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ORIGINAL ARTICLE

Risk factors for acute kidney injury after intracranial hemorrhage

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Abstract

OBJECTIVE: This study investigated the risk factors for acute kidney injury (AKI) occurrence in patients with spontaneous intracerebral hemorrhage.
METHODS: The clinical data of patients with spontaneous intracerebral hemorrhage who were hospitalized in the Department of Intensive Care Medicine of Mingguang People's Hospital from January 2016 to August 2020 were retrospectively analyzed. The patients were divided into AKI group and non-AKI group according to whether the patient had secondary AKI, and the clinical data of the two groups were compared. Logistic regression analysis was used to screen out the risk factors for secondary AKI in patients with spontaneous intracerebral hemorrhage.
RESULTS: Three hundred thirty-seven patients were included in this study, whereby 186 males (55.2%) and 151 females (44.8%). A total of 65 patients developed AKI, of whom 44 patients were (67.69%) in stage 1, 12 patients (18.46%) in stage 2, and 9 patients (13.85%) in stage 3. Univariate logistic regression analysis showed that Acute Physiology, Age and Chronic Health Evaluation (APACHE II score), diabetes, chronic kidney disease, fasting blood glucose level and amount of mannitol used were risk factors for AKI in patients with intracerebral hemorrhage. Multivariate logistic regression analysis showed APACHE II score (OR: 1.846, 95% CI: 1.319 to 2.585, $p<0.001$), diabetes (OR: 3.609, 95% CI: 1.596 to 8.163, $p=0.002$) and amount of mannitol use (OR: 3.495, 95% CI: 1.910~3.395, $p<0.001$) are the independent risk factors for AKI after intracranial hemorrhage.
CONCLUSION: In summary, APACHE II score, diabetes, and total mannitol use are independent risk factors for AKI in patients with spontaneous intracerebral hemorrhage. It is necessary to monitor renal function frequently in patients with high APACHE II scores and control the amount of mannitol administrated in the prevention of AKI after intracranial hemorrhage. The intervention of the above

factors is expected to reduce the risk of secondary AKI.

Abbreviations:

AKI	- acute kidney injury
APACHE II score	- Acute Physiology, Age and Chronic Health Evaluation
SIH	- spontaneous intracerebral hemorrhage
SAH	- subarachnoid hemorrhage
SCr	- serum creatinine
KIDIGO	- kidney disease improving global outcomes
CHAID	- Chi-squared automatic interaction detection
GCS	- Glasgow Coma Score
ICU	- intensive care unit
HHS	- hyperosmolar hyperglycemic state.

INTRODUCTION

Spontaneous intracerebral hemorrhage (SIH) is a critical and severe disease seriously damaging human health, with high mortality and disability rates (Chinese Society of Neurology & Chinese Stroke Societ, 2019). After intracerebral hemorrhage, various clinical complications, such as gastrointestinal hemorrhage, water and electrolyte disturbance, and acute kidney injury (AKI), may occur due to the damage to the central autonomic nerve, the disturbance of neuro-humoral regulation, and the use of various drugs (Zhang, 2005).

Stroke is a common disease with a high mortality and an extremely high disability rate (An *et al.* 2017; Fu *et al.* 2013). A previous study has shown that secondary AKI is associated with higher mortality or morbidity three months after onset in patients with hemorrhagic stroke (Qureshi *et al.* 2020). Nevertheless, a previous study indicated that acid-base imbalance, electrolyte metabolism disorder, and volume overload caused by AKI are reversible (Lazzeri *et al.* 2018). Therefore, identifying the risk factors and incipient signs of AKI in patients with cerebral hemorrhage may help prevent the occurrence of AKI and reduce the damages caused by AKI. In this study, we collected the clinical data of patients with spontaneous intracerebral hemorrhage and divided the patients into AKI group and non-AKI group according to whether the patient developed secondary AKI. The potential risk factors for AKI after intracranial hemorrhage were examined in order to provide reference for clinicians.

METHODS

Study Design

This is a retrospective study involving 337 patients with spontaneous intracerebral hemorrhage (SIH) at Mingguang People's Hospital. The patients were divided into AKI group (n=65) and Non-AKI group (n=272) according to whether the patient developed secondary AKI. The clinical parameters of the patients were analyzed to assess potential risk factors for secondary AKI after intracranial hemorrhage. This study was approved by the medical research ethics committee of Mingguang People's Hospital (Approval No. 2015-0003645).

Subjects

Patients with SIH who were hospitalized in the Department of Intensive Care Medicine in Mingguang People's Hospital from January 2016 to August 2020 were selected for a retrospective study. Inclusion criteria: diagnoses of spontaneous acute cerebral hemorrhage by clinical manifestation analyses and imaging examinations, including subarachnoid hemorrhage (SAH), parenchymal hemorrhage, and primary ventricular hemorrhage. Exclusion criteria: hospitalization time less than 48 hours without serum creatinine re-examination; main diagnosis of this hospitalization not being cerebral hemorrhage.

Patient data records

1. The clinical data of cerebral hemorrhage patients were collected, including basic characteristics, medical history, the evaluation after admission, pre-AKI vital signs, laboratory examination changes, and clinical therapeutic intervention. The patients were divided into AKI group (n=65) and Non-AKI group (n=272). The clinical data of the two groups were compared, and the risk factors for secondary AKI in patients with cerebral hemorrhage were identified by Logistic regression analysis.
2. Diagnostic criteria for AKI: Increase in serum creatinine (SCr) by over 26.5umol/L within 48 hours; or increase in SCr to over 1.5 times the baseline within seven days. The diagnostic criteria for AKI were defined according to the creatinine criteria classified by the Kidney Disease Improving Global Outcomes (KIDIGO) (Khwaja, 2012).
3. Disease severity assessment: The Acute Physiology, Age and Chronic Health Evaluation (APACHE) II score and Glasgow Coma Score (GCS) were used to evaluate the severity of the disease and AKI conditions. The details of the parameters used in (APACHE) II score and Glasgow Coma Score (GCS) were summarized in Supplementary Table.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 statistical software. The normally distributed measurements were expressed as mean ± standard deviation, and t-test was used to compare groups; the non-normally distributed measurements were expressed with median and quartiles, and the Wilcoxon rank sum test was used to compare groups. Enumeration data were expressed as frequencies and rates, and comparisons between groups were performed using chi-square test or Fisher's exact test. Logistic regression was used for multivariate analysis. Univariate analysis was performed on the variables, and then the variables with statistical significance in univariate analyses were included in the multivariate analysis for model fitting. In Logistic regression analysis, the stratification of variables was analyzed

Tab. 1. Patient demography in AKI group and non-AKI group

Groups	AKI group (n=65)	Non-AKI group (n=272)	X^2/t/Z value	*p* value
Gender [male (%)]	32 (49.23)	154 (56.61)	1.158	0.282
Age	68 (52,73)	64 (55,72)	-0.845	0.398
APACHE II	17.78±4.97	15.00±4.91	4.097	<0.001
GCS	7 (5,10)	9 (6,12)	-3.305	0.001
Length of stay in ICU (hours)	247.33 (135.45,456.50)	219.55 (144.63,353.12)	-1.257	0.209
Complication	59	231		
Hypertension [n (%)]	53 (81.54)	228 (83.82)	0.198	0.657
Diabetes [n (%)]	15 (23.08)	20 (7.35)	13.94	<0.001
Heart disease [n (%)]	4 (6.15)	12 (4.41)	—	0.523
Chronic liver disease [n (%)]	2 (3.08)	2 (0.74)	—	0.169
Chronic kidney disease [n (%)]	7 (10.77)	3 (1.10)	17.03	<0.001
Chronic respiratory disease [n (%)]	9 (13.85)	22 (8.09)	2.082	0.149
Admission vital signs				
Body temperature (°C)	36.50 (36.30,36.70)	36.50 (36.20,36.80)	-0.339	0.735
Heart rate (bpm)	79.00 (68.50,93.50)	75.00 (66.00,87.00)	-1.4	0.162
Respiration rate	20.00 (17.00,22.00)	19.00 (17.00,21.00)	-0.406	0.684
MAP (mmHg)	124.79±24.18	126.61±19.44	-0.646	0.519
Admission laboratory examination				
BUN (mmol/L)	5.46 (3.60,7.05)	5.04 (3.93,6.38)	-0.918	0.359
Scr (μmol/L)	55.40 (43.25,80.65)	56.5 (45.15,70.15)	-0.157	0.875
GLU (mmol/L)	9.55±3.54	8.23±2.51	3.48	0.001
K^+ (mmol/L)	3.28 (3.00,3.82)	3.5 (3.11,3.8)	-1.664	0.096
Na^+ (mmol/L)	140 (136.08,142.88)	139 (136.82,141.30)	-0.893	0.372
Hb (g/L)	130 (94.75,144.75)	131 (116,147)	-0.457	0.648

AKI: acute kidney injury; APACHE II: Acute Physiology, Age and Chronic Health Evaluation II; GCS: Glasgow Coma Score; ICU: Intensive care unit; MAP: Mean Arterial Pressure; BUN: Blood Urea Nitrogen; Scr: serum creatinine; GLU: fasting blood glucose level; Hb: Hemoglobin.

by the Exhaustive CHAID (Chi-squared Automatic Interaction Detection) model. In order to prevent over-fitting of the classification tree model, the significance test levels of model parameter splitting and merging were both 0.05. The minimum sample sizes in parent node (upper node) and child node (lower node) were set as 50 and 20.

RESULTS

Patients demography, diseases, and AKI status

Three hundred thirty-seven patients were included in this study, whereby 186 males (55.19%) and 151 females (44.81%). The patients were divided into AKI group (n=65) and Non-AKI group (n=272) according to whether the patient developed secondary AKI. Of them, 211 patients (62.61%) received improved outcomes, 10 patients died (2.97%), and 116 patients (34.42%) were discharged voluntarily. The average onset time of the AKI group was 95.87 hours, and the median was 96.61 hours. AKI group showed a significantly higher APACHE II score (p<0.001) but a lower GCS score (p=0.001) (Table 1). There were 59 (90.77%) AKI patients with at least one chronic comorbidity. The percentage of diabetes was significantly higher in AKI group compared to non-AKI group (p<0.001), while there was no significant difference in hypertension, coronary heart disease, chronic liver disease, or chronic respiratory disease between two groups (Table 1, p>0.05). In addition, there was no significant difference between the two groups in basic vital signs at admission (p>0.05), but the fasting blood glucose level (after 18 hour fasting) in AKI group was significantly higher than that of non-AKI group (Table 1, p=0.001). As expected, the percentage of chronic kidney disease was significantly higher in AKI group (Table 1, p<0.001).

Therapeutic intervention in AKI and non-AKI patients

Both groups were given symptomatic treatments such as blood pressure control and dehydration to lower intracranial pressure after admission. The therapeutic interventions in both groups were recorded, including

Tab. 2. Therapeutic intervention in AKI group and non-AKI group

Groups	AKI group(n=65)	Non-AKI group(n=272)	X^2/t/Z value	*p* value
surgery [n (%)]	29(44.62)	139(51.10)	0.883	0.347
Mechanical Ventilation [h]	18.66 (0.00,112.08)	1.17 (0.00,45.96)	-1.570	0.116
Norvancomycin [n (%)]	2 (3.08)	21 (7.72)	—	0.273
Contrast agent [n (%)]	3 (4.62)	27 (9.93)	1.825	0.177
Norepinephrine [n (%)]	12 (18.46)	31 (11.40)	2.352	0.125
Total Mannitol (g)	1325 (640,1613)	1259 (580,1495)	-4.303	<0.001
Length of Mannitol application (d)	9 (5.50,15.50)	12.50 (8.00,17.00)	-5.09	<0.001
Highest single-day mannitol application (g)	150.00 (120.00,160.00)	120.00 (120.00,160.00)	-0.97	0.332
Glycerol fructose [n (%)]	31 (47.69)	163 (59.93)	3.215	0.073
Furosemide [n (%)]	20 (30.77)	76 (27.94)	0.206	0.65
human albumin [n (%)]	14 (21.54)	56 (20.59)	0.029	0.865

AKI: acute kidney injury

surgery, mechanical ventilation, norvancomycin, contrast agent, norepinephrine, total mannitol dosage, length of mannitol application, highest single-day mannitol application, glycerol fructose, furosemide and human albumin (Table 2). Statistical comparison of different therapeutics between the two groups revealed that patients who developed AKI had been administered higher doses of mannitol than those who did not develop AKI (p<0.001) whereas patients who did not develop AKI had been given longer duration of mannitol (Table 2, p<0.001). However, there was no statistical difference in other therapeutics administrated.

Univariate logistic regression analysis of the association of parameters with AKI status

The following variables were stratified for regression analysis: APACHE II score, GCS score, fasting blood glucose level, total mannitol dosage, serum potassium level, and days of mannitol use between AKI group (n=65) and Non-AKI group (n=272). The APACHE II score was further divided into four levels: ≤14; 15-19; 20-24; ≥25. GCS score was divided into three levels: ≤7; 8-10; ≥11. Fasting blood glucose level (mmol/L) was divided into four levels: ≥11.2; 7.8-11.1; 6.2-7.7; 3.9-6.1. The serum potassium level (mmol/L) was divided into three levels: ≤3.5; 3.6-5.5; ≥5.6. The GCS score was divided into three levels: ≤7; 8-10; ≥11. The total dosage of mannitol (g) was divided into two levels: ≤1012.5; ≥1012.6. The length of mannitol use was divided into three levels: ≤9; 10-17; ≥18.

Univariate Logistic regression analysis showed that APACHE II score, diabetes, chronic kidney disease, fasting blood glucose level, and total mannitol dosage were closely associated with AKI group (Table 3, p<0.001), indicating that they may serve as risk factors for AKI patients with cerebral hemorrhage.

Tab. 3. Univariate regression analysis of different parameters with AKI status

	p value	Odds Ratio	95%CI
APACHE II	<0.001	1.809	1.332 - 2.457
GCS	0.244	0.666	0.336 - 1.319
Diabetes	<0.001	3.780	1.813 - 7.883
Chronic kidney disease	0.001	10.822	2.717 - 43.10
GLU	0.018	1.473	1.069 - 2.030
K^+	0.885	1.038	0.626 - 1.721
Total Mannitol	<0.001	3.953	2.230 - 7.007
Length of Mannitol application (d)	0.084	0.619	0.357 - 10.67
human albumin	0.865	1.059	0.547 - 2.049

APACHE II: Acute Physiology, Age and Chronic Health Evaluation II; GCS: Glasgow Coma Score; GLU: fasting blood glucose level.

Tab. 4. Multivariate logistic regression analysis of different parameters with AKI status

	p value	Odds Ratio	95%CI
APACHE II	<0.001	1.846	1.319 - 2.585
Diabetes	0.002	3.609	1.596 - 8.163
Total Mannitol	<0.001	3.495	1.910 - 3.395

APACHE II: Acute Physiology, Age and Chronic Health Evaluation II

Multivariate logistic regression analysis the association between parameters with AKI status

Multivariate logistic regression analysis between AKI group (n=65) and Non-AKI group (n=272) indicated that APACHE II score (OR: 1.846, 95% CI: 1.319-2.585, $p<0.001$), combined diabetes (OR: 3.609, 95% CI: 1.596-80163, $p=0.002$), and total mannitol dosage (OR: 3.495, 95% CI: 1.910-3.395, $p<0.001$) were independent risk factors for AKI in patients with cerebral hemorrhage (Table 4).

DISCUSSION

This study selected patients with intracranial hemorrhage as research subjects to analyze the risk factors for AKI. An excessively high APACHE II score indicates a poor prognosis in patients with severe intracranial hemorrhage (Huang *et al.* 2016). A previous report indicated that high APACHE II scores are associated with the occurrence of AKI (Søvik *et al.* 2019). The APACHE II scoring standard includes options such as serum creatinine value, acute renal failure, etc. The score is positively correlated with the APACHE II score, which may be the reason why the APACHE II score can indicate AKI. In addition, the APACHE II score is an index to evaluate the overall condition and severity of the ICU (intensive care unit) patients. The higher the APACHE II score, the more critical the patient's condition, the higher the risk factors associated with AKI, and the higher the risk of AKI.

Some complications of diabetes, such as chronic renal insufficiency, cardiovascular disease, and heart failure, as well as medications, make diabetic patients more likely to develop AKI (Advani, 2020). The pathogenesis of diabetic nephropathy is multifactorial. One study showed increased apoptosis in proximal tubule cells when exposed to high glucose after ATP depletion or severe hypoxia; its researcher identified the activation of an apoptotic endogenous pathway characterized by mitochondrial Bax protein accumulation and cytochrome c release and suggested that hyperglycemia sensitizes mitochondria to Bax attack, cytochrome c release, and apoptosis during acute injury, leading to mitochondrial fragmentation (Peng *et al.* 2015). Acute intracranial hemorrhage as stress can trigger a transient increase in blood glucose, and the blood glucose level in diabetic patients is more susceptible. Hyperosmolar hyperglycemic state (HHS) is often accompanied by dehydration and predisposes patients to suffer AKI. HHS itself may be accompanied by rhabdomyolysis, further increasing the propensity to develop AKI.

Mannitol is the most commonly used dehydrating agent in neurosurgery. Although previous animal study has shown that mannitol can improve the symptoms of AKI, it has not shown efficacy in human trials (O'Kane *et al.* 2019). A systematic review concluded that there is insufficient evidence for the perioperative use of mannitol to prevent AKI (Waskowski *et al.* 2019). Results of a double-blind randomized trial in patients with partial nephrectomy showed that patients who received mannitol had no better renal function six months after surgery than patients who did not receive mannitol (Spaliviero *et al.* 2018). In this study, the total dosage of mannitol was a risk factor for AKI (OR=3.495), which means that the total dosage of mannitol is positively correlated with the occurrence of AKI, and similar outcome was observed by Xu *et al.* (2010). Possible reasons for AKI caused by mannitol include: (1) Large doses of mannitol can lead to increased intratubular osmotic pressure, dehydration and necrosis of renal tubular epithelial cells; (2) The rapid entry of a large amount of mannitol into the blood circulation can increase the flow of the distal convoluted tubules, cause tube-globular feedback, and significantly reduce the glomerular filtration rate; and (3) After excessive diuresis, the patient's blood volume decreased, resulting in prerenal oliguria and AKI.

A previous report found that high-dose contrast agents (≥180 mL) are a risk factor for contrast-induced AKI and an independent risk factor for death in patients with contrast-induced AKI (Li *et al.* 2013). In this study, the use of contrast media was not suggested as a risk factor for AKI, which may be due to the lower usage of contrast media by patients with intracerebral hemorrhage. With the gradual development of interventional surgery and the increased use of contrast agents, positive results may occur, which needs to be confirmed by further statistical studies.

This study has certain limitations. First, the study is a single-center study, which cannot represent all patients with intracranial hemorrhage in terms of patient data and quality; secondly, the treatment process of patients with intracranial hemorrhage is complicated, and all factors affecting renal function cannot be included in the study; finally, the diagnosis of AKI was based on the

SCr criteria in the KIDGO guidelines, but due to insufficient continuous statistics on urine volumes, it was not included in the diagnostic criteria, which led to an underestimation of AKI incidence.

In conclusion, APACHE II score, diabetes, and total mannitol use are independent risk factors for AKI in patients with spontaneous intracerebral hemorrhage. For patients with high APACHE II scores, it is necessary to monitor renal function for early detection and treatment of AKI. Clinicians should strictly control blood glucose levels in such patients. While ensuring the dehydration effect, attention should be paid to controlling the total amount of mannitol used. More prospective, multi-center, and well-informed studies are needed for further demonstration in the follow-up.

COMPLIANCE WITH ETHICAL STANDARD

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest.

ETHICS APPROVAL

This study is approved by relevant Ethics Committee of Mingguang People's Hospital.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

AVAILABILITY OF DATA AND MATERIALS

The datasets used during the present study are available from the corresponding author upon reasonable request.

REFERENCES

1 Advani A. (2020) Acute Kidney Injury: A Bona Fide Complication of Diabetes. Diabetes. **69**(11): 2229–2237.
2 An SJ, Kim TJ, Yoon BW. (2017) Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. J Stroke. **19**(1): 3–10.
3 Chinese Society of Neurology & Chinese Stroke Society. (2019) Chinese guidelines for diagnosis and treatment of acute intracerebral hemorrhage 2019. Chin J Neurol. **52**(12): 994–1005.
4 Fu X, Wong KS, Wei JW, Chen X, Lin Y, Zeng J, et al. (2013) Factors associated with severity on admission and in-hospital mortality after primary intracerebral hemorrhage in China. Int J Stroke. **8**(2): 73–9.
5 Huang Y, Chen J, Zhong S, Yuan J. (2016) Role of APACHE II scoring system in the prediction of severity and outcome of acute intracerebral hemorrhage. Int J Neurosci. **126**(11): 1020–4.
6 Khwaja A. (2012) KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. **120**(4): c179–84.
7 Lazzeri E, Angelotti ML, Peired A, Conte C, Marschner JA, Maggi L, et al. (2018) Endocycle-related tubular cell hypertrophy and progenitor proliferation recover renal function after acute kidney injury. Nat Commun. **9**(1): 1344.
8 Li X, Li D, Zhang P. (2013) Analysis of risk factors for acute kidney injury and death caused by contrast media. Chin J Pract Intern Med. **33**(01): 42–45.
9 O'Kane D, Baldwin GS, Bolton DM, Ischia JJ, Patel O. (2019) Preconditioning against renal ischaemia reperfusion injury: the failure to translate to the clinic. J Nephrol. **32**(4): 539–547.
10 Peng J, Li X, Zhang D, Chen JK, Su Y, Smith SB, et al. (2015) Hyperglycemia, p53, and mitochondrial pathway of apoptosis are involved in the susceptibility of diabetic models to ischemic acute kidney injury. Kidney Int. **87**(1): 137–50.
11 Qureshi AI, Huang W, Lobanova I, Hanley DF, Hsu CY, Malhotra K, et al. (2020) Antihypertensive Treatment of Cerebral Hemorrhage 2 Trial Investigators. Systolic Blood Pressure Reduction and Acute Kidney Injury in Intracerebral Hemorrhage. Stroke. **51**(10): 3030–3038.
12 Søvik S, Isachsen MS, Nordhuus KM, Tveiten CK, Eken T, Sunde K, et al. (2019) Acute kidney injury in trauma patients admitted to the ICU: a systematic review and meta-analysis. Intensive Care Med. **45**(4): 407–419.
13 Spaliviero M, Power NE, Murray KS, Sjoberg DD, Benfante NE, Bernstein ML, et al. (2018) Intravenous Mannitol Versus Placebo During Partial Nephrectomy in Patients with Normal Kidney Function: A Double-blind, Clinically-integrated, Randomized Trial. Eur Urol. **73**(1): 53–59.
14 Waskowski J, Pfortmueller CA, Erdoes G, Buehlmann R, Messmer AS, Luedi MM, et al. (2019) Mannitol for the Prevention of Peri-Operative Acute Kidney Injury: A Systematic Review. Eur J Vasc Endovasc Surg. **58**(1): 130–140.
15 Xu Z, Fang L, Hen B. (2010) Mannitol is an independent risk factor of acute kidney injury in traumatic brain injury patients. Chin J Neahrol. **26**(04): 264–270.
16 Zhang W. (2005) Medical treatment of cerebral hemorrhage and its complications. J. Intern Intensive Med. **11**(5): 233–239.

Supplementary Table 1. APACHE II scoring system

Score			0	1	2	3	4
1.Acute Physiology Score (APS)	1. Anal temperature (°C)		36.0~38.4	34~35.9 or 38.5~38.9	32~33.9	30~31.9 or 39~40.9	≤29.9 or≥41
	2. Mean arterial pressure (mmHg)		70~109		50~69 or 110~129	130~159	≤49 or≥160
	3. Heart rate		70~109		55~69 or 110~139	40~54 or 140~179	≤39 or ≥180
	4. Respiration rate		12~24	10~11 or 25~34	6~9	35~49	≤5 or ≥50
	5. Oxygenatio n (mmHg)	FiO2<0.5 measuring PaO2	>70	61~70		55~60	<55
		FiO2>0.5 Measuring AaDO2	<200		200~349	350~499	≥500
	6.	Arterial blood pH	7.33~7.49	7.5~7.59	7.25~7.32	7.15~7.24 or 7.60~7.69	≥7.7 or <7.15
		Veinous blood HCO3 (mmol/L) (without arterial blood gas)	22~31.9	32~40.9	18~21.9	15~17.9 or 41~51.9	<15 or ≥52
	7. Plasma sodium (mmol/L)		130~149	150~154	120~129 or 155~159	111~119 or 160~179	≤110 or ≥180
	8. Plasma potassium (mmol/L)		3.5~5.4	3.0~3.4 or 5.5~5.9	2.5~2.9	6.0~6.9	<2.5 or ≥7
	9.	Serum creatinine (mg/dL)	0.6~1.4		<0.6 or 1.5~1.9	2.0~3.4	≥3.5
		Serum creatinine (μmol/L)	53~127		<53 or 128~171	172~304	≥305
		acute renal failure	Yes	No			
	10. Hematocrit (%)		30~45.9	46~49.9	20~29.9 or 50~59.9		<20 or ≥60
	11. WBC (×10^9/L)		3~14.9	15~19.9	1~2.9 or 20~39.9		<1 or ≥40

2. Age score	0	2	3	5	6
	≤44	45~54	55~64	65~74	≥75

3. Chronic health status score (with severe organ system dysfunction or immune impairment)	2	5	0
	non-surgical or after elective surgery	Unable to operate or after emergency operation	None of above

Explanation	APACHE II scoring system is composed of acute physiology score (APS), age score and chronic health score, and the final score is the sum of the three. The highest theoretical score is 71, and the higher the score, the worse the disease.
Notes	1. Data collection shall be the worst value within 24 hours after the patient enters the ICU or rescue begins. 2. Average arterial pressure=(systolic pressure+2 * diastolic pressure)/3. If there is direct arterial pressure monitoring, the direct arterial pressure shall be recorded. 3. Respiratory rate The patient's spontaneous respiratory rate should be recorded. 4. If the patient has acute renal failure, the score of serum creatinine should be doubled on the original basis. 5. Severe organ dysfunction refers to: ① heart: heart function grade IV; ② Lung: chronic hypoxia, obstructive or restrictive ventilation disorder, poor exercise tolerance; ③ Kidney: chronic dialysis patients; ④ Liver: liver cirrhosis, portal hypertension, history of upper gastrointestinal bleeding, liver coma, and history of liver failure. 6. Immune impairment: such as receiving radiotherapy, chemotherapy, long-term or massive hormone treatment, including leukemia, lymphoma, AIDS, etc. 7. The "inoperable" in Item C shall be understood as those who cannot receive surgical treatment due to the critical condition of the patient.

Supplementary Table 2. Glasgow Coma Score (GCS)

GCS score		6	5	4	3	2	1
Items	Eye opening response			Automatic eye opening	Eye opening upon speech call	Eye opening upon pain	Unable to open the eye
	Language reaction		Answer to the point	Answer not to the point	Irrelevant answer	Unintelligible sounds	Unable to pronounce
	Body movement	Act as instructed	Can locate the puncture site	Can avoid puncture	Limb flexion upon puncture	Limb stretch upon puncture	Unable to move the limbs
	Note	Glasgow Coma Score (GCS) is a medical method to evaluate the degree of coma of patients. The degree of coma is evaluated by the sum of the three scores. The higher the score, the better the state of consciousness. The evaluation of Glasgow Coma Index includes three aspects: eye opening response, language response and body movement. The total score of the three aspects is the coma index of the patient.					