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Relationship between the Value of $PvaCO_2$ Gap with *Near Infrared Spectroscopy* for Assessing Oxygen Perfusion of Cerebral Network in Sepsis Patients with Decreased Consciousness in the Intensive Treatment Room of Adam Malik Hospital, Medan

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Abstract:-
Background: The tissue perfusion marker (lactate, $ScVO_2$) has limitations. Therefore, the $PvaCO_2$ gap is described as a parameter reflecting tissue hypoperfusion. Since occult regional ischemia, ie undetected at the systemic level, is considered a major contributor to morbidity and mortality after major trauma and in other critically ill patients, early detection of regional hypoxia is necessary. Traditionally, oxygenation is measured with invasive devices. NIRS is further used as a noninvasive monitoring technique that assesses regional brain oxygen saturation.

Objective: To determine the relationship between $PvaCO_2$ gap and NIRS to assess cerebral tissue oxygen perfusion in septic patients with decreased consciousness.

Methods: This study is a descriptive analytic study looking for the relationship between $PvaCO_2$ gap and NIRS in septic patients with decreased consciousness in the intensive care unit to assess cerebral tissue oxygen perfusion. Measurements were made with NIRS and examination blood gas of carotid and jugular. The normality test used with a sample size of less than 50, namely the Shapiro-wilk test. The hypothesis test used to compare the $PvaCO_2$ gap compared to NIRS in patients is the Pearson correlation test. Comparison of the value of discrimination using two measuring instruments using NIRS compared to the $PvaCO_2$ gap is presented in the form of a scatter plot.

Results: Right and left StO_2 levels have a negative correlation direction to the $PvaCO_2$ gap value. There is no significant correlation between the $PvaCO_2$ gap and NIRS.

Conclusion: $PvaCO_2$ gap does not correlate with NIRS to assess cerebral tissue oxygen perfusion in septic patients with decreased consciousness.

Keywords:- *$PvaCO_2$ gap, NIRS, StO_2, Sepsis.*

I. INTRODUCTION

Blood gas measurements are used to assess acid-base status and oxygenation. Many of these patients suffer from sepsis, it is estimated that it affects more than 30 million people each year and contributes significantly to the number of hospital deaths (Shastri, 2021).Several studies have shown that oxygen parameters are normalized at the time of ICU admission, suggesting that initial resuscitation may be partially or completely accomplished. Thus, several studies have shown that oxygen saturation values are not sufficient to describe regional or tissue perfusion abnormalities (Araujo, 2019).

Adequate tissue perfusion markers (lactate, $ScVO_2$) have limitations. Hyperlactataemia does not necessarily reflect tissue hypoxia or anaerobic metabolism and can be nonspecific. Central venous oxygen saturation ($ScVO_2$), which is used as a marker of hypoxia, can be normal despite microcirculation disturbances. Therefore, the difference in partial pressure of venous to central arterial CO 2 ($CO_2 gap$) has been described as a parameter reflecting tissue hypoperfusion (Huette, 2021).

The difference between venous carbon dioxide and arterial carbon dioxide pressure ($PvaCO_2 gap$) has been described as a parameter reflecting tissue hypoperfusion in critically ill patients who are not adequately resuscitated. $PvaCO_2 gaps$ have been proposed to better describe the correlation between systemic blood flow and global metabolic demand as it provides information not provided by other parameters (Department of Anesthesia of South Valley University, 2021).Through a prospective observational study over a 1 year period, which included a total of 150 high-risk surgical patients, it was observed that a high $PvaCO2_{gap}$ (≥6 mmHg) was associated with more organ failure, longer duration of mechanical ventilation, and length of hospital stay. (Department of Anesthesia of South Valley University, 2021).The high $PvaCO_{2\ group}$ was associated with a higher incidence of complications and organ failure than the normal $PvaCO_{2\ group}$. Regarding the length of stay in the ICU and mechanical ventilation days were also longer in the high $PvaCO_{2\ group}$ although the difference was not statistically significant (Department of Anesthesia of South Valley University, 2021).

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It is recommended that ICU patients be resuscitated with a target value of 70% ScvO $_2$ met, but a PcvaCO $_2$ of less than 6 mmHg can be a better marker (Department of Anesthesia of South Valley University, 2021).Sepsis, which occurs when the body's response to infection results in dysfunction of one or more organ systems, is a common condition in the ICU. Furthermore, sepsis is the most common cause of death in hospitals. Cerebral oxygenation has also been shown to be significantly lower in septic shock patients with decreased consciousness, suggesting that poor cerebral perfusion may contribute to its development. Furthermore, decreased consciousness has been associated with dysfunctional cerebral autoregulation, which may indicate secondary neurologic injury. To date, there is no feasible marker to measure cerebral perfusion non-invasively in ICU patients (Wood, 2021).

Neurological complications, associated with longer hospital stays and increased mortality. For this reason, neurological monitoring is essential to detect and potentially limit neurological complications. Among the tools that can be used to monitor the brain in such patients, the NIRS may have an important role. This non-invasive monitoring technique can provide a continuous value of forehead regional tissue oxygen saturation, which represents the balance between cerebral oxygen delivery and cerebral oxygen consumption (Pozzebon, 2018).*Near infrared spectroscopy* (NIRS) has gained popularity as a patient monitoring tool in intensive care and emergency departments. NIRS is very popular in many clinical areas, especially as a neuromonitoring tool for oxygenation adequacy and/or as a general hemodynamic assessment tool (Öztürk, 2019).

II. RESEARCH METHODS

A. *Research design*

This research is a descriptive analytic study that looks for the relationship between the PvaCO $_{2\ .\ value}$*gap* and NIRS values in septic patients with decreased consciousness in the intensive care unit to assess cerebral tissue oxygen perfusion.

B. *Place and time of research*

The study was conducted at the Haji Adam Malik General Hospital Medan from January 1, 2022 to February 28, 2022.

C. *Population and Research Sample*

A septic patient with decreased consciousness who was admitted to the intensive care unit of Haji Adam Malik General Hospital, Medan. Affordable population that meets the inclusion criteria and exclusion criteria.

D. *Inclusion Criteria*

- Patients aged 18 years and over.
- Patients on mechanical ventilation.

E. *Exclusion Criteria*

- The patient's family refused to be included in the study.
- The patient is declared brain stem dead.
- Patients with cerebral abnormalities in the frontal region.

F. *Drop Out Criteria*

The patient was in cardiac arrest at the time of examination.

G. *Procedure*

Collecting data on research samples, namely patients who were treated in the intensive care room at Haji Adam Malik General Hospital Medan who met the inclusion and exclusion criteria. An explanation to the patient's family who is the subject of the study regarding the purpose, method and benefits of this examination and then to the patient's family who will be asked to first sign the *informed consent*. Basic data recording was carried out by researchers in the intensive care room at Adam Malik General Hospital, Medan, such as name, gender.

Performing a vital examination of vital signs, in the form of blood pressure, MABP, pulse and SpO $_2$. Before using NIRS, the patient's forehead is cleaned first with wet gauze and alcohol, then dried so that it is clean from disturbances such as oily or watery face. Then turn on the NIRS device, put it in a stable position, connect the NIRS electrode to the INVOS machine and attach it according to the number on the frontal area of the research subject in a parallel position at the same time to show the right and left sides. Attachment position according to Figure 3.2. The measurable results on the NIRS (at the time the jugular vein sample was taken, described in the next point) were recorded on the study sheet. Clean the blood collection area, on the right or left neck with povidone iodine, after a while with alcohol and then dry with gauze.Through ultrasound guidance, blood samples were taken using a 3 ml syringe, on the carotid artery for examination of AGDA and internal jugular vein for examination of Venous Blood Gas Analysis with both at the same level, then inserted into 2 *vacuum tubes* containing lithium heparin accompanied by lactate test. The shooting position is adjusted to the image. Each time blood is drawn, then compression is carried out at the collection site for approximately 5-10 minutes until there is no visible active bleeding or swelling due to accumulation of blood under the skin.

H. *Analasys statistics*

The data in this study are numerical data with a normal distribution displayed in the average value of SD (*Standard Deviation)* . Categorical data is displayed in numbers (percentages). The normality test used with a sample size of less than 50 is the Shapiro-Wilk test. Hypothesis test used to compare the value of PvaCO $_2$*gap* compared to NIRS in patients, namely the Pearson correlation test because the data are normally distributed. Comparison of the value of discrimination using two measuring instruments using NIRS compared to PvaCO $_2$*gap* is presented in the form of a *scatter plot* .

III. RESULT

A. *Characteristics of Research Parameters*

This study was followed by as many as 30 research subjects, the characteristics of the research subject parameters can be seen in table 4.1 as follows:

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Characteristics	n=30	p value [a]
Age	47.07 ± 17.63	0.40
Gender n (%)		
Man	18 (60)	0.08
Woman	12 (40)	
BMI	24.19±4.71	0.23
Pulse	106.64 ± 27.62	0.08
FOLDER	87.47 ± 19.97	0.71
SpO2 _	95.80 ± 7.47	0.24
GCS	7.17 ± 2.91	0.03
Lactate	0.05±0.32	0.03
Hb	10.96 ± 2.98	0.93
StO 2 Right	53.87±20.00	0.60
StO 2 Left	56.27 ± 18.66	0.46
PvaCO 2*gap*	8.03±7.22	0.08

Table 1: Characteristics of Research Parameters

[a] Shapiro Wilk

Based on the table above, it can be seen that the average age of the research subjects was 47 years with the majority of men as many as 18 people (60%) and women as many as 12 people (40%). The mean BMI was 24 kg/m ^{2} , the mean pulse was 106 beats / min, the mean MAP was 87, the mean SpO 2 was 95.8%, the right StO 2 was 53.87%, the left StO 2 was 56.27%, the mean GCS score was 7.17 , mean lactate 0.05, and mean PvaCO 2*the gap* is 8.03. Categorical data is presented in the form of frequency distribution (%) and numerical data is presented in the form of mean ± standard deviation.

B. Characteristics of PvaCO 2Gaps in Assessing Oxygen Perfusion

The following is a table regarding the characteristics of PvaCO 2*gap in assessing oxygen perfusion,* which is said to be PvaCO2 *gap* is high if 6 and PvaCO 2 low *gap* if <6 :

Parameter	Frequency (%)	p value
High PvaCO2 _	19 (63.3%)	0.08 [a]
Low PvaCO2 _	11 (36.7%)	

Table 2: Characteristics of PvaCO 2*Gaps* in Assessing Oxygen Perfusion

[a] Shapiro Wilk

Based on the table above, it can be seen that PvaCO 2 high *gap* as many as 19 subjects (63.3%) and PvaCO 2 a low *gap* of 11 subjects (36.7%) with a p value > 0.05 which means the data is normally distributed.

C. Difference NIRS (StO 2) Right and Left

The following is a table regarding the characteristics of NIRS (StO 2) on the right and left sides in assessing cerebral oxygen perfusion with the following results:

Parameter	N	Average ± SD	Correlation coefficient (r)	p value
Right StO2	30	53.87±20.00	0.955 [a]	0.001 [b]
Left StO2	30	56.27 ± 18.66		

Table 3: NIRS . Correlation (StO 2) Right and Left

[a] Pearson Correlation
[b] Test T

Based on the results of the analysis of the difference in the values of StO 2 right and StO 2 left, there was a statistically significant difference with a value of p = 0.001 (p < 0.05) and a positive correlation with a value of r = 0.955.

D. Right and Left NIRS (StO 2) Correlation of PvaCO 2gap

The following is a table regarding the correlation of NIRS (StO 2) on the right and left side of PvaCO 2*gaps* :

	PvaCO2 Correlation coefficient (r)	p value
Right StO2	-1.36	0.475
Left StO2	-0.64	0.738

The following is a *scatter plot graph of the* right and left StO 2 correlation test against PvaCO 2*gaps* :

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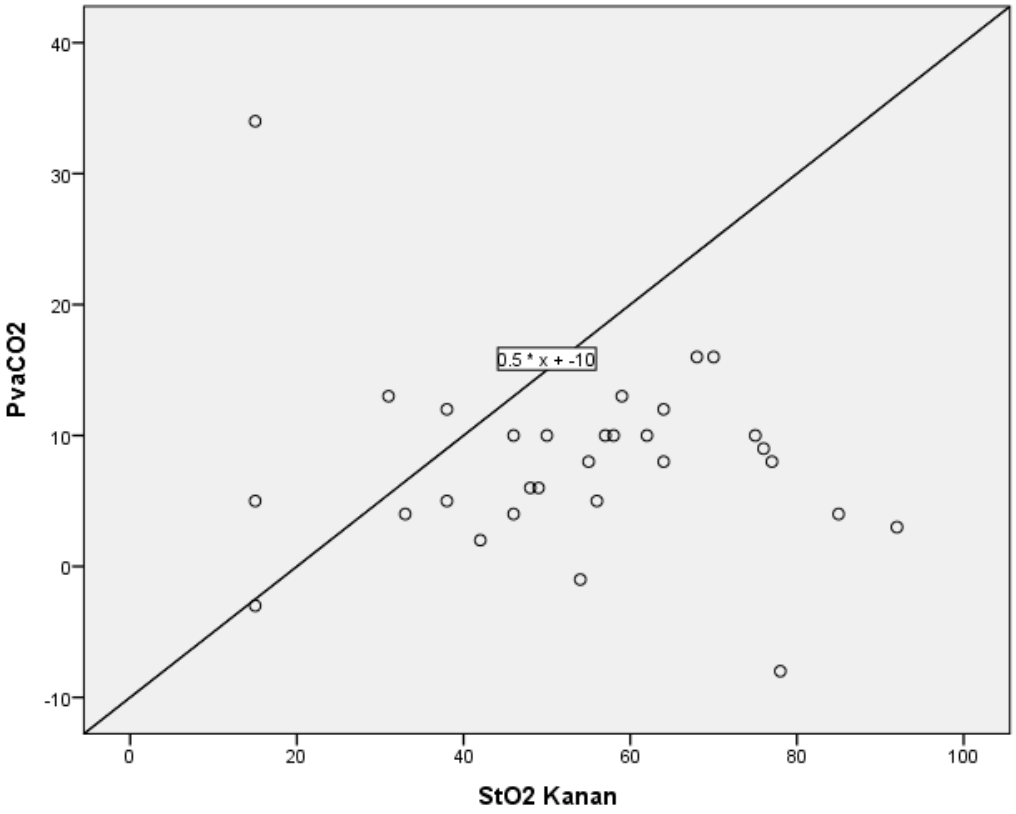

Fig. 1: *Scatter P lot*Correlation of StO ₂Right with PvaCO ₂*gap*

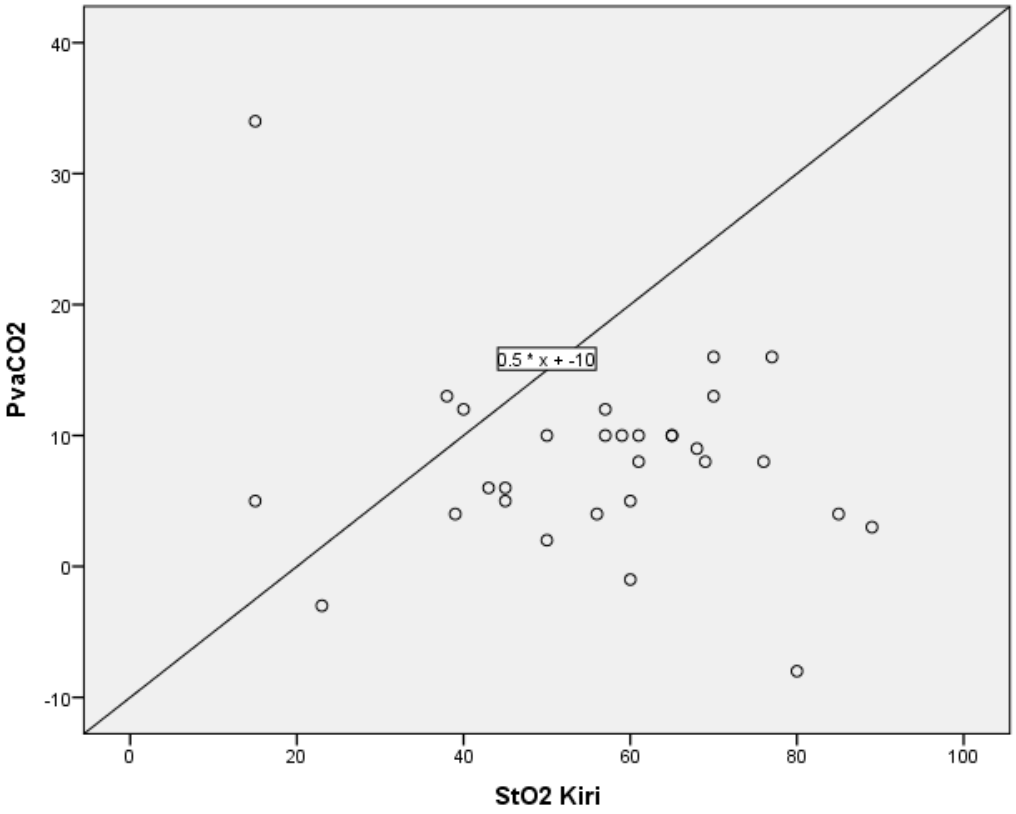

Fig. 2: *Scatter Plot*Correlation of Left StO ₂ with PvaCO ₂*gap*

StO ₂ levels have a negative correlation direction to the PvaCO ₂ . value*gaps* . However, based on the analysis, there is no statistically significant correlation between NIRS and PvaCO ₂*gap* with p value > 0.05.

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IV. DISCUSSION

In this study, the mean PvaCO $_2$*gap* is 8.03 where PvaCO $_2$ high *gap* as many as 19 subjects (63.3%) and PvaCO $_2$ low *gap* of 11 (36.7%) in septic patients. A prospective blinded observational study conducted by Bitar with 28 samples with severe sepsis and septic shock subjected to PvaCO2 examination *gap* at the time of admission and 6 hours after admission to the critical care unit it was found that PvaCO $_2$ a high *gap* has a mortality of 30% and at PvaCO $_2$ a low *gap* of 20% for septic patients. PvaCO $_2$*gap* is an important hemodynamic variable in the management of sepsis-induced circulatory failure, can be a marker of adequacy of cardiac output in severe sepsis and can assess an important prognosis in septic patients (Bitar, 2020).

Because of the higher solubility of CO2 $_{\text{than}}$ O2 in the blood, the waste CO2 $_{\text{from hypoxic}}$ tissues is higher than that of O2 in the low-flow state . Thus PvaCO $_2$*gap* can be used as a marker of tissue hypoperfusion rather than a tool for detecting tissue hypoxia. PvaCO $_2$*gap* is suggested to be used as a guide for shock resuscitation (Scheeren, 2018).

In this study, the NIRS was actually intended to describe the microcirculation in the brain, and a significant positive and significant correlation was found for the parameters MAP, Hb, and PvaCO2 *gaps* . In fact, this confirms the theory of oxygen delivery, in which the components of oxygen delivery take into account the *cardiac output component* , which is represented by MAP, and oxygen content, which consists of several components, such as Hb, SaO $_2$, and PaO $_2$.

Furthermore, what was studied was the difference in StO $_2$ on the right and left sides. Based on the normality test, the distribution is normal, so it is continued with the correlation test, with the result that the right and left StO $_2$ are different, with a value of 53.87 with 56.27. Actually it shows that the StO $_{2\ \text{level}}$ on one side cannot describe the situation on the two different sides, so for this examination, two electrodes are installed on both sides.

StO $_{2\ \text{values}}$ on both the right and left sides have a negative correlation with the PvaCO $_{2\ .\ \text{value}}$*gap* , although analytically, there is no significant correlation. The conclusion that can be drawn, although the correlation is not statistically significant, is that if the StO2 value is $_{\text{high}}$, the PvaCO2 value is otherwise *the gap* will be low, whereas if the value of StO $_2$ is low then the value of PvaCO $_2$*the gap* will be high. This has disproved the hypothesis of this study which states that NIRS is associated with PvaCO $_2$*gaps* .

Several other studies also did not find a significant relationship between NIRS and PvaCO $_2$*gap* , for example a study conducted by Das that assessed cerebral oxygenation levels using NIRS in septic shock patients, and found a significant relationship between cerebral oxygenation levels, MAP, lactate levels, and central venous saturation in shock patients, not to PvaCO $_2$*gaps* . The positive association between cerebral oxygenation, MAP, and central venous saturation persisted for up to 72 hours with 6-hour monitoring, and there was a significant negative relationship between cerebral oxygenation and lactate levels in

NIRS cannot stand alone, it is necessary to examine other necessary parameters before continuous NIRS examination is carried out to be able to describe the state of cerebral oxygen perfusion optimally so that patient care and management can be carried out optimally.

V. CONCLUSION

PvaCO $_2$*gap* does not correlate with the NIRS statistically to assess cerebral tissue oxygen perfusion in septic patients with decreased consciousness. PvaCO Value $_2$*The gap* was found to increase in septic patients with decreased consciousness, while the NIRS value was found to be within the normal range in sepsis patients with decreased consciousness.

REFERENCES

[1.] Abou-Arab O, Braik R, Huette P, Bouhemad B, Lorne E, Guinot PG. The Ratios of Central Venous to Arterial Carbon Dioxide Content and Tension to Arteriovenous Oxygen Content are not Associated with Overall Anaerobic Metabolism in Postoperative Cardiac Surgery Patients. Plos one. 2018 Oct 26; 13(10): 1-11.

[2.] Araujo DT, Felice VB, Meregalli AF, Friedman G. Value of Central Venous to Arterial CO_2 Difference after Early Goal-directed Therapy in Septic Shock Patients. Indian Journal of Critical Care Medicine. 2019 Oct; 23(10): 449-453.

[3.] Bitar ZI, Maadarani OS, El-Shably AM, Elshabasy RD, Zaalouk TM. The Forgotten Hemodynamic PCO_2 Gap in Severe Sepsis. Critical Care Research and Practice. 2020 Jan 7: 1-5.

[4.] Dahlan MS. Sample Size and Method of Sampling in Medical and Health Research. Edition 3. Jakarta. Salemba Medika. 2010.

[5.] Das D, Mitra K, Das S. Brain Co-oximetry: An Useful Non-Invassive Parameter Adjuvant to Standard Perfusion Parameters in Septic Shock. Journal of Anesthesia and Clinical Research. 2021 Feb 4; 12(1): 1-5.

[6.] Department of Children, Airlangga University, Surabaya. Acid Base Balance Disorders. PGD09. 2017; 3:491-520.

[7.] Department of Anesthesia, South Valley University, Qena, Egypt. The Impact of Early Goal Directed Therapy and PCO $_2$ Gap Protocol on Outcomes of High-Risk Surgical Patients Admitted to ICU: A Prospective Study. Journal of Anesthesia & Clinical Research. 2021 Jul 29; 12(7): 1-5.

[8.] Eyeington CT, Ancona P, Osawa EA, Cutuli SL, Eastwood GM, Bellomo R. Modern Technology-derived Normative Values for Cerebral Tissue Oxygen Saturation in Adults. Journal of Anesthesia and Intensive Care. 2019 Oct 12; 47(1): 69-75.

[9.] Hamrin TH, Radell PJ, Flaring U, Berner J, Eksborg S. Performance of Regional Oxygen Saturation Monitoring by NIRS in Pediatric Inter-hospital Transports with Special Reference to Air Ambulance

Transports: A Methodological Study. Journal of Clinical Monitoring and Computing. 2017 Dec 28: 1-7.
[10.] Huette P, Beyls C, Mallat J, Martineau L, Besserve P, Haye G, et al. Central Venous to Arterial CO_2 Difference is a Poor Tool to Predict Adverse Outcomes After Cardiac Surgery: a Retrospective Study. Canadian Journal of Anesthesia. 2021 Jan 6; 68: 467-476.
[11.] Lian C, Li P, Wang N, Lu Y, Shangguan W. Comparison of Basic Regional Cerebral Oxygen Saturation Values in Patient of Different Ages: A Pilot Study. Journal of International Medical Research. 2020 Jun 3; 48(8): 1-9.
[12.] Mahrous RSS, Ismail TI. Evaluation of Two Different Fluids Regimens on Central Venous to Arterial Carbon Dioxide Difference (PCO_2 Gap) - A Randomized Controlled Trial. Egyptian Journal of Anaesthesia. 2021 Mar 7; 37(1): 113-122.
[13.] Muller G, Mercier E, Vignon P, Lagarrigue MH, Kamel T, Desachy A, et al. Prognostic Significance of Central Venous to Arterial Carbon Dioxide Difference During The First 24 Hours of Septic Shock in Patients with and without Impaired Cardiac Function. British Journal of Anaesthesia. 2017 Jul 14; 119(2): 239-248.
[14.] Murkin JM, Arango M. Near-Infrared Spectroscopy as an Index of Brain and Tissue Oxygenation. British Journal of Anaesthesia. 2009 Mar 23; 103: 3-13.
[15.] Öztürk NY, Aygün B, Uyar E, Girgin FI. Comparison of Bilateral Cerebro-Renal Tissue Oxygenations in Healthy Children. The Indian Journal of Pediatrics. 2019 Dec 16: 1-6.
[16.] Pozzebon S, Ortiz AB, Franchi F, Cristallini S, Belliato M, Lheureux O, et al. Cerebral Near-Infrared Spectroscopy in Adult Patients Undergoing Veno-Arterial Extracorporeal Membrane Oxygenation. Neurocritical Care Society. 2018 Mar 20; 29: 94-104.
[17.] Sastroasmoro S. Dasar-dasar Metodologi Penelitian Klinis. Edisi 4. Jakarta. Sagung Seto. 2011.
[18.] Scheeren TWL, Wicke JN, Teboul JL. Understanding The Carbon Dioxide Gaps. Current Opinion in Critical Care. 2018; 24: 181-189.
[19.] Shastri L, Kjærgaard B, Rees SE, Thomsen LP. Changes in Central Venous to Arterial Carbon Dioxide Gap (PCO_2 Gap) in Response to Acute Changes in Ventilation. BMJ Open Respiratory Research. 2021 Mar 18: 1-5.
[20.] Valeanu L, Bubenek-Turconi S, Carmen Ginghina C, Balan C. Hemodynamic Monitoring in Sepsis: A Conceptual Framework of Macro-and Microcirculatory Alterations. Diagnostics. 2021 Aug 28; 11(1559): 1-21.
[21.] Vesoulis ZA, Mintzer JP, Chock VY. Neonatal NIRS Monitoring: Recommendations for Data Capture and Review of Analytics. Journal of Perinatology. 2021 Feb 15; 41: 675-688.
[22.] Wood MD, Boyd JG, Wood N, Frank J, Girard TD, Ross-White A, et al. The Use of NIRS and/or Non-Invasive Markers of Cerebral Perfusion in Adult Sepis Patients with Delirium: A Systematic Review. Journal of Intensive Care Medicine. 2021 Feb 3; 37(3): 408-422.