Relationship between cerebral hemodynamics, tissue oxygen saturation, and delirium in patients with septic shock: a pilot observational trial

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Abstract

Background Patients with septic shock are prone to have impaired cerebral autoregulation and to have an imbalance in cerebral oxygen metabolism. Transcranial doppler (TCD) and tissue oxygen saturation monitoring were performed to observe the changes in cerebral hemodynamic indices of the middle cerebral artery, and in cerebral and peripheral tissue oxygen saturation (StO₂) to identify risk factors for sepsis-associated delirium (SAD).

Methods Patients with septic shock that were admitted to the Department of Critical Care Medicine of Xiangya Hospital of Central South University from May 2018 to March 2019 were prospectively enrolled, which were divided into an SAD group and a non-SAD group according to the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Both groups were compared with respect to patient characteristics, blood gas analysis indexes, organ function indicators, cerebral hemodynamic index, cerebrovascular automatic regulation function (transient hyperemia response rate, THRR index), the changes in regional cerebral oxygen saturation, and peripheral tissue oxygen saturation.

Results The incidence of SAD was 39% (20/51). The overall 28-day mortality rate was 43% (22/51). Compared with the non-SAD group, patients in the SAD group required a longer mechanical ventilation time (5 days [95% confidence interval (CI) 2, 6] vs 1 day [95% CI 1, 4], $p=0.015$) and ICU stay (9 days [95% CI 5, 20] vs 5 days [95% CI 3, 9], $p=0.042$) and has a higher 28-day mortality rate (65% vs 29%, $p=0.011$). Multivariate regression analysis showed that the THRR index (OR=5.770, 95% CI:1.222-27.255; $p=0.027$) and mean value of regional cerebral oxygen saturation (rSO₂) <55% (OR=3.864, 95% CI:1.026-14.550; $p=0.046$) were independent risk factors for SAD.

Conclusions SAD has a high incidence in septic patients and is associated with poor prognosis. Our results provide a clinical basis for improving early detection and treatment of SAD.

Background

Sepsis-associated delirium (SAD) is considered a diffuse cerebral dysfunction caused by a systemic inflammatory response to an infection without evidence of a central nervous system involvement (i.e., infection). SAD can develop in a short time and fluctuate transiently with time [1–2]. Studies have found that neuroinflammation, abnormal cerebral perfusion, neurotransmitter imbalances and neuronal degeneration may be involved in the pathogenesis of SAD [3–6]. Other studies suggest that changes in cerebral blood flow caused by hemodynamic instability, decreased brain oxygen uptake, blood-brain barrier disruption and cerebral edema are important predisposing factors for SAD [7–8]. Transcranial Doppler (TCD) ultrasound can visually detect the changes of cerebral perfusion and cerebral autoregulation in patients with sepsis. Pfister et al. [9] found a significant correlation between cerebral vascular autoregulation disorders and SAD. Some studies have found that the changes of cerebral hemodynamics detected by TCD ultrasound are closely related to the clinical symptoms of SAD [10].

Hypotension and hypoxia not only increase neuronal apoptosis but are also directly associated with poor prognosis [11]. At present, for both central venous oxygen saturation($ScvO_2$)and Mixed venous oxygen saturation(SvO_2), the monitoring is non-continuous, requires invasive procedures, and does not allow specific monitoring of local brain tissue, which makes it impossible to quickly and effectively identify patients with sepsis who are at risk of brain or brain-tissue hypoxia [12]. Regional cerebral oxygen saturation (rSO_2) and tissue oxygen saturation (StO_2) monitoring which are derived from near infrared spectroscopy (NIRS) can provide non-invasive assessment of cerebral oxygen metabolism and local tissue oxygen metabolism, providing real-time and continuous information of the balance of oxygen supply and demand. In addition, rSO_2 is a sensitive indicator of global cerebral hypoperfusion [13]. Studies have revealed a good correlation between tissue oxygen saturation monitoring and clinical evaluation of sepsis or septic shock [14–15].

Therefore, our study uses TCD and tissue oxygen saturation monitoring to observe the changes in cerebral hemodynamic indices of the middle cerebral artery, and in cerebral and peripheral tissue oxygen saturation (StO_2) to identify risk factors for sepsis-associated delirium (SAD).

Materials And Methods

Patients

Fifty-one patients with septic shock who were admitted to the Department of Intensive Care Unit, Xiangya Hospital of Central South University from May 2018 to March 2019 were enrolled in our study. Our study was a pilot observational trial with inclusion criteria were in accordance with the definition of sepsis 3.0. All included patients were treated according to the 2016 International Guidelines for the Treatment of Sepsis and Septic Shock [16] (i.e., Mean arterial pressure (MAP) reached 65 mmHg and lactic acid normalization was the target of initial resuscitation). Patients with diagnostic criteria for septic shock [17] were included in the study. Exclusion criteria: (1) age < 18 years ; (2) previous history of mental disorders or craniotomy; (3) neurological diseases (clear intracranial lesions such as cerebral hemorrhage, subarachnoid hemorrhage, craniocerebral trauma, stroke, intracranial infection, etc.); (4) liver failure with hepatic encephalopathy suspected; (5) pregnancy; (6) abnormal findings upon cervical vascular examination, by head MRI/CT and TCD ultrasound (such as carotid plaque with hemodynamically significant stenosis (eg > 50%)., thrombosis, etc.); (7) inability to detect blood flow signals in the temporal window by TCD. The primary outcome was delirium from admission to the ICU to Day 7 or discharge from the ICU. The secondary outcome was the 28-day mortality rate.

Ethics approval and consent to participate

This study was conducted in line with the standards of medical ethics. It was approved by the Central South University Xiangya Hospital Ethics Committee (Ethics No.:2018101082), and informed consent was obtained from the patient's immediate families.

Evaluation method of delirium

The diagnosis of delirium was based on the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), which was performed twice a day by trained researchers at the ICU (10:00–11:00 am; 16:00–17:00 for at first day of ICU admission up to 7 days. Patient assigned to the "SAD group" on the basis of a twice positive CAM-ICU screen performed by two researchers. All patients with septic shock were classified into a SAD group and non-SAD group according to the presence or absence of delirium, respectively.

Data collection

General data, Acute physiological and chronic health status assessment scores (APACHE II) score, sequential [sepsis-related] organ failure assessment (SOFA) score, administration of sedation and analgesia drugs, continuous renal replacement therapy (CRRT) mechanical ventilation time (days), ICU time (days), and 28-day mortality (%) of septic shock patients were determined.

Circulating hemodynamic management indicators

Arterial and central venous blood gas indicators, lactate clearance, Central venous pressure (CVP), Norepinephrine dosage, total resuscitation fluid, and urine output. Patients with septic shock included in the study completed critical echocardiography within 1 hour of admission, which measured cardiac output (CO), left ventricular ejection fraction (LVEF%), inferior vena cava diameter (IVCD), and Inferior Vena cava collapse index (IVC-CI).

Organ function and biochemical markers

Blood samples were monitored immediately after admission to the ICU, including organ function was assessed using routine blood indicators, liver and kidney function indicators, and routine coagulation indicators. Sepsis-associated biomarker indicators were procalcitonin (PCT); Neuron Specific Enolase (NSE), Central Nervous System Specific Protein (S100 β).

TCD monitoring index

TCD ultrasound (Shenzhen Delikai, EMS-9A dual channel, 1.6 MHz TCD probe) was used to obtain the bilateral middle cerebral arteries (MCAs) flow signal through the temporal window after 6 hours of initial resuscitation in patients with septic shock. Recording the diastole velocity of middle cerebral arteries ($V_{d_{MCA}}$), mean blood flow velocity (the mean velocity of middle cerebral arteries; $V_{m_{MCA}}$), systolic velocity of middle cerebral arteries ($V_{s_{MCA}}$), pulsatility index (PI ; $PI = (V_{s_{MCA}} - V_{d_{MCA}}) / V_{m_{MCA}}$), and calculation of cerebral blood flow index (CBFi, $CBFi = 10 \times MAP / 1.47 PI$), record whether the S_1 and S_2 peaks are fused during systole, and complete the dynamic assessment of cerebrovascular autoregulation. Dynamic cerebrovascular autoregulation was assessed by the transient hyperemia response rate (THRR) method. That is, the blood flow velocity of the middle cerebral artery was stably decreased to 30–50% of the baseline value by confirmed carotid artery compression for 3–9 seconds, and then the ratio of the blood flow velocity to the baseline blood flow velocity was measured. A THRR index > 1.09 is considered evidence for a dynamic cerebrovascular autoregulation function, conversely, at a THRR index ≤ 1.09 cerebrovascular autoregulation is considered to be impaired [18].

Tissue oxygen saturation was determined using the non-invasive tissue oxygen saturation monitor (CASMED, FORE-SIGHT) to continuously collect forehead cerebral oxygen saturation (rSO₂) (Large probe, detection depth 2.5 cm below the skull) and the thenar eminence tissue oxygen saturation (StO₂) (small probe, detection depth 0.5-2 cm). rSO₂ and StO₂ values were continuously recorded for at least 1 hour after 6 hours of initial resuscitation in patients with septic shock, and these data were uniformly processed in the later period. The rSO₂ and StO₂ data were analyzed at multiple thresholds (≥65%, < 60%, < 55%, and < 50%) to determine 1 suitable for comparison[19].

Data analysis

SPSS version 24.0 (SPSS Inc, Armonk, New York) was used for data analysis. The data were tested for normality. The data of the continuous variable that conformed to or approximated the normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$). The comparison between two samples was performed by independent student t test. Data that did not conform to the normal distribution were expressed as median [interquartile range; IQR], and the comparison between the two samples was performed using the Wilcoxon rank-sum test. The chi-square (χ^2) test was used to compare categorical data. When the theoretical frequency was < 5, the continuous correction method was adopted. When the theoretical frequency was < 1, the exact probability method was adopted. Multivariate logistic regression analysis was used to detect independent predictors of delirium, the predictor variables were selected from the risk factors displaying $p < 0.05$ in tables. The Pearson analysis method was used to analyze the correlation of the above-mentioned normal distribution variables. $P < 0.05$ was considered statistically significant.

Results

Of a total of 121 patients with septic shock that were screened in this study, 66 patients met the exclusion criteria and 4 patients did not complete delirium evaluation. Therefore, 51 patients were enrolled in the study after CAM-ICU evaluation was successfully completed. SAD incidence was 39%. (Fig. 1).

General clinical data and prognosis

Of the 51 patients with septic shock, the average age was 53 ± 11 years, including 31 males, accounting for 61%. Patients in the SAD group had a higher SOFA score (12 ± 5 vs 6 ± 3 , $p < 0.001$) and a higher APACHE II score (21 ± 7 vs 15 ± 6 , $p = 0.003$) (Table 1). The overall median mechanical ventilation time was 5 [1, 5] days and median ICU stay was 6 [3, 12] days. Compared with the non-SAD group, the SAD group needed a longer mechanical ventilation time (5 [2, 6] days vs 1 [1, 4] days, $p = 0.015$), and ICU stay (9 [5, 20] days vs 5 [3, 9] days, $p = 0.042$). The 28-day mortality rate was 43% for the entire cohort and was significantly higher in the SAD group (65% vs 29%, $p = 0.011$) (Table 1).

Table 1
Patient characteristics and co-morbidities.

Characteristic	The overall population (n = 51)	SAD group (n = 20)	Non-SAD group(n = 31)	p value
Age(years) ^a	53 ± 11	56 ± 11	52 ± 14	0.239
Gender(man) ^b	31(61)	13(65)	18(58)	0.620
BMI(kg/m ²) ^a	22.59 ± 2.50	23.05 ± 2.48	22.29 ± 2.51	0.294
Education(years) ^b				0.884
≤6	19(37)	8(40)	11(36)	
6–9	13(25)	4(20)	9(29)	
9–12	11(22)	5(25)	6(19)	
12–16	8(16)	3(5)	5(16)	
Hypertension ^b	14(27)	6(30)	8(26)	0.743
Coronary heart disease ^b	8(16)	4(20)	4(13)	0.775
Diabetes mellitus ^b	9(18)	3(15)	6(19)	0.982
Temperature(°C) ^a	37.2 ± 0.9	37.2 ± 0.7	37.2 ± 1.0	0.936
Heart rate(beats/min) ^a	109 ± 17	112 ± 18	106 ± 16	0.276
Breaths(/min) ^a	22 ± 6	22 ± 6	22 ± 6	0.864
Pulse oxygen saturation (%) ^a	98 ± 3	97 ± 4	98 ± 3	0.211
Blood glucose(mmol/L) ^a	9.0 ± 4.5	9.4 ± 5.3	8.7 ± 3.9	0.597
MAP(mmHg) ^a	81 ± 14	82 ± 18	80 ± 11	0.687
SOFA ^a	8 ± 5	12 ± 5	6 ± 3	≤0.001
APACHE II ^a	18 ± 7	21 ± 7	15 ± 6	0.003
Sedative ^b	25(49)	11(55)	14(45)	0.493

a values shown as mean ± standard deviation; b values shown as number of patients (%); c values shown as as median [IRQ].

Characteristic	The overall population (n = 51)	SAD group (n = 20)	Non-SAD group(n = 31)	p value
Analgesic ^b	34(67)	15(75)	19(61)	0.311
Detection rate of pathogenic bacteria ^b	29(57)	13(65)	16(52)	0.242
CRRT ^b	16(31)	9(45)	7(23)	0.092
Mechanical ventilation time (days) ^c	2[1, 5]	5[2, 6]	1[1, 4]	0.002
ICU stay (days) ^c	6[3, 12]	9[5, 20]	5[3, 9]	0.030
28-day mortality ^b	22 (43)	13 (65)	9(29)	0.011
a values shown as mean $\pm$ standard deviation; b values shown as number of patients (%); c values shown as as median [IRQ].				

Circulating hemodynamics indicators

Compared with the non-SAD group, the SAD group had significantly higher blood lactate (Lac) (t6h) (5.2 ± 4.3 mmol/L vs 2.1 ± 1.3 mmol/L, $p = 0.005$), lower lactate clearance rate (t6h) (-0.36 ± 0.73 mmol/L vs -0.002 ± 0.35 mmol/L, $p = 0.049$), and lower oxygenation index (t6h) (230 ± 116 vs 322 ± 121 , $p = 0.01$). There were no significant differences in critical echocardiography indicators ($p > 0.05$). An additional file shows this in more detail. [See Additional file 1 in Supplementary materials].

Organ function and biochemical markers

The white blood cell count (WBC) was significantly higher in the SAD group than in the non-SAD group (21.38 ± 14.16 vs 12.55 ± 11.61 , $p = 0.019$). Likewise, urea nitrogen (BUN) ($9.6 [5.7, 16.9]$ mmol/L vs $5.8 [2.8, 11.2]$ mmol/L, $p = 0.046$) and neuron specific enolase (NSE) ($18.24 [13.29, 27.08]$ vs $9.55 [6.13, 18.11]$, $p = 0.031$) were significantly higher in the SAD group than in the non-SAD group. An additional file shows this in more detail. [See Additional file 2 in Supplementary materials].

Cerebral hemodynamics in the middle cerebral artery detected by TCD

Compared with the non-SAD group, the SAD group had a lower cerebral artery diastolic blood flow velocity (V_{dMCA}) (49.7 cm/s ± 20.3 vs 61.9 ± 17.3 , $p = 0.026$), and a higher pulsation index (PI) (0.98 ± 0.19 vs 0.84 ± 0.20 , $p = 0.019$). The dynamic cerebrovascular dysfunction (ie, THRR index < 1.09) was 22% in the entire cohort, but was significantly higher in the SAD group compared with the non-SAD group (40% vs 10%, $p = 0.01$) (Table 2).

Table 2

Comparison of cerebral blood flow parameters of TCD between the sepsis-associated delirium (SAD) group and the non-SAD group.

Variable	The overall population (n = 51)	SAD group (n = 20)	Non-SAD group (n = 31)	P value
MAP (mmHg) ^a	81 ± 14	82 ± 18	80 ± 11	0.687
V _{S_{MCA}} (cm/s) ^a	127.9 ± 37.9	122.0 ± 50.2	131.7 ± 27.7	0.436
V _{m_{MCA}} (cm/s) ^a	79.2 ± 26.6	74.0 ± 29.7	82.7 ± 24.3	0.258
V _{d_{MCA}} (cm/s) ^a	57.1 ± 19.3	49.7 ± 20.3	61.9 ± 17.3	0.026
PI ^a	0.89 ± 0.21	0.98 ± 0.19	0.84 ± 0.20	0.019
CBFi ^a	648.73 ± 180.02	596.72 ± 196.38	682.28 ± 163.15	0.098
S ₁ S ₂ coalesce ^b	30(59)	11(55)	19(61)	0.656
THRR index $\times$ 1.09 ^b	11(22)	8(40)	3(10)	0.010
a values shown as mean $\pm$ standard deviation; b values shown as number of patients (%).				

Tissue oxygen saturation monitoring

The mean rSO₂ value of the SAD group was lower than that of the non-SAD group (55 ± 7 vs 60 ± 6, p = 0.01). In the overall study cohort, 16 patients had an average rSO₂ value of < 55%, and this was significantly more predominant in the SAD group than in the non-SAD group (50% vs 19%, p = 0.021). In addition, 15 patients had a mean StO₂ < 60%, which was also significantly more predominant in the SAD group than in the non-SAD group (45% vs 19%, p = 0.049) (Table 3).

Table 3
Tissue oxygen saturation. SAD group vs. non-SAD group.

	The overall population (n = 51)	SAD group (n = 20)	Non-SAD group(n = 31)	p
rSO ₂ value(%) ^a				
rSO ₂ min	55 ± 7	53 ± 7	56 ± 6	0.055
rSO ₂ max	62 ± 6	60 ± 6	63 ± 6	0.056
rSO ₂ mean	58 ± 7	55 ± 7	60 ± 6	0.010
Number of patients ^b				
rSO ₂ mean ≥ 60%	29(57)	14(70)	15(48)	0.128
rSO ₂ mean ≥ 55%	16(31)	10(50)	6(19)	0.021
rSO ₂ mean ≥ 50%	7(14)	5(25)	2(6)	0.144
StO ₂ value(%) ^a				
StO ₂ min	63 ± 8	62 ± 9	64 ± 7	0.391
StO ₂ max	70 ± 7	69 ± 9	71 ± 6	0.373
StO ₂ mean	67 ± 7	65 ± 9	68 ± 6	0.335
Number of patients ^b				
StO ₂ mean ≥ 65%	16(31)	9(45)	7(23)	0.092
StO ₂ mean ≥ 60%	15(29)	9(45)	6(19)	0.049
StO ₂ mean ≥ 55%	6(12)	4(20)	2(6)	0.307
a values shown as mean ± standard deviation; b values shown as number of patients (%).				

Multivariate analysis of SAD risk factors

Multivariate regression analysis of risk factors which focus on the brain parameters for SAD, Logistic regression analysis showed that there were a number of independent risks for predicting SAD, including the THRR index < 1.09 (odds ratio (OR) = 5.77, 95% confidence interval (CI) : 1.222–27.255, p = 0.027), and the mean rSO₂ < 55% value (OR = 3.864, 95% CI: 1.026 to 14.550, p = 0.046) (Table 4).

Table 4

Multivariate regression analysis of risk factors which focus on the brain parameters for sepsis-associated delirium (SAD).

Variable	B	S.E.	Wals	p	Exp(B)	95% C.I. for EXP(B)	
						upper	lower
PI	1.160	2.109	0.303	0.582	3.191	0.051	199.021
V _{dMCA}	-0.035	0.024	2.177	0.140	0.965	0.921	1.012
THRR index $\times$ 1.09	1.753	0.792	4.896	0.027	5.770	1.222	27.255
rSO2 mean	-0.083	0.058	2.045	0.153	0.921	0.822	1.031
rSO2mean $\times$ 55%	1.352	0.676	3.993	0.046	3.864	1.026	14.550
Sig. = significance; EXP(B) = Estimated odds ratio.							

Discussion

Impaired cerebral hemodynamics and imbalance of cerebral oxygen metabolism play an important role in the development of SAD. Our study confirmed a high incidence of SAD among patients with sepsis, which was associated with poor prognosis. Cerebrovascular autoregulation dysfunction (THRR index < 1.09) and mean cerebral oxygen saturation < 55% were found to be independent risk factors for SAD.

First, our study showed that the incidence of SAD in patients with septic shock was 39% (20/51), and that the SAD group required longer mechanical ventilation and ICU stay, and had a significantly higher 28-day mortality rate, which highlighted the need for identifying risk factors allowing early identification of SAD. In the ICU, early identification of reversible risk factors is very important for improving the prognosis of patients with sepsis or septic shock [20]. Tse et al. [21] proposed that age as well as certain pre-existing diseases and conditions are predictors of delirium after cardiac surgery. There are no recommended drugs or drug regimens to prevent delirium, so the focus should be on non-pharmaceutical interventions, including active communication, early detection of patients' psychological problems, family companionship, early activities, noise reduction, and good sleep [22].

Second, our study showed that cerebral vascular autoregulation dysfunction was an independent risk factor for delirium in patients with septic shock. This suggests that there is a decrease in cerebral perfusion and a decrease in cerebral vascular compliance in patients with SAD 6 hours after initial resuscitation. These changes may further affect cerebrovascular autoregulation. Cerebral hemodynamics and cerebral oxygen metabolism disorders play a crucial role in the development of SAD, which also lays the foundation for clinical hemodynamic management strategies targeting cerebral perfusion. Central nervous system dysfunction caused by sepsis is closely related to cerebral hypoperfusion caused by decreased cerebral blood flow. TCD ultrasound can monitor the systolic, diastolic, and mean blood flow

velocity of anterior, posterior, and middle cerebral arteries to evaluate cerebral perfusion [23]. TCD also provides an indirect assessment of the cerebral circulation including cerebral vascular autoregulation. When the cerebral vascular autoregulation is impaired, the changes of cerebral ischemia or cerebral congestion that may occur with the changes of perfusion pressure may cause nerve damage, which may adversely affect the prognosis. As early as 1997, Smielewski et al. [24] found that the disappearance of the transient cerebral congestion response rate (THRR) was associated with poor prognosis in patients with severe craniocerebral injury. Although TCD and THRR index evaluation cannot completely replace the results of brain imaging, they can provide early continuous monitoring of cerebrovascular autoregulation in patients with sepsis and septic shock [25]. The timely detection of the dysfunction of cerebrovascular autoregulation, will improve timely implementation of intervention measures.

Third, determining an imbalance between oxygen supply and demand in the optimization of cerebral perfusion requires real-time dynamic monitoring of oxygen saturation of brain. Our study found a lower mean rSO_2 value in the SAD group than in the non-SAD group, and multivariate regression showed that a mean $rSO_2 < 55\%$ was an independent risk factor for delirium in patients with septic shock. It is suggested that the overall trend of cerebral oxygen saturation in SAD patients persists at a low level. The mismatch between cerebral oxygen supply and oxygen consumption is crucial for the development of SAD, which also requires a continuous monitoring of cerebral oxygen saturation in patients with septic shock. It should be used as a routine monitoring indicator followed by blood pressure, heart rate, respiration, and pulse oxygen saturation. Studies have reported that intraoperative regional $rSO_2 < 40\%$ is an independent predictor of cognitive impairment after cardiac surgery [26]. De Tournay-Jette et al. [27] also reported that patients with $rSO_2 < 50\%$ during surgery experienced more post-operative cognitive dysfunction after 4 to 7 days of surgery ($p = 0.04$), and that a greater than 30% reduction in baseline rSO_2 was associated with cognitive impairment 1-month post-surgery ($p = 0.03$). Monitoring of oxygen saturation provides important information about oxygen in brain tissues at risk of various diseases. [28].

Fourth, the mean value of StO_2 fluctuated between 60–74% after initial resuscitation in patients with septic shock. In optimizing hemodynamics in critically ill patients, although global parameters are normalized, microcirculation and regional perfusion may change. The persistence of these changes is associated with poor prognosis. StO_2 can serve as an early warning signal for the initiation of low perfusion and tissue hypoxia [29].

There are certain limitations to this study. First, the effectiveness of TCD ultrasound is influenced by the operator's technique. Second, we only evaluated the changes of cerebral hemodynamics, and cerebral and peripheral tissue oxygen saturation 6 hours following the initial resuscitation and without combined neuroimaging or neurophysiological results. In addition, in view of the small sample size and the observational nature of our study, large-scale randomized controlled clinical trials may be needed for further verification of our results.

Conclusions

This group of septic patients had a high incidence of SAD and this was associated with poor prognosis. Cerebrovascular dysregulation (THRR < 1.09), and mean cerebral oxygen saturation < 55% are independent risk factors for SAD. The high-quality and adequately powered RCTs are warranted in the future.

Abbreviations

BMI body mass index; MAP = mean arterial pressure; SOFA = Sequential [sepsis-related] organ failure assessment; APACHE II=Acute physiological and chronic health status assessment scores; CRRT = Continuous renal replacement therapy. MAP = mean arterial pressure; VsMCA = systolic velocity of middle cerebral arteries; VmMCA= mean velocity of middle cerebral arteries; VdMCA= diastole velocity of middle cerebral arteries; PI = pulsatility index; CBFi=calculation of cerebral blood flow index; THRR = transient hyperemia response rate. rSO2 = regional cerebral oxygen saturation; StO2 = tissue oxygen saturation.

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Contributions

Qing Feng performed statistical analyses, searched the scientific literature and drafted the manuscript. Meilin Ai, Li Huang, Qianyi Peng helped to collect the data. Yuhang Ai, contributed to conception, design, and data interpretation. Lina Zhang contributed to conception, design, data interpretation, manuscript revision for critical intellectual content, and supervision of the study. All authors read and approved the manuscript.

Ethics declarations

Ethics approval and consent to participate

We performed a prospective observation study at an urban academic hospital in China. All subjects provided written informed consent to participate in the study. All procedures of this study were approved

by the ethics committee of Xiangya Hospital of Central South University (ethics no: 2018101082).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Study flow diagram. 121 patients with septic shock were screened, of which 66 patients met various exclusion criteria and 4 patients did not complete CAM-ICU assessment. A total of 51 patients were enrolled in our study, of which 20 (39%) were positive for CAM-ICU (SAD group) and 31 (61%) were negative for CAM-ICU (non-SAD group).

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