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Cerebral oximetry and autoregulation monitoring in shock patients

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ABSTRACT:

Background: Data on regional cerebral oxygen saturation (rSO_2) and cerebral autoregulation monitoring in shock patients are limited. This study aimed to find the optimal range of rSO_2 and cerebral oximetry index (COx), an autoregulation index correlated with adequate tissue perfusion determined by standard clinical and laboratory assessment.

Methods: We plan to monitor cerebral oximetry using near-infrared spectroscopy in shock patients admitted to the medical intensive care unit (MICU) at Siriraj Hospital. The rSO_2 are continuously recorded for 72 hours [48] after admission or 24 hours after cessation of vasopressor infusion. The COx is calculated from the correlation coefficient between rSO_2 and MAP. Data on patient demographics, treatments, physiologic parameters, and outcomes are recorded. The primary objective is to identify the optimal rSO_2 and COx correlated with adequate tissue perfusion assessed by the current standard method. Adequate tissue perfusion as is defined as MAP ≥65 mmHg and two of the following criteria: urine ≥0.5 ml/kg/hour, capillary refill time ≤3 seconds, improvement in consciousness, lactate reduction ≥10% in 1 hour, serum lactate <2 mmol/L, or central venous oxygen saturation ($ScVO_2$) ≥70%. Since the optimal values of rSO_2 and COx in shock patients are unknown, we are unable to perform the sample size calculation. Thus, for this study, we plan to collect data on rSO_2 and COx in 30 patients.

Hypothesis: We hypothesize that the values of rSO_2 and COx are different between patients with adequate and inadequate tissue perfusion.

Ethics: The study was reviewed and approved by the Human Research Protection Unit of Siriraj Hospital, Mahidol University (certificate of approval no. si 410/2022).

Keywords: Near-infrared spectroscopy, Regional cerebral oxygen saturation, Cerebral oximetry index, Cerebral autoregulation, Shock, Tissue perfusion.

BACKGROUND

Shock is the stage of inadequate cellular oxygen utilization.[1] Septic shock is the most common type of shock in clinical practice, and the reported mortality rate in our institution was 53%.[2] The patients who survived might have poor functional outcomes and cognitive impairment.[3-5] While mean arterial pressure (MAP) is targeted at ≥65 mmHg in current practice, optimal MAP may vary for individual patients.[6,7] The current methods to assess the adequacy of tissue perfusion cannot be performed continuously and have many limitations; for example, sedative agents may obscure the evaluation of the level of consciousness, low urine output may be caused by acute kidney injury rather than inadequate renal blood flow, central venous oxygen saturation ($ScVO_2$) cannot be measured in the absence of central venous catheter insertion, and a reduction in lactate level may be interfered with by a high dose of catecholamines, abnormal liver function and, some medications.

Cerebral oxygen saturation can be continuously recorded noninvasively by near-infrared spectroscopy (NIRS). The principle of this brain monitoring is to use near-infrared light (700 – 950 nanometers), which can penetrate through the superficial layers of the scalp and skull and illuminate the cerebral tissue for measuring cerebral oxygen saturation in each region. This average of oxygen saturation is calculated to regional cerebral oxygen saturation (rSO_2) from different ratios of light absorption between oxyhemoglobin and deoxyhemoglobin by a modified Beer-Lambert law's equation.[8-11] Normal range of rSO_2 is 60% to 75% [8]. Reduction of rSO_2 by 20% and/or less than 50% of rSO_2 indicates cerebral ischemia.[11] Whose sensitivity of 80% and specificity of 82.2% had been reported [9]. Also, patients with severe sepsis had significantly lower than thenar muscle rSO_2 values (p=0.031) than healthy volunteers.[48] Cerebral autoregulation can also be monitored by calculating the correlation coefficient between rSO_2 and MAP, which may be used to personalize MAP targets for individual patients.[12-15] The baselines of rSO_2 in each patient may vary; thus, monitoring the changes in rSO_2 is preferred.[16-17] However, there are some limitations, including ; 1) it measures rSO_2 merely in the focal area of the brain ; 2) the measured rSO_2 includes vessels of the skin at the forehead and skull ; and 3) it has less accuracy than $PbtO_2$.[18-20]

Autoregulation is an intrinsic property of cerebral vessels to maintain constant CBF when MAP changes. The cerebral autoregulation can be monitored using the changes in MAP and cerebral oximetry because rSO_2 correlates with cerebral blood flow (CBF), and MAP correlates with cerebral perfusion pressure (CPP). The cerebral oximetry index (COx), an autoregulation index, can be calculated using Pearson's correlation coefficient (r) between MAP and rSO_2.[21] When autoregulation is intact, rSO_2 remains unchanged despite changes in MAP. This results in a zero or negative COx value. But when autoregulation is impaired, changes in rSO_2 go in the same direction as changes in MAP. This results in a positive COx value.[21] This value can be automatically calculated by ICM+ software (University of Cambridge, United Kingdom). Cerebral autoregulation has been used to guide optimal blood pressure in sepsis, ischemic stroke, and post-cardiac arrest patients.[22-25]

KEY MESSAGES:

- This study is an observational, prospective cohort study that reported the rSO_2, and COx value during shock resuscitation and shock reversal determined by standard clinical and laboratory assessment. The primary endpoint is a Correlation between rSO_2, COx and MAP to be applied to monitor cerebral autoregulation for personalized each appropriate target blood pressure.

OBJECTIVES

This study aims to determine the optimal range of rSO_2 and the cerebral autoregulation index, the cerebral oximetry index (COx), correlated with adequate tissue perfusion determined by standard clinical and laboratory assessment. Adequate tissue perfusion is defined as MAP ≥65 mmHg and two of the following criteria: urine ≥0.5 ml/kg/hour, capillary refill time ≤3 seconds, improvement in consciousness, lactate reduction ≥10% in 1 hour, serum lactate <2 mmol/L or central venous oxygen saturation ($ScVO_2$) ≥70% with the difference in central venous and arterial partial pressure of carbon dioxide ($PvaCO_2$) <6 mmHg.[26]

MATERIALS AND METHODS

Study design

A prospective cohort study.

Study setting

The patients admitted to the medical intensive care units (MICUs) at Siriraj Hospitals, Mahidol University, Bangkok, Thailand.

Eligibility criteria

Inclusion criteria

1) Age ≥ 18 years.
2) Admission to the MICUs at Siriraj Hospital.
3) Duration from the onset of shock ≤ 24 hours.
4) Circulatory shock diagnosed by MAP < 65 mmHg or receiving vasopressors including norepinephrine, epinephrine, or dopamine to maintain MAP ≥65 mmHg with one of the following:
    4.1) Altered mental status with GCS < 15.
    4.2) Capillary refill time test > 4 seconds.
    4.3) Amount of urine output < 0.5 ml/kg/hr.
    4.4) Serum lactate level > 2 mmol/L.
5) Received invasive arterial blood pressure monitoring.

Exclusion criteria

1) Patients who decline life-sustaining therapy, including cardio-pulmonary resuscitation, endotracheal intubation, vasopressor therapy, etc.

2) Patients who received extracorporeal membrane oxygenation (ECMO) before enrollment.

3) Patients with advanced-stage cancer.

4) Patients with cardiac arrest before the enrollment.

Withdrawal criteria

Participants who desire to quit the study are allowed to withdraw.

INTERVENTION

After enrolling the shock patient, who has informed consent and was admitted to the medical intensive care units (MICUs) at Siriraj Hospitals, the cleaned equipment piece of cerebral oximetry monitoring named INVOS 7100 (by Medtronic, USA.) is attached on either the right or left side of the patient's forehead.

Values of regional cerebral oxygen saturation (rSO_2) are recorded continuously every 10 seconds for 72 hours or until vasopressors are stopped for 24 hours. The records are transferred to analyze for cerebral oximetry index (COx) in ICM+ software from the University of Cambridge, United Kingdom. These values from Cox are identified as the optimal MAP for each shock patient. Optimal MAP stands for maximum or minimum MAP, which relates to the lowest value of COx, and COx is still ≤ 0 (Figure 1). MAP is calculated by cerebral perfusion pressure (CPP) plus intracranial pressure (ICP). If it happens, reduce rSO_2 by 20% and/or less than 50%, check for other parameters of current standard practice for shock reversal, and resuscitate until reaching a good hemodynamic goal. The collected data include;

1) Fundamental data: Age, Gender, Body weight and height, Principal diagnosis, Types of shock, Baseline functional status by evaluated clinical performance category (CPC), Previous underlying diseases, Disease severity (SOFA score, APACHE II score).

2) Treatments consisted of inotropic drugs/vasopressors (norepinephrine, epinephrine, dopamine, dobutamine, milrinone, terlipressin, others.), invasive mechanical ventilation, renal replacement therapy, sedative agents and neuromuscular blocking agents (fentanyl, morphine, midazolam, propofol, dexmedetomidine, cisatracurium, others.)

3) Hemodynamics are evaluated during the first 72 hours of ICU admission, which include mean arterial pressure (MAP), Glasgow coma scale (GCS), amount of urine output, and capillary refill time (CRT).

4) Laboratories during the first 72 hours of ICU admission, which include the serum lactate level, central venous oxygen saturation ($ScvO_2$), and difference in arterial and mixed venous partial pressure of carbon dioxide ($Pv\text{-}aCO_2$).

5) Record the date and time of collected data to compare with values of rSO_2 and COx until a good hemodynamic goal is achieved, as shown in Table 1.

A good hemodynamic goal as per current standard practice for shock reversal is comprised of mean arterial pressure (MAP) ≥ 65 mmHg, amount of urine output ≥ 0.5 ml/kg/hr, capillary refill time (CRT) ≤ 3 seconds, Glasgow coma scale (GCS) returning to 15 points or the previous baseline of the patient's GCS, Serum lactate ≤ 2 mmol/L, Lactate reduction rate ≥ 10% in 1 hour, $ScvO_2$ ≥ 70%, $Pv\text{-}aCO_2$ gap ≤ 6 mmHg with $ScvO_2$ ≥ 70%.

6) Follow up Glasgow coma scale (GCS) and ICU Delirium evaluated by CAM-ICU daily for the first seven days until sedative agents are stopped.

7) Treatment outcome includes mortality rate in hospitals, Glasgow coma scale (GCS) and cerebral performance category on the day of discharge from hospitals, number(s) of the day which received some inotropic drugs or vasopressors, mechanical ventilator, renal replacement therapy and also the length of stay in ICU and hospitals.

8) Complications include the rate of acute kidney injury within the first week of ICU admission, the initiation of renal replacement therapy and the need for renal replacement therapy after discharge, Delirium during the

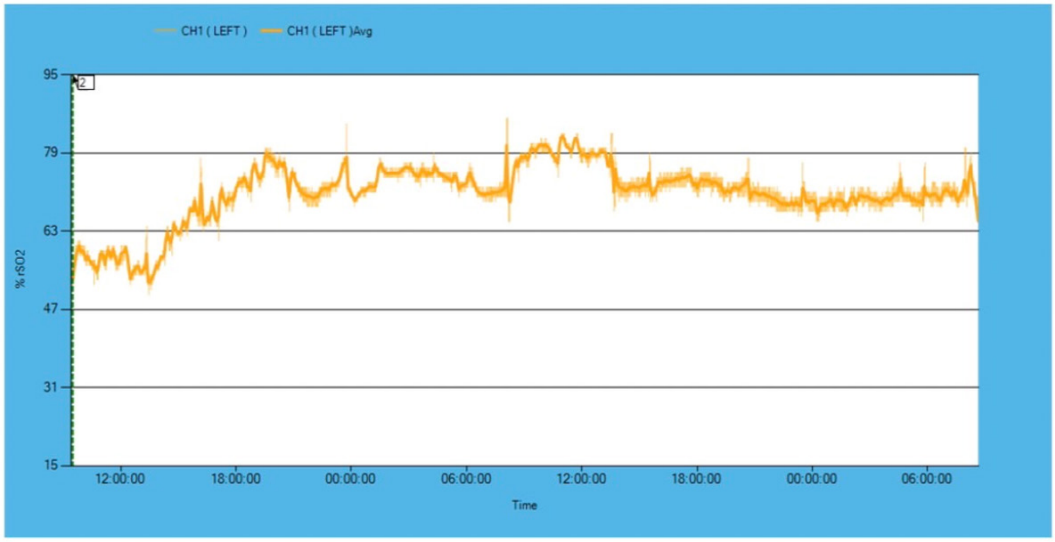


Figure 1. $PrSO_2$ trend data corelated with adequate tissue perfusion determined by standard clinical and laboratory assessment.

Table 1. Monitoring rSO_2 and COx until the good hemodynamic goal is achieved.

Clinicals	Hypotension and inadequate tissue perfusion with or without inotropes/ vasopressors	Normotension with inotropes/ vasopressors but inadequate tissue perfusion	Normotension with inotropes/ vasopressors with adequate tissue perfusion	Normotension and adequate tissue perfusion without inotropes/ vasopressors
Definition	MAP < 65 mmHg with ≥ 2 followings: - urine < 0.5 ml/kg/hr - CRT > 3 seconds - GCS < 15 or below patient's baseline - Serum lactate > 2 mmol/L and lactate reduction rate < 10% - $ScvO_2$ < 70% - Pv-aCO_2 gap > 6 mmHg and $ScvO_2$ ≥ 70%	MAP ≥ 65 mmHg with ≥ 2 followings: - urine < 0.5 ml/kg/hr - CRT > 3 seconds - GCS < 15 or below patient's baseline - Serum lactate > 2 mmol/L and lactate reduction rate < 10% - $ScvO_2$ < 70% - Pv-aCO_2 gap > 6 mmHg and $ScvO_2$ ≥ 70%	MAP ≥ 65 mmHg with ≥ 2 followings: - urine ≥ 0.5 ml/kg/hr - CRT ≤ 3 seconds - GCS 15 or equal to patient's baseline - Serum lactate ≤ 2 mmol/L and lactate reduction rate < 10% - $ScvO_2$ ≥ 70% - Pv-aCO_2 gap ≤ 6 mmHg and $ScvO_2$ ≥ 70%	MAP ≥ 65 mmHg with ≥ 2 followings: - urine ≥ 0.5 ml/kg/hr - CRT ≤ 3 seconds - GCS 15 or equal to patient's baseline - Serum lactate ≤ 2 mmol/L and lactate reduction rate < 10% - $ScvO_2$ ≥ 70% - Pv-aCO_2 gap ≤ 6 mmHg and $ScvO_2$ ≥ 70%
Date and time				
rSO_2				
COx				

first seven days of ICU admission, some ischemic complications (acute limb ischemia, mesenteric ischemia, etc.), other complications.

OUTCOME MANAGEMENT

Primary outcomes

1) Correlation between rSO_2 and mean arterial blood pressure (MAP) during shock and in patients at shock reversal.

2) Correlation between COx and mean arterial blood pressure (MAP) during shock and in patients at shock reversal.

To be applied to monitor cerebral autoregulation for personalized each appropriate target blood pressure.

Secondary outcomes

1) Incidence and risk factors of cerebral desaturation during shock resuscitation and reversal of shock.

2) Incidence and risk factors of cerebral autoregulation impairment during shock resuscitation and shock reversal.

DATA ANALYSIS PLAN

Sample size calculations

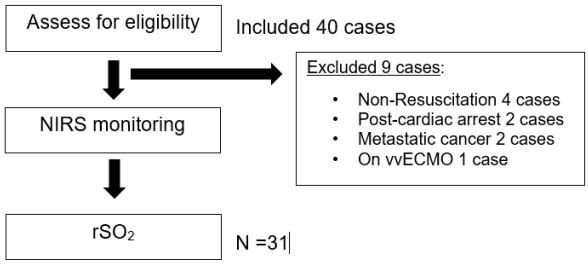
Since the optimal value of rSO_2 and COx in shock is unknown, we are unable to perform the sample size calculation. Thus, we plan to collect the data on rSO_2 and COx in 30 patients for this pilot and feasibility study [43].

Statistical analysis

Demographic and clinical variables are summarized using descriptive statistics. Continuous variables are described as means and SD or medians and interquartile ranges (IQR) depending on the distribution of the data. Categorical variables are described as frequencies, percents, or proportions, with a 95% confidence interval (CI). The comparison between the intervention group and the control group is interpreted by an independent t-test, a Mann-Whitney U test for continuous variables, and Chi-square test or Fisher's exact test for categorical variables.

The correlation between rSO_2, COx, and mean arterial blood pressure (MAP) during shock and in patients at shock reversal is calculated using Pearson correlation. A p-value of a two-tailed test less than 0.05 is considered statistically significant. PASW statistic v.18 is used for statistical analysis.

STUDY FLOW



DATA MANAGEMENT AND DATA MONITORING

Input data and monitoring method

- Monitoring rSO_2 and COx until the good hemodynamic goal is achieved (Table 1).
- Baseline patient characteristic variables (Table 2).
- Monitoring of parameters until shock(s) is/are reversed and timing to compare with rSO_2 and COx (Table 3).
- ICU-related variables (Table 4).
- Treatment outcomes on the day of discharge-related variables (Table 5).
- Complication-related variables (Table 6).

Table 2. Baseline patient characteristic variables.

Baseline patient characteristics	Collection method
Age/Gender.	Chart review
Body weight/height.	Chart review
Type(s) of shock. - Hypovolemic shock - Cardiogenic shock - Septic shock - Anaphylactic shock - Adrenal shock - Neurogenic - Cardiac tamponade - Pulmonary embolism - Tension pneumothorax - Other shock(s)	Chart review
Comorbidities. - Diabetes mellitus - Hypertension - Chronic kidney disease(s) - Long-term dialysis - Coronary artery disease(s) - Chronic liver disease(s) - Peripheral arterial disease(s) - Malignancy - Alcohol use - Smoking - Dementia - Mild cognitive impairment - Ischemic stroke - Intracerebral hemorrhage - Subarachnoid hemorrhage - Parkinsonism - Others	Chart review
Baseline cerebral performance category. - CPC 1, conscious and alert with good cerebral performance or minor disability. - CPC 2, conscious and alert with moderate cerebral performance (function is sufficient for independent ADL). - CPC 3, conscious with severe cerebral disability (conscious but disabled). - CPC 4, comatose or in persistent vegetative state (no obvious cortical function)	Chart review
Disease severity. - SOFA score - APACHE II score	Chart review

Table 3. Monitoring parameters until shock(s) is/are reversed and timing to compare with rSO_2 and COx.

Shock monitoring	Date/Time	Date/Time	Date/Time	Date/Time	Date/Time
Parameters					
Mean arterial pressure (mmHg)					
Heart rate (beat/min)					
Capillary refill time (Seconds)					
Urine output (ml/hr)					
Glasglow coma scale (GCS; 3-15 points)					
Central venous Pressure (mmHg)					
Laboratories					
Serum Lactate (mmol/L)					
$ScVO_2$ (%)					
Pv-aCO_2 gap (mmHg)					

Table 4. ICU treatment-related variables.

ICU Treatment	Duration (hours)	Max used doses (mcg/kg/min)
Type of Inotropes/Vasopressors: - Norepinephrine - Epinephrine - Dopamine - Dobutamine - Milrinone - Terlipressin - Others	Chart review	Chart review
Invasive mechanical ventilator	Chart review	
Type of Renal replacement therapy: - No - Intermittent hemodialysis (IHD) - Sustained low-efficiency dialysis (SLED) - Continuous renal replacement therapy (CRRT) - Peritoneal hemodialysis (PD)	Chart review	Chart review
Sedative agents	**Duration (hours)**	**Max used doses (mg/kg)**
- Fentanyl - Midazolam - Propofol - Dexmedetomidine - Morphine - Cisatracurium - Others	Chart review	Chart review

Table 5. ICU Treatment outcomes on the day of discharge-related variables.

ICU Treatment outcome	Collection method
Average Glasglow coma score (GCS)	Chart review
Average Richmond agitation and sedation scale (RAAS) score	Chart review
Incidence of ICU delirium: - No - Hypoactive - Hyperactive	Chart review
Amount of creatinine within the first week of ICU admission (mg/dl). - Baseline Creatinine before admission - Creatinine at the first hour of ICU admission - Maximum Creatinine after 48 hours of ICU admission - Maximum Creatinine after the first week of ICU admission	Chart review
Mortality rate	Chart review
At discharge: - Cerebral Performance Category (CPC) - Glasglow coma score (GCS)	Chart review
Length of stay (days) - ICU - Hospitals	Chart review

Table 6. Complication-related variables.

Incidence of Complication	Collection method
Acute kidney injury within the first week of ICU admission.	Chart review
RRT initiation	Chart review
RRT requirement after discharge	Chart review
Delirium during the first week of ICU admission	Chart review
Ischemic complications	Chart review
Other complications	Chart review

Definition of variables

Shock reversal is defined as maintenance of mean arterial pressure (MAP) of more than 65 mmHg with adequate tissue perfusion with at least two following criteria: the amount of urine output ≥ 0.5 ml/kg/hr, capillary refill time (CRT) ≤ 3 seconds, Glasgow coma scale (GCS) returns to 15 points or previous baseline of patient's GCS, Serum lactate ≤ 2 mmol/L, Lactate reduction rate ≥ 10%, $ScvO_2$ ≥ 70%, Pv-aCO_2 gap ≤ 6 mmHg with $ScvO_2$ ≥ 70% [1].

Near-infrared spectroscopy (NIRS) is a spectroscopic method that uses the near-infrared region of the electromagnetic spectrum to measure brain tissue oxygen saturation constantly. It is commonly used in operative room [38].

Regional cerebral oxygen saturation (rSO_2) is a non-invasive monitoring technique that uses Near-infrared spectroscopy (NIRS) to measure oxygen saturation of superficial brain cortex regions, which are among the most vulnerable to ischemic-hypoxic injury [38].

Cerebral pressure autoregulation is defined as maintaining constant cerebral blood flow (CBF) in the face of changing cerebral perfusion pressure (CPP)[39].

Cerebral oximetry index (COx) is an index of autoregulatory vasoreactivity derived from a time-domain analysis as a moving linear correlation coefficient between CPP and INVOS cerebral oximeter waveforms. Lowering/Rising in ABP below/above the breakpoint of autoregulation leads to loss of cerebral autoregulation caused by hypotension or hypertension, respectively [39].

Cerebral ischemia is a common mechanism of acute brain injury that results from impaired blood flow to the brain. Cerebral ischemia represents a medical emergency; if untreated, it can result in cerebral infarctions or global hypoxic-ischemic encephalopathy, which can result in death or permanent disability [44]. It is often defined as a 20% relative decrease from baseline or an absolute rSO_2 value of 50% [47].

Cerebral desaturation is compromised perfusion and oxygen delivery to the brain — is a common and serious event during cardiac surgery. It affects up to 25-37% of all cardiac surgery patients and up to 69-76% of high-risk cardiac surgery patients [45-46]. It is often defined a decrease in saturation values below 70% of baseline for 1 min or longer [11].

Research instruments

The cerebral performance category (CPC) score is widely used in research and quality assurance. The CPC ranges from 1 to 5, with 1 representing intact function, 2 as moderate disability, 3 as severe disability, 4 as coma and 5 as brain death [40].

Sequential Organ Failure Assessment score (SOFA score) is used to assess organ dysfunction during ICU admission by evaluating six organ systems (respiratory, cardiovascular, hepatic, renal, central nervous system, and coagulation). Variables representing each system are scored from 0 to 4. A higher score indicates higher severity [41].

Acute Physiology and Chronic Health Evaluation II (APACHE II) is used to assess disease severity on admission, containing three sections: 12 physio-logic variables to determine the degree of acute illness, age, and chronic health status. Age and chronic health status are weighted according to their relative impact. A higher score indicates a more severe disease.

Richmond Agitation Sedation Scale (RASS) is used to assess consciousness level. It comprises a 10-point scale ranging from -4 to +5, with RASS score of 0 indicating a calm and alert patient. Positive RASS scores indicate agitation or aggressive symptom ranging from +1 (mild rest - restlessness) to +4 (dangerous agitation). Negative RASS scores indicate drowsiness, stupor, or coma differentiated by the response to verbal command (score -1 to -3) and response to physical stimulation (score -4), and no response (score -5).

Confusion Assessment Method Intensive Care Unit (CAM-ICU) is used worldwide to assess delirium in critically ill patients. It has demonstrated pooled sensitivity of 80%, pooled specificity of 95.9%, and pooled area under the summary receiver operating characteristic curve (AUC) of 0.97. CAM-ICU comprises four features that assess the following: acute change or fluctuation of mental status, inattention, altered level of consciousness, and disorganized thinking. The Thai version of CAM-ICU has established validity and reliability with a sensitivity of 92.3%, specificity of 94.7%, and inter-rater reliability (Cohen's + = 0.81) [42].

Acute kidney injury (AKI) is defined as any of the followings; an increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26.5 umol/L) within 48 hours or an increase in serum creatinine to ≥ 1.5 times baseline within the previous 7 days or urine volume < 0.5 ml/kg/hr for 6 hours (KDIGO 2012).

ETHICS

We plan to apply for funding from the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, which takes no part in the design, conduct, analysis, review, or approval of the manuscript. We continuously review evolving scientific literature and evidence related to the safety of the study over the trial duration. The trial receives ethics approval from Siriraj Institutional Review Board (SIRB Protocol No. 314/2565 (IRB2), COA No. Si 410/2022), and enrollment has begun.

DISCUSSION

The study was conducted to identify the correlation between rSO_2, COx, and mean arterial blood pressure (MAP) in critically ill medical patients in shock and shock reversal in the medical intensive care unit (MICU). However, previously published studies had never demonstrated using NIRS for rSO_2 and COx values at the MICU [49]. It could be used to evaluate adequate tissue perfusion for each shock patient at MICU. The parameters for shock reversal in current standard practice were recorded by time to compare with values of rSO_2 and COx until a good hemodynamic goal was achieved. The correlation between change in mean arterial blood pressure (MAP) and rSO_2, COx was observed and analyzed by either a positive or

negative trend. In shock resuscitation, it could be monitored in real-time with mean arterial blood pressure (MAP).

For shock patients with an intracranial lesion, comatose (GCS <8), status epilepticus, and comatose from drug addiction and known metabolic causes, which affect this study, we did not exclude those data to compare between all data and data with those conditions excluded in the difference of change in rSO_2 and COx.

Studies of cerebral blood flow (CBF) autoregulation in sepsis suggest that patients with early sepsis or septic encephalopathy frequently manifest impaired CBF autoregulation, possibly as a result of BP below the lower limit of autoregulation. Early detection of this dysregulation might prevent poor functional outcomes, for example, AKI, stroke, prolonged invasive mechanical ventilation > 48 hours, prolonged inotrope use > 24 hours, and cognitive impairment. [50-52] The future study of rSO_2 monitoring using NIRS and clinically monitoring CBF autoregulation could provide insight into the cerebral pathophysiology of sepsis and offer more precise treatments that may improve functional and cognitive outcomes for survivors of sepsis.

If this hypothesis is proven effective, the correlation between rSO_2, COx, and mean arterial blood pressure (MAP) could be applied to monitor cerebral autoregulation. It could be personalized to appropriate target blood pressure as a surrogate monitoring shock resuscitation in the medical intensive care unit (MICU).

The strengths of the study are, first, non-invasive and continuous monitoring of cerebral oxygen saturation and autoregulation as a surrogate for the ultimate goal of shock resuscitation in the medical intensive care unit (MICU). Second, equipment pieces with NIRS technology, which use wavelengths between 700 and 950 nm, are harmless and can be used for every shock patient in the medical intensive care unit (MICU). Last, enrolling in this study entailed no selection bias.

The limitations of the study are, first, that it measures cerebral oxygen saturation only in the local area, which is attached by an equipment piece and includes vessels in the skin at the forehead and skull of that part. Second, most shock patients enrolled in this study are partially treated with intravenous fluid and vasopressors. It is difficult to monitor cerebral oxygen saturation at the beginning of shock resuscitation compared to the standard parameters for shock reversal in current practice.

CONFIDENTIALITY

Informed consents are obtained in the ICU/ward-prepared counseling room. Code is used and recorded instead of the patient's name, hospital number, and admission number. Date of birth, initials of name-surname, or other personal information are not collected. This study's data are recorded only in research record form and password protected in investigators' personal computers. When the study is concluded, data and documents recorded in physical form (paper) will be destroyed as per the destruction of document policy of Siriraj Hospital. Data and documents recorded in digital format will be permanently deleted from all investigators' computers.

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None

AUTHORS' CONTRIBUTIONS

(I) Conceptualization: Jirapat Lohpratana, Tanuwong Viarasilpa; (II) Data curation: Jirapat Lohpratana, Tanuwong Viarasilpa; (III) Formal analysis: Jirapat Lohpratana, Tanuwong Viarasilpa; (IV) Funding acquisition: Tanuwong Viarasilpa; (V) Methodology: Jirapat Lohpratana, Tanuwong Viarasilpa; (VI) Project administration: Jirapat Lohpratana, Tanuwong Viarasilpa; (VII) Visualization: Jirapat Lohpratana, Tanuwong Viarasilpa; (VIII) Writing – original draft: Jirapat Lohpratana, Tanuwong Viarasilpa; (IX) Writing – review & editing: Jirapat Lohpratana, Tanuwong Viarasilpa.

SUPPLEMENTARY MATERIALS

1 figures

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