



# The Association between Mean Arterial Pressure, Central Venous Pressure, Cerebral Perfusion Pressure, Lung Oxygenation, and Glasgow Coma Scale in Sepsis Patients in the Intensive Care Unit

Bastian Lubis<sup>1,2\*</sup>, Putri Amelia<sup>2,3</sup>, Muhammad Akil<sup>1</sup>, Vincent Viandy<sup>1</sup>

<sup>1</sup>Department of Anesthesiology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia; <sup>2</sup>Functional Medical Unit of Anesthesiology, H. Adam Malik Central Hospital, Medan, Indonesia; <sup>3</sup>Department of Child Health, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

## Abstract

**Edited by:** Mirko Spiroski  
**Citation:** Lubis B, Amelia P, Akil M, Viandy V. The Association between Mean Arterial Pressure, Central Venous Pressure, Cerebral Perfusion Pressure, Lung Oxygenation, and Glasgow Coma Scale in Sepsis Patients in the Intensive Care Unit. Open Access Maced J Med Sci. 2022 Mar 17; 10(T7):38-41.  
https://doi.org/10.3889/oamjms.2022.9285

**Keywords:** Mean arterial pressure; Central venous pressure; Cerebral perfusion pressure; Lung oxygenation; Glasgow Coma Scale

**\*Correspondence:** Bastian Lubis, Department of Anesthesiology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. E-mail: bastian.lubis@usu.ac.id

**Received:** 03-Aug-2021

**Revised:** 29-Nov-2021

**Accepted:** 08-Mar-2022

**Copyright:** © 2022 Bastian Lubis, Putri Amelia, Muhammad Akil, Vincent Viandy

**Funding:** This article was supported by Universitas Sumatera Utara by Talenta research implementation contracts 2020, number: 4142/UN5.1.R/PPM/2020.

**Competing interests:** The authors have declared that no competing interests exist

**Open Access:** This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

**BACKGROUND:** Sepsis is the most frequent condition encountered in the intensive care unit (ICU). One of the neurological features of sepsis is sepsis-associated encephalopathy (SAE). The exact pathophysiology of SAE remains unclear. Many factors have been linked to SAE, such as hypotension, hypoxemia, and other metabolic abnormalities. However, alteration of cerebral blood flow is thought to be the main culprit behind SAE.

**AIM:** This study aims to evaluate and find correlations between mean arterial pressure (MAP), central venous pressure (CVP), cerebral perfusion pressure (CPP), PaO<sub>2</sub>/FiO<sub>2</sub> (PF) ratio, Glasgow Coma Scale (GCS), and level of consciousness.

**METHODS:** A cross-sectional study was conducted from March 2020 to October 2020 in the ICU of H. Adam Malik Central Hospital, Medan, Indonesia. Patients over 18 years old with sepsis were included in this study. We recorded the demographic data, MAP, CVP, CPP, PF ratio, and GCS in the 1<sup>st</sup> h of ICU admission. The data were then analyzed to find the correlation between these parameters.

**RESULTS:** The total subjects in this study were 62 patients, with an equal ratio of male-to-female. A quarter of the patients were intubated, affecting the GCS assessment. The median of GCS was 12. Most patients (46.8%) were determined to be somnolence. The mean age of the subjects is 54.84 ± 13.25 years old. There was no correlation between MAP, CVP, CPP, PF ratio, GCS, and level of consciousness in this study.

**CONCLUSIONS:** Our study found no correlation between MAP, CVP, CPP, PF ratio, GCS, and level of consciousness in sepsis patients.

## Introduction

The mortality rate of sepsis patients in the intensive care unit (ICU) remains very high, ranging from 30% for sepsis to 80% for septic shock. The high mortality usually aligns with delay in diagnosis and treatment of sepsis. In critically ill patients, a worsening condition may occur when oxygen delivery fails to meet tissue oxygen demands. The result is compensation in the form of increased oxygen extraction. If the imbalance between oxygen delivery and extraction is not corrected rapidly, the compensatory response will slow down, causing oxygen deprivation, systemic tissue hypoxia, anaerobic metabolism, and an increase in lactate production [1], [2]

Sepsis-associated encephalopathy (SAE) is one of the most common and poorly understood neurological manifestations of sepsis. The presentation of SAE may vary, from a mild altered level of consciousness to deep coma. In sepsis patients,

the brain can be affected by systemic disturbances, such as hypoxemia and hypotension. Inflammation by itself also causes profound alterations in cerebral homeostasis. Alterations of the cerebral blood flow (CBF) may represent a key component for developing SAE. Hypotension will cause reduce CBF and oxygen extraction by the brain. Other possible explanations include disruption of the blood-brain barrier and cerebral edema that may arise from inflammatory mediators, an abnormal neurotransmitter of the reticular activating system, and neuronal degeneration [3], [4], [5], [6].

Central venous pressure (CVP) is often used in ICU to monitor hemodynamic status. Factors that can reduce CVP are hypovolemia and vasodilation. Reduction in CVP may cause hypotension, resulting in lower mean arterial pressure (MAP) and CPP. Increased level of CVP has been associated with poor outcomes [7]. Tissue hypoxia can be caused by three general abnormalities: Impaired oxygen delivery, hypoxemia, and impaired cellular oxygen uptake. Hypoxemia is a condition when the PaO<sub>2</sub> · 80 mmHg.

Managing hypoxia traditionally involves improving oxygen delivery and focuses on blood oxygenation (PaO<sub>2</sub> and hemoglobin) and cardiac output (CO) [8], [9]

Based on these connections, we conducted this study to evaluate whether there are correlations between MAP, CVP, CPP, and lung oxygenation with the outcome of reducing GCS in sepsis ICU patients.

## Methods

An analytic study with a cross-sectional design was conducted from March to October 2020 in the ICU of H. Adam Malik Central Hospital, Medan. The sampling method in this study was consecutive sampling. All patients over 18 years old with sequential organ failure assessment (SOFA) or quick SOFA (qSOFA) scores of more than two were included in this study. The parameter of lung oxygenation used in this study was PaO<sub>2</sub>/FiO<sub>2</sub> ratio which PaO<sub>2</sub> obtained from arterial blood gas analysis. All measurements were performed within the 1<sup>st</sup> h of ICU admission. The demographic data, CVP, CPP, MAP, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and GCS were analyzed. The GCS of intubated patients were evaluated with a method that was developed by Brennan *et al.*, which can be seen in Figure 1 [10].

After obtaining the GCS, we classified it further into four categories which were Compos Mentis (GCS = 15), Somnolence (GCS = 12–14), Sopor (GCS = 8–11), and Comatose (GCS = 3–7). This classification was reported by Hartanto *et al.* [11].

Data were analyzed using SPSS version 22.0. Quantitative variables were expressed as means and standard deviations, while categorical variables were described by their absolute (n) and relative (%) frequencies. Spearman's correlation was used to assess the associations between all numeric variables as most of the data were not normally distributed. As for the correlation of categoric variables (level of consciousness) and numeric variables, we used the Kruskal–Wallis test to find the correlation.  $p < 0.05$  was considered statistically significant. This study was approved by the Ethics Committee of the Faculty of Medicine of Universitas Sumatera Utara.

## Results

During this study period, 62 patients were admitted, comprising 31 males and 31 females with a mean age of  $54.84 \pm 13.25$  years. Sixteen subjects (25.8%) were intubated in this study. The baseline characteristics of subjects are seen in Table 1.

**Table 1: Characteristics of subjects**

Characteristics	Descriptive (n = 62)
Gender	
Male	31 (50%)
Female	31 (50%)
Intubated patients	16 (25.8%)
Age, (mean $\pm$ SD)	54.84 $\pm$ 13.25 years
MAP, (mean $\pm$ SD)	96.23 $\pm$ 19.78 mmHg
CVP, (mean $\pm$ SD)	8.15 $\pm$ 2.75 mmHg
CPP, (mean $\pm$ SD)	88.1 $\pm$ 20.46 mmHg
GCS, median	12 (10–14)
(Percentile 25–75)	
Compos mentis (15)	11 (17.7%)
Somnolence (12–14)	29 (46.8%)
Sopor (8–11)	14 (22.6%)
Coma (3–7)	8 (12.9%)
PF ratio, (mean $\pm$ SD)	291.09 $\pm$ 114.38

Table 2 shows p-value of correlation between MAP, CVP, CPP, and PF ratio to GCS using Spearman's correlation. All four tests have  $p > 0.05$ . There was no correlation between MAP, CVP, CPP, PF ratio, and GCS.

**Table 2: Correlation of MAP, CVP, CPP, PF ratio, and GCS**

Variables	p value
MAP $\times$ GCS	0.546
CVP $\times$ GCS	0.886
CPP $\times$ GCS	0.569
PF ratio $\times$ GCS	0.716

Table 3 shows the mean rank of each variable when paired with the level of consciousness.  $p$ -values in these four groups were also  $>0.05$ . No correlation was found between MAP, CVP, CPP, PF ratio, and level of consciousness.

**Table 3: Correlation of MAP, CVP, CPP, PF ratio, and level of consciousness**

Level of consciousness	Level of consciousness				p value
	Mean rank	Compos mentis n = 11	Somnolence n = 29	Sopor n = 14	
MAP	28.41	30.24	38.93	27.31	0.352
CVP	25.09	34.17	31.68	30.31	0.560
CPP	29.45	29.66	39.04	27.81	0.401
PF ratio	35.68	27.83	36.57	30.19	0.359

## Discussion

In sepsis patients, the brain function may be affected by several systemic disturbances such as abnormal glucose level, hypotension, hypoxemia, and organ dysfunction, for example, high ammonia or urea. Aside from these metabolic effects, inflammation itself also plays a key role in managing cerebral homeostasis [4].

Severe hypotension was found to be the only predictor of sepsis-associated delirium in a multiple logistic regression analysis. MAP tends to be lower in severe sepsis and septic shock patients. Accordingly, the level of CPP is low as well. When MAP drops

Step 1	E + M	2	3	4	5	6	7	8	9	10	
Step 2	+ V	Add 1					2	4	5		
Step 3	EVM	3	4	5	6	7	9	12	13	15	

**Figure 1: Visual aid to the imputation of verbal score with eye and motor score [10]**

significantly, blood flow won't be able to perfuse cerebral tissues and, therefore, causes loss of consciousness and probably neuronal death. Based on the formula below, we can conclude that CPP is directly proportional to MAP [11], [12], [13].

$$\text{CPP} = \text{MAP} - \text{ICP}$$

CPP = Cerebral Perfusion Pressure

MAP = Mean Arterial Pressure

ICP= Intracranial Pressure

In our patients, MAP was controlled very tightly, sometimes with vasopressor or fluid, explaining why we did not find an association between MAP and GCS. The concept of inadequate cerebral perfusion as one contributor to brain damage in sepsis is supported by earlier work showing reduced CBF in patients with sepsis utilizing the xenon-133 clearance technique [11].

Near infra-red spectroscopy (NIRS) is an increasingly used non-invasive tool to assess cerebral oxygenation. The tissue oxygenation index has been satisfactorily validated, and recent work has confirmed that it is not influenced by external factors such as hemoglobin concentration or skull thickness. The use of NIRS and transcranial Doppler (TCD) in detecting CPP has shown excellent results [6].

CVP is also used to estimate a patient's preload. It is considered one of the indices of IVS (Intravascular Volume Status) and cardiac function. Based on Frank Starling Law, vascular resistance should match CO as determined by CVP gradient. Changes of CO will affect blood pressure and, thus, affect MAP. Changes in CO that is associated with CVP are very crucial concerns in treatment of critically ill patients (Table 4) [14], [15].

**Table 4: Indicative of CO and CVP changes [15].**

CO	CVP	Indicative
Increase	Increase	Responsive of fluid challenge
Increase	Decrease	Improvement of the right heart function
Decrease	Increase	Primary decrease in cardiac function
Decrease	Decrease	Primary decrease in return function or decrease in volume

New evidence suggests no absolute direct correlation between CVP and the total blood volume present in the circulation. CVP was found to be a poor predictor of fluid responsiveness. Another reason is that the measurement of CVP may vary from one person to another. A survey reported that 75% of respondents made an error in the measurement of CVP [16], [17].

One of the limitations of this study was our inability to determine CPP using the method of TCD or NIRS in measuring CPP. Instead, we obtained CPP from the subtraction of MAP with CVP. This method was more inferior than NIRS and TCD. A few subjects in this study were also mechanically ventilated and sedated. Therefore, sedation may cause bias in GCS and level of consciousness.

## Conclusion

In this study, we found no correlation between CVP, MAP, CPP, PF ratio, and GCS with the level of consciousness in ICU sepsis patients. Further study is required to investigate this correlation with a better approach (NIRS or TCD) and larger subjects.

## References

- PERDICI. Penatalaksanaan Sepsis dan Syok Septik Optimalisasi Fasthugsbid. 1<sup>st</sup> ed. Jakarta: PERDICI; 2017. p. 3.
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, *et al*. The third international consensus definition for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801-10. <https://doi.org/10.1001/jama.2016.0287> PMID:26903338
- Chaudhry N, Duggal AK. Sepsis associated encephalopathy. *Adv Med*. 2014;2014:762320. <https://doi.org/10.1155/2014/762320> PMID:26556425
- Burkhart CS, Siegemund M, Steiner LA. Cerebral perfusion in sepsis. *Crit Care*. 2010;14(2):215. <https://doi.org/10.1186/cc8856> PMID:20236459
- Taccone FS, Scolletta S, Franchi F, Donadello K, Oddo M. Brain perfusion in sepsis. *Curr Vasc Pharmacol*. 2013;11(2):170-86. <https://doi.org/10.2174/1570161111311020007> PMID:23506496
- Pfister D, Siegemund M, Dell-Kuster S, Smielewski P, Ruegg S, Strebel SP, *et al*. Cerebral perfusion in sepsis-associated delirium. *Crit Care*. 2008;12(3):R63. <https://doi.org/10.1186/cc6891> PMID:18457586
- Lubis B, Amelia P, Akil M. The Association between daily fluid balance and mean perfusion pressure as a critical sign in the intensive care unit of Adam Malik central hospital, Medan. *Open Access Maced J Med Sci*. 2021;9(T3):52-5.
- MacIntyre NR. Tissue hypoxia: Implications for the respiratory clinician. *Respir Care*. 2014;59(10):1590-6.
- Samuel J, Franklin C. Hypoxemia and hypoxia. In: *Common Surgical Diseases*. New York: Springer; 2008. p. 391-4.
- Brennan PM, Murray GD, Teasdale GM. A practical method for dealing with missing Glasgow Coma Scale verbal component scores. *J Neurosurg*. 2020;1(1):1-6. <https://doi.org/10.3171/2020.6.JNS20992> PMID:32898843
- Hartanto AS, Basuki A, Juli C. Correlation of Glasgow Coma Scale Score at hospital admission with stroke hemorrhagic patient mortality at Hasan Sadikin hospital. *J Med Health*. 2019;2(4):938-44.
- Vedel AG, Holmgaard F, Rasmussen LS, Paulson OB, Thomsen C, Danielsen ER, *et al*. Perfusion pressure cerebral infarct (PPCI) trial the importance of mean arterial pressure during cardiopulmonary bypass to prevent cerebral complications after cardiac surgery: Study protocol for a randomised controlled trial. *Trials*. 2016;17(1):247. <https://doi.org/10.1186/s13063-016-1373-6> PMID:27189028
- Wijdicks EF, Stevens M. The role of hypotension in

- septic encephalopathy following surgical procedures. Arch Neurol. 1992;49(6):653-6. <https://doi.org/10.1001/archneur.1992.00530300093015>  
PMid:1596202
14. Naghipour B, Faridaalae G. Correlation between central venous pressure and inferior vena cava sonographic diameter; determining the best anatomic location. Emergency. 2016;4(2):83-7.  
PMid:27274518
15. Su L, Pan P, Li D, Zhang Q, Zhou X, Long Y, et al. Central venous pressure (CVP) reduction associated with higher cardiac output (CO) favors good prognosis of circulatory shock: A single-center, retrospective cohort study. Front Med. 2019;6:216. <https://doi.org/10.3389/fmed.2019.00216>  
PMid:31681775
16. Bowton DL, Bertels NH, Prough DS, Stump DA. Cerebral blood flow is reduced in patients with sepsis syndrome. Crit Care Med. 1989;17:399-403. <https://doi.org/10.1097/00003246-198905000-00004>  
PMid:2495896
17. Shah P, Oduah MT, Podder V, Louis MA. Physiology, Central Venous Pressure. Treasure Island, FL: StatPearls; 2019.