Group A (OS ≤3 months)	Group B (OS >3 months)	*P*
Number of cases (*n*)	97	135	
Gender (*n*, %)			
Female	28 (28.9)	44 (32.6)	0.545
Male	69 (71.1)	91 (67.4)	
Age (mean, yrs)	59.1±12.8	60.1±13.2	0.829
Admission GCS	6.0±3.1	9.1±3.5	<0.001
Volume (mean, ml) of ICH	52.8±31.8	33.3±25.1	0.002
Location (*n*, %)			
Cerebral hemisphere	13 (13.4)	43 (31.9)	<0.001
Basal ganglia/thalamus	24 (24.7)	47 (34.8)	
Ventricle intrusion	51 (52.6)	34 (25.2)	
Infratentorial structure	9 (9.3)	11 (8.1)	
Obesity (*n*, %)			
Yes	15 (15.5)	31 (23.0)	0.158
No	82 (84.5)	104 (77.0)	
Hypertensive crisis (*n*, %)			
Yes	53 (54.6)	86 (63.7)	0.165
No	44 (45.4)	49 (36.3)	
Diabetes (*n*, %)			
Yes	9 (9.3)	19 (14.1)	0.269
No	88 (90.7)	116 (85.9)	
Time for surgery (median, hours)	3.7	3.5	0.763
Duration of ventilatory support (median, days)	8.5	3.5	0.001
Postoperative seizures (%)			
Yes	10 (10.3)	13 (8.9)	0.714
No	87 (89.7)	122 (91.1)	
Infection			
Yes	49 (50.5)	29 (21.5)	<0.001
No	48 (49.5)	106 (78.5)	
Cardiac failure (*n*, %)			
Yes	20 (20.6)	11 (8.1)	0.006
No	77 (79.4)	124 (91.9)	
eGFR (ml/min 1.73 m^2)			
Admission eGFR	91.9±45.1	108.1±45.7	<0.001
Postoperative eGFR	82.5±42.2	106.5±40.7	<0.001
3-day postoperative eGFR	73.5±44.7	111.5±46.6	<0.001
7-day postoperative eGFR	75.2±58.2	109.6±46.3	<0.001
3-day postoperative ABG			
FiO_2 (%)	44.6±13.1	41.7±11.0	0.073
pCO_2 (mmHg)	36.1±7.3	36.1±7.0	0.753
TCO_2 (mmHg)	24.1±4.0	25.9±3.4	<0.001
pH	7.41±0.01	7.45±0.04	<0.001
HCO_3^- (mmol/L)	22.7±4.3	24.8±3.3	<0.001
HCO_{3std} (mmol/L)	24.0±3.1	25.8±2.1	<0.001
BE (mmol/L)	-1.2±3.9	1.0±2.7	<0.001
BEecf (mmol/L)	-1.6±4.4	0.8±3.2	<0.001
Lactate (mmol/L)	2.0±1.1	1.4±0.5	<0.001

ICH, intracranial hemorrhage, GCS, Glasgow Coma Scale, eGFR, estimated glomerular filtration rate, ABG, arterial blood gas analysis, V-SIMV (volume-synchronized intermittent mandatory ventilation) or P-SIMV (pressure-synchronized intermittent mandatory ventilation) for sedated patients. For patients who were spontaneously breathing, we employed CPAP (continuous positive airway pressure) or PSV (pressure support ventilation), PH, pondus hydrogenii, BE, base excess, BEecf, extracellular fluid base excess, TCO_2, total partial pressure of carbon dioxide, HCO_{3std}^-, standard HCO_3^-

The prevalence of obesity (body mass index ≥28), diabetes, and hypertension crisis was also similar in both subgroups (all $P > 0.05$, Table 1).

However, patients with a bleak prognosis (OS <3 months) exhibited certain distinct characteristics compared to those with a more favorable prognosis. Specifically, the group A

cases had lower admission GCS scores (mean for group A and B cases: 6.0 ± 3.1 vs. 9.1 ± 3.5, $P < 0.001$), larger hematoma volumes (mean for group A and B cases: 52.8 ± 31.8 vs. 33.3 ± 25.1 ml, $P = 0.002$), a higher incidence of ventricular intrusion (52.6% vs. 25.2%, $P < 0.001$), infection (50.5% vs. 21.5%, $P < 0.001$), and a higher prevalence of cardiac failure (20.6% vs. 8.1%, $P = 0.006$).

Importantly, we observed a substantial difference in kidney function between these two subgroups. The admission eGFR for group A cases was significantly lower compared to group B cases (91.9 ± 45.1 vs. 108.1 ± 45.7 ml/min·1.73 m^2, $P < 0.001$). This finding suggests that a good reserve of kidney function may be crucial for the prognosis of hypertension-related ICH cases undergoing surgical intervention. Overall, these results indicate that factors such as lower GCS scores, larger hematoma volumes, ventricular intrusion, cardiac failure, and impaired kidney function are associated with poorer outcomes in patients who underwent surgical intervention due to hypertension-related ICH cases.

Distinct dynamic kidney function changes were observed in 3-month dead and alive cases

We collected eGFR data at four-time points in this case set, revealing distinct dynamic trends among the subgroups [Figure 2a and Table 1]. In group A, there was a substantial worsening of eGFR from admission to postoperative, 3-day postoperative, and 7-day postoperative time points (mean values: 91.9 ± 45.1, 82.5 ± 42.2, 73.5 ± 44.7, 75.2 ± 58.2 ml/min·1.73 m^2, respectively). In contrast, no significant change in eGFR was observed in group B (mean values: 108.1 ± 45.7, 106.5 ± 40.7, 111.5 ± 46.6, 109.6 ± 46.3 ml/min·1.73 m^2, respectively). These findings suggest that during the treatment of patients who underwent surgical intervention due to hypertension-related ICH, certain treatments may have adverse effects on kidney function, particularly in patients with limited reserves. Furthermore, we performed ROC analysis to evaluate the prognostic significance of eGFR at different time points. The results revealed that the eGFR at the 3-day postoperative time point had the highest prognostic predictive value in this case set (AUC for admission, postoperative, 3-day postoperative, and 7-day postoperative: 0.617, 0.675, 0.737, 0.730, Figure 2b).

Based on these findings, we utilized the 3-day postoperative eGFR instead of the admission eGFR for subsequent survival analysis, as it demonstrated superior prognostic accuracy.

Disturbed acid-base equilibrium was closely associated with insufficient kidney function

The kidney plays a vital role in maintaining acid-base equilibrium by regulating the secretion of hydrogen ions (H^+). Given the substantial difference in 3-day eGFR between groups A and B, we further investigated the acid-base equilibrium balance in these two subgroups. We observed imbalances in several acid-base parameters, indicating disrupted equilibrium.

In patients with a bleak prognosis (3-month dead subgroup), we observed lower pH values (mean for dead and alive patients:

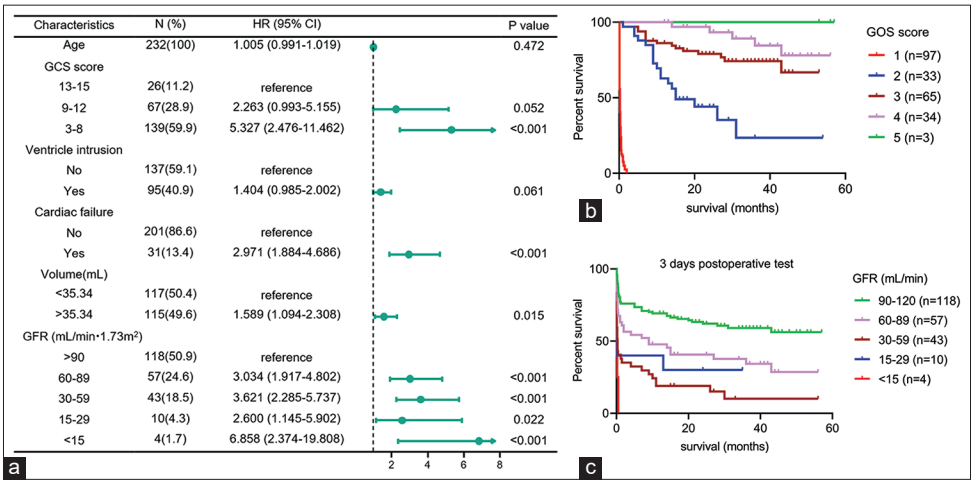

Figure 2: Patients were divided into group A (OS ≤3 months) and group B (OS >3 months) to determine factors correlative with survival. (a) The eGFR substantially worsened in group A (mean for admission, postoperative, 3-day postoperative, and 7-day postoperative: 91.9 ± 45.1, 82.5 ± 42.2, 73.5 ± 44.7, 75.2 ± 58.2 ml/min 1.73 m^2, respectively), while no significant change was observed in group B (mean for admission, postoperative, 3-day postoperative, and 7-day postoperative: 108.1 ± 45.7, 106.5 ± 40.7, 111.5 ± 46.6, 109.6 ± 46.3 ml/min 1.73 m^2, respectively). (b) ROC curves revealed that the 3-day eGFR was the best prognostic predictor in this case set (AUC for enrollment, postoperative, 3-day postoperative, and 7-day postoperative: 0.617, 0.675, 0.737, 0.730). c-f, Lower PH (group A and B, 7.41 ± 0.01 vs. 7.45 ± 0.04, $P < 0.001$, c-a), higher lactate (2.0 ± 1.1 vs. 1.4 ± 0.5 mmol/L, $P < 0.001$, c-b), lower BE (−1.2 ± 3.9 vs. 1.0 ± 2.7 mmol/L, $P < 0.001$, d-a) and BEecf (−1.6 ± 4.4 vs. 0.8 ± 3.2 mmol/L, $P < 0.001$, d-b), lower TCO2 (24.1 ± 4.0 vs. 25.9 ± 3.4 mmHg, $P < 0.001$, e-b) instead of pCO2 (36.1 ± 7.3 vs. 36.1 ± 7.0 mmHg, $P = 0.753$, e-a), and lower HCO3$^-$ (22.7 ± 4.3 vs. 24.8 ± 3.3 mmol/L, $P < 0.001$, f-a) and HCO_3std^- (24.0 ± 3.1 vs. 25.8 ± 2.1 mmol/L, $P < 0.001$, f-b) in group A revealed comprehensive out-of-regulation for acid-base equilibrium, which could intensify the brittle homeostasis and lead to death. Abbreviations: eGFR, estimated glomerular filtration rate, PH, pondus hydrogenii, BE, base excess, BEecf, extracellular fluid base excess, TCO2, total partial pressure of carbon dioxide, $HCO3_{std}^-$, standard HCO3$^-$

7.41 ± 0.01 vs. 7.45 ± 0.04, $P < 0.001$, Figure 2c-a), higher lactate levels (2.0 ± 1.1 vs. 1.4 ± 0.5 mmol/L, $P < 0.001$, Figure 2c-b), lower base excess (BE) levels (-1.2 ± 3.9 vs. 1.0 ± 2.7 mmol/L, $P < 0.001$, Figure 2d-a) and extracellular fluid base excess (BEecf) levels (-1.6 ± 4.4 vs. 0.8 ± 3.2 mmol/L, $P < 0.001$, Figure 2d-b), lower total partial pressure of carbon dioxide (TCO_2) levels (24.1 ± 4.0 vs. 25.9 ± 3.4 mmHg, $P < 0.001$, Figure 2e-b) but similar partial pressure of carbon dioxide (pCO_2) levels (36.1 ± 7.3 vs. 36.1 ± 7.0 mmHg, $P = 0.753$, Figure 2e-a), as well as lower bicarbonate ($HCO3^-$) levels (22.7 ± 4.3 vs. 24.8 ± 3.3 mmol/L, $P < 0.001$, Figure 2f-a) and standard bicarbonate ($HCO3std^-$) levels (24.0 ± 3.1 vs. 25.8 ± 2.1 mmol/L, $P < 0.001$, Figure 2f-b).

These findings collectively indicate comprehensive dysregulation of acid-base equilibrium in the 3-month dead subgroup. Such imbalances can further disrupt homeostasis and potentially contribute to fatal outcomes.

Survival analysis demonstrated the hierarchy of kidney function as an independent prognosis risk factor

With a median follow-up period of 15.0 months, a total of 137 (59.1%) ICH cases in our study population had succumbed, resulting in a median OS of 10.0 months. Several adverse factors were identified as predictors of survival, including advanced age, low GCS score (3–8), ventricle intrusion of hematomas, cardiac failure, long duration of ventilatory support (>6 days), infection, larger hematoma volume (>35.34 ml), and lower 3-day postoperative GFR. These findings are summarized in Table 2. In the multivariate analysis, low GCS score, infection, cardiac failure, larger hematoma volume, and lower 3-day postoperative GFR remained significant predictors of survival [Table 2 and Figure 3a].

Although the Glasgow Outcome Scale (GOS) scores were effective in predicting hierarchical outcomes for this case set [Figure 3b], the lag in GOS assessment made it less ideal as a prognostic factor. Instead, we employed GCS scores, which provided a more timely and precise prediction. Additionally, the 3-day postoperative eGFR demonstrated efficient predictive capability for outcomes in hypertensive ICH cases, and a clear inverse correlation was observed between kidney function stage and OS [Figure 3c].

To further enhance prognostic prediction, we developed a nomogram model that incorporated GCS score, cardiac failure, hematoma volume, infection, and lower 3-day postoperative eGFR. The nomogram highlighted the crucial importance of the 3-day eGFR in predicting OS [Figure 4a]. By assigning scores to each parameter, we were able to accurately assess the 1-year probabilities. Calibration plots demonstrated good agreement between the observed fraction survival probability and the nomogram-estimated survival probability [Figure 4b]. Furthermore, the DCA confirmed the predictive capacity of the model, affirming the significance of all the key characteristics [Figure 4c].

Discussion

The acute phase of hypertensive ICH is often accompanied by kidney failure or the worsening of existing compromised renal reserves,[18,19] especially for surgically treated cases. The development of oliguria and anuria due to kidney failure can ultimately lead to refractory and potentially fatal fluid and electrolyte imbalances, as well as disturbances in acid-base equilibrium.[20] Therefore, recognizing the critical role of kidney function in managing patients who undergo surgical intervention for hypertension-related ICH is crucial

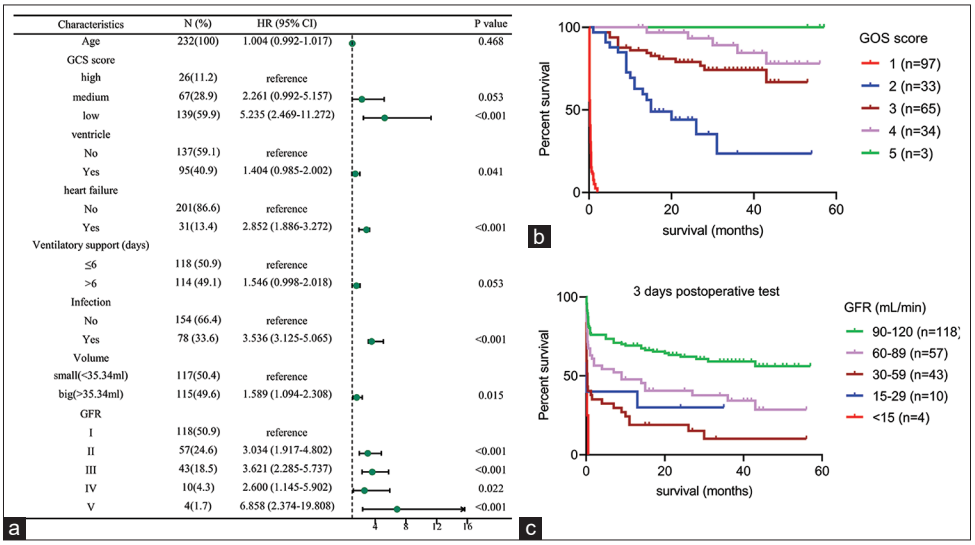

Figure 3: Survival analysis for hypertensive ICH cases who underwent surgical intervention. (a) the low GCS score, ventricle intrusion of the hematoma, heart failure, infection, larger hematoma volume, and lower 3-day postoperative eGFR were independent risk factors for overall survival in multivariate analysis. (b) Though GOS scores could effectively and precisely predict hierarchal outcomes for this set [Figure 2b], the hysteresis of GOS assessment rendered it an unideal factor to predict prognosis and we employed GCS scores instead. (c) the 3-day postoperative eGFR could also efficiently predict outcomes for hypertensive ICH cases and an inverse correlation was observed between kidney function stage and OS

Table 2: Cox hazards regression analysis for patients who underwent surgery due to hypertension-related ICH of OS

Characteristics	Total (*n*,%)	Univariate analysis		Multivariate analysis	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Age	232 (100)	1.015 (1.002–1.029)	0.028	1.004 (0.992–1.017)	0.468
Gender	232 (100)				
Male	160 (69.0)	Reference			
Female	72 (31.0)	0.950 (0.662–1.363)	0.779		
GCS score	232 (100)				
13–15	26 (11.2)	Reference			
9–12	67 (28.9)	1.358 (0.612–3.014)	0.452	2.261 (0.992–5.157)	0.053
3–8	139 (59.9)	4.179 (2.027–8.616)	<0.001	5.235 (2.469–11.272)	<0.001
Ventricle intrusion	232 (100)				
No	147 (63.4)	Reference			
Yes	85 (36.7)	1.926 (1.374–2.700)	<0.001	1.404 (0.985–2.002)	0.041
Obesity	232 (100)				
Yes	46 (19.8)	Reference			
No	186 (80.2)	1.395 (0.884–2.202)	0.153		
Hypertension crisis	232 (100)				
No	139 (59.9)	Reference			
Yes	93 (40.1)	1.280 (0.913–1.795)	0.153		
Diabetes	232 (100)				
No	204 (87.9)	Reference			
Yes	28 (12.1)	0.818 (0.479–1.399)	0.464		
Cardiac failure	232 (100)				
No	201 (86.7)	Reference			
Yes	31 (13.3)	2.258 (1.470–3.469)	<0.001	2.852 (1.886–3.272)	<0.001
Duration of ventilatory support (days)					
≤6	118 (50.9)	Reference			
>6	114 (49.1)	1.571 (1.116–2.212)	<0.010	1.546 (0.998–2.018)	0.053
Infection					
No	154 (66.4)	Reference			
Yes	78 (33.6)	3.689 (2.156–5.278)	<0.001	3.536 (3.125–5.065)	<0.001
Hematoma volume (ml)	232 (100)				
<35.34	117 (50.4)	Reference			
>35.34	115 (49.6)	2.594 (1.827–3.682)	<0.001	1.572 (1.091–2.411)	0.017
3-day eGFR (ml/min 1.73 m^2)	232 (100)				
≥90	118 (50.9)	Reference			
60–89	57 (24.6)	2.640 (1.735–4.016)	<0.001	3.001 (1.324–4.300)	<0.001
30–59	43 (18.5)	4.518 (2.927–6.973)	<0.001	3.263 (2.162–4.213)	<0.001
15–29	10 (4.3)	3.193 (1.439–7.085)	0.004	2.631 (1.231–5.065)	0.031
<15	4 (1.7)	7.718 (2.733–21.793)	<0.001	5.586 (2.651–11.256)	<0.001

ICH, intracranial hemorrhage

for guiding treatment planning. Our study results indicate that preserving adequate kidney function is of paramount importance in dealing with the acute phase of ICH for surgically treated patients. It is important to note that the treatment of ICH itself can exacerbate kidney dysfunction or even lead to renal failure, resulting in unfavorable outcomes. Therefore, protecting kidney function should be carefully considered to promote more favorable outcomes in surgically treated patients.

By identifying the significant association between kidney function and prognosis, our study highlights the need to incorporate renal assessment and preservation strategies into the management of patients with surgically treated hypertension-related ICH. Strategies aimed at minimizing the potential negative impact of ICH treatments on kidney function, such as adjusting dosages, utilizing alternative medications, or implementing supportive measures, should be considered. Additionally, close monitoring of renal function parameters, including GFR and acid-base balance, should be an integral part of the clinical management plan.

Further research is warranted to explore the underlying mechanisms linking kidney function and ICH outcomes in surgically treated patients. Understanding the intricate interplay between renal dysfunction and the pathophysiology of ICH could potentially lead to the development of targeted interventions and improved therapeutic strategies.

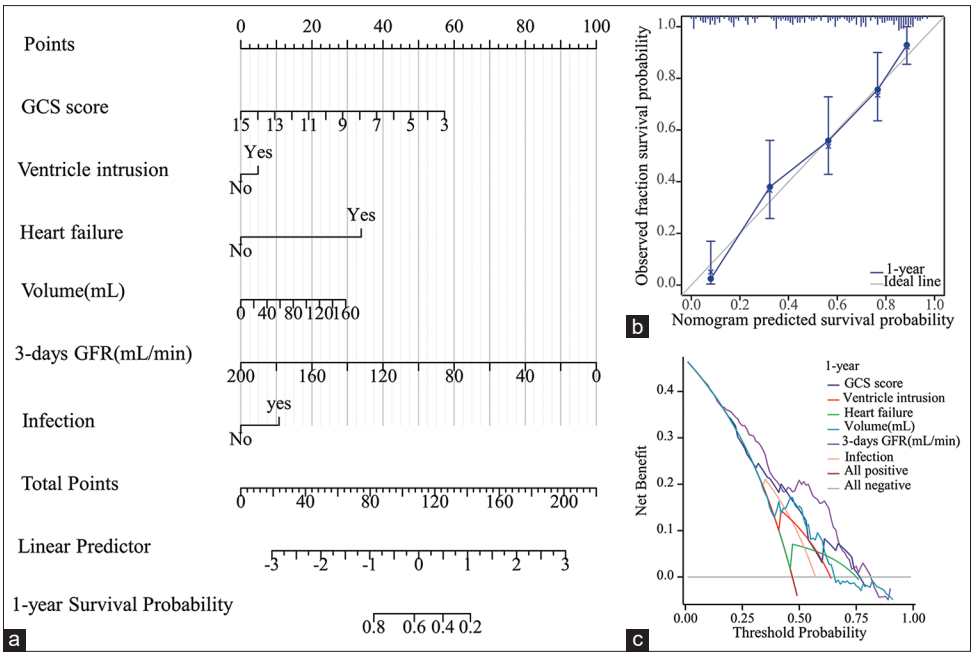

Figure 4: Nomogram model for predicting OS in hypertensive ICH cases who underwent surgical intervention. (a) A nomogram model incorporating GCS score, ventricle intrusion of hematoma, heart failure, hematoma volume, lower 3-day postoperative eGFR, and infection to assess survival probability and the nomogram showed the vital importance of 3-day eGFR in predicting OS (b) calibration plots graphically showed good agreement between the observed fraction survival probability and the nomogram-estimated survival probability. (c) The DCA analysis assessed the model endowing all the crucial characteristics with satisfying predicting capacity

By prioritizing the preservation of kidney function in the management of surgically treated hypertension-related ICH, we can strive for better patient outcomes and a more comprehensive approach to care.

Dehydration treatment, particularly the use of mannitol, plays a crucial role in reducing cerebral edema caused by hematomas.[21,22] However, it is important to recognize that mannitol can have adverse effects on kidney function.[23,24] Our study revealed a persistent decline in eGFR among patients with poor prognosis, indicating a correlation between mannitol usage and kidney function deterioration. High doses of mannitol can lead to constriction of the glomerular arterioles, resulting in reduced renal blood flow and subsequent kidney dysfunction or failure.[23,24] It is acknowledged that mannitol can cause osmotic diuresis, which may result in a temporary decrease in eGFR. This diuretic effect can potentially lead to an acute decline in renal function. Moreover, mannitol has been associated with other renal effects, such as alterations in tubular function and electrolyte imbalances. These factors suggest a plausible relationship between mannitol administration and reduced eGFR in our study population. Therefore, careful monitoring of kidney function is essential during the treatment of ICH. Consideration should be given to reducing or discontinuing mannitol administration, and alternative options such as furosemide or glycerin fructose may be considered to address cerebral edema.

Patients with diabetes often experience structural changes in the glomerulus due to long-term hyperglycemia and insulin hyposecretion.[25-28] These changes include a reduction in heparan sulfate glycoproteins in the basement membrane and a deficiency of negative charges, leading to impaired kidney function.[28] In our study, although the number of patients with diabetes was limited (27/232, 11.6%), it is important to carefully monitor and manage blood glucose levels to promote wound healing and protect kidney function in these individuals.

Advanced age is frequently accompanied by comorbidities such as hypertension, diabetes, and cardiac insufficiency.[29] The compensatory capacity of elderly patients is often compromised due to aging and the cumulative effects of these diseases. Consequently, these factors contribute to acute kidney failure and poorer prognosis in surgically treated ICH patients. Univariate analysis revealed that age was a risk factor for poor prognosis, highlighting the need for increased attention and individualized treatment protocols for these patients.

A significant portion of the patients in our study presented with surgically treated hypertensive ICH and a deep coma status (GCS score ≤8) (54.7%, 127/232). This subgroup experienced more disease manifestations, including larger hemorrhage volumes, ventricle intrusion, and advanced age. The sudden and massive intracranial bleeding directly leads to increased intracranial pressure and profound neuroendocrine changes, resulting in vasoconstriction and inadequate renal blood perfusion. Additionally, factors such as intractable vomiting, gastrointestinal bleeding, insufficient fluid intake, and the use of dehydrating agents further exacerbate blood volume depletion and can ultimately lead to circulatory

failure.[30] These pathological changes collectively contribute to the compromised renal blood supply. Moreover, the dose of mannitol usage positively correlates with the severity of ICH, indicating a more pronounced impact on kidney function in patients with lower GCS scores.

Furthermore, we identified cardiac failure, larger hematoma volume, and ventricle intrusion as independent adverse factors for overall survival. The neuroendocrine and circulatory alterations associated with hypertensive ICH increase the risk of cardiovascular events, particularly in patients with insufficient functional reserves. Larger hematoma volume and ventricle intrusion can lead to life-threatening cerebral herniation, acute obstructive hydrocephalus, and delayed vasospasm, ultimately resulting in respiratory and circulatory failure.[30-32] Therefore, protecting cardiac function is crucial in the context of surgically treated hypertensive ICH to enhance patient survival.

There are limitations to consider in our study, primarily due to its retrospective design and single-center nature, which introduce the possibility of selection bias. Additionally, the variation in post-discharge rehabilitation and supportive care provided to the patients may have influenced survival outcomes. Factors such as blood pressure control, timing of craniectomy, duration of hospital stay, duration of ventilatory support, and occurrence of postoperative seizures can influence the outcomes of patients. Despite these limitations, our study provides valuable insights into the assessment of kidney function in patients with hypertensive ICH and highlights impaired renal function as an adverse prognostic factor. Further research is warranted.

Conclusion

For patients with hypertensive intracerebral hemorrhage (ICH), the protection of kidney function is of paramount importance in the pursuit of favorable prognoses. Impaired 3-day postoperative glomerular filtration rate (eGFR) was identified as an independent risk factor for overall survival. Moreover, the use of furosemide or glycerin fructose as alternatives to mannitol can safely lower intracranial pressure and alleviate cerebral edema. By prioritizing the preservation of kidney function and implementing appropriate treatment strategies, healthcare professionals can contribute to improving the prognoses of patients with hypertensive ICH.

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Authors' contributions

Literature search, study design, data collection, data interpretation, writing: Jian Wang, Rui Wang, Hu Qin, Lei Zuo

Data availability

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Xinjiang Medical University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Written informed consent was waived by the Institutional Review Board.

Abbreviations

ICH, intracranial hemorrhage, GCS, Glasgow Coma Scale, GOS, Glasgow Outcome Scale, OS, overall survival, eGFR, estimated glomerular filtration rate, ABG, arterial blood gas analysis, PH, pondus hydrogenii, BE, base excess, BEecf, extracellular fluid base excess, TCO_2, total partial pressure of carbon dioxide, $HCO3_{std}^-$, standard $HCO3^-$

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Conflicts of interest

There are no conflicts of interest.

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