ORIGINAL ARTICLE

Correlation between Peripheral and Central Venous Blood Partial Pressure of Carbon Dioxide in Critically Ill Patients with Shock

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Objective: To determine the correlation and relationship between upper extremity peripheral and central venous blood partial pressure of carbon dioxide ($PcvCO_2$) in critically ill patients with shock.

Materials and Methods: The present study was a single center, observational study. A paired sample of upper extremity peripheral and central venous blood was taken from critically ill adult patients receiving vasopressor or inotropic drug for blood gas analysis. Correlation of carbon dioxide tension of venous blood from the two sites were determined.

Results: Thirty paired samples were obtained from 12 patients, by two medical and one surgical intensive care units, aged between 53 and 90 years who received norepinephrine infusion that ranged from 0.01 to 0.95 mcg/kg/minute actual body weight. The intraclass correlation revealed that peripheral venous carbon dioxide tension ($PpvCO_2$) was excellently correlated with $PcvCO_2$ (ICC 0.98, 95% CI 0.96 to 0.99, p<0.001). The Bland-Altman plot demonstrated mean bias of 0.2 with the limits of agreement of –5.3 to 5.8.

Conclusion: The present study revealed excellent correlation between $PpvCO_2$ and $PcvCO_2$ in critically ill patients with shock. Clinical implications of the findings require further study.

Keywords: Carbon dioxide gap; Blood gas analysis; Peripheral venous blood; Central venous blood, Shock

Received 21 June 2024 | Revised 29 December 2024 | Accepted 8 January 2025

J Med Assoc Thai 2025;108(2):94-8

Website: http://www.jmatonline.com

Adequacy of oxygen delivery during shock resuscitation is crucial. Oxygen content and cardiac output need to be assessed and interpreted to guide resuscitation. While optimizing hemoglobin level, arterial oxygen saturation can be guided by basic laboratory testing, but optimizing cardiac output is more complicated. The demand for cardiac output varies from patient to patient and by conditions. Either inadequate or excessive cardiac output can lead to catastrophic outcomes[1,2]. As a result, there is no specific reference range for guiding resuscitation.

The venous-arterial partial pressure of carbon dioxide gap (va-PCO_2 gap, va-CO_2 gap, Pv-a CO_2 gap, or CO_2 gap) refers to the difference in the partial pressure of carbon dioxide (PCO_2) between venous and arterial blood[3,4]. This gap is commonly used to assess the adequacy of cardiac output[3,4]. Ideally, venous blood should be sampled from mixed venous blood. However, central venous PCO_2 has demonstrated good agreement with mixed venous PCO_2 and is accepted to be used as a surrogate for venous PCO_2 in CO_2 gap calculations[3-8]. While obtaining central venous blood is less complicated than mixed venous blood, the use of a central venous catheter is still required. Only a few patients who have a newly developed shock would already have central venous catheter in place and the process of installing one requires time and skill. This may result in delayed treatment and cause complications. Previous studies had demonstrated various levels of correlation of several chemical components between central and peripheral venous blood[9-11]. The current study was designed to evaluate the correlation of partial pressure of carbon dioxide between central, superior vena cava ($PcvCO_2$), which receives venous

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How to cite this article:

Karnjanarachata C, Pravitharangul T, Morakul S, Theerawit P. Correlation between Peripheral and Central Venous Blood Partial Pressure of Carbon Dioxide in Critically Ill Patients with Shock. J Med Assoc Thai 2025;108:94-8.

DOI: 10.35755/jmedassocthai.2025.2.94-98-01185

blood from upper part of the body, and peripheral upper extremities venous blood ($PpvCO_2$) in critically ill patients with shock.

Materials and Methods

The protocol of this observational study was registered to the ClinicalTrials.gov Identifier: NCT03269448 and the ethical approval was provided by the Institutional Ethics Committee (Ethical Clearance Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University: ID 09-60-61).

Central and peripheral venous blood were taken from participants after written consent was obtained. In cases that the patient was not fully conscious, the consent was obtained from the patient's next of kin in accordance with the guideline established by the Institutional Ethics Committee. The patients admitted in one of three institutional intensive care units, including two medical and one surgical, older than 18 years, who were receiving vasopressor or inotropic drug at time of sample collection, with central venous catheter with tip in superior vena cava confirmed by chest radiograph and had order for venous blood sampling were included. The patients participating in other clinical trials, receiving intravenous sodium bicarbonate, receiving intravenous fluid infusion in both upper extremities, those with difficult peripheral venous blood sampling or tourniquet time for peripheral venous blood sampling over ten minutes, interval between peripheral and central venous blood sampling over ten minutes were excluded. To limit overfitting due to multiple samples from a single patient, one venous blood sampling from central venous catheter and another from upper extremity peripheral vein were taken as a paired sample once per calendar day per patient and not more than three pairs of samplings per patient.

The sampling was done by collecting an additional 1 milliliter of venous blood from the distal port of the central venous catheter and the upper extremity peripheral vein when the venous blood test was ordered by the attending physician using preset blood gas syringes and aseptic technique. Then the paired samples would be immediately sent to the hospital central laboratory for blood gas analysis (Stat Profile® Critical Care Xpress, Nova Biomedical Corporation, Waltham, MA, USA). The patient's demographic data, vital signs, dosages of vasopressor or inotropic drug, and location of peripheral blood sampling were recorded. Tourniquet time, and interval between central and peripheral sampling were self-reported by performer in minute time unit.

Table 1. Patient characteristic and demographic data (n=12)

Male; n (%)	9 (75%)
Age (years); mean±SD	77.47±12.27
Weight (kg); mean±SD	63.84±11.17
Norepinephrine dose (mcg/kg/min); median (IQR)	0.1 (0.05, 0.23)
Mean arterial pressure (mmHg); mean±SD	78.63±10.53
Heart rate (beats per minute); mean±SD	102.43±17.57
Tourniquet time (minutes); mean±SD	2.73±0.87
Interval between drawing 2 sampling site (minutes); mean±SD	3.00±1.23

SD=standard deviation; IQR=interquartile range

Initially, thirty pairs of samples were collected and analyzed for intraclass correlation coefficient (ICC) between $PpvCO_2$ and $PcvCO_2$. Thereafter, with the data from initial analyses, the actual sample size needed for the study was then calculated and data collection would continue until the calculated sample size reached.

In the present study, the ICC was employed to assess the reliability and consistency between two techniques, specifically evaluating the extent to which $PpvCO_2$ reflects $PcvCO_2$. Given that the primary focus was on examining the reliability of these measurements, the ICC provided a suitable method for quantifying their consistency. Additionally, a Bland-Altman analysis was conducted to assess the level of agreement between $PpvCO_2$ and $PcvCO_2$. A regression line was plotted to further showed relationship between PCO_2 from both sampling sites and linear regression analysis was performed. All statistical analyses were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant.

Results

Thirty paired samples from 12 patients were collected between January 2018 and March 2018 and analyzed. All characteristic and demographic data are demonstrated in Table 1. All patients were receiving norepinephrine as a vasopressor at time of sample collection. No patient had other type of vasopressor or inotropic medication. For peripheral venous blood sampling site, ten samples (33.3%) were collected from right upper extremities and 20 samples (66.6%) were collected from the left upper extremities.

After completing the pilot study of 30 paired samples, the ICC between $PcvCO_2$ and $PpvCO_2$ was

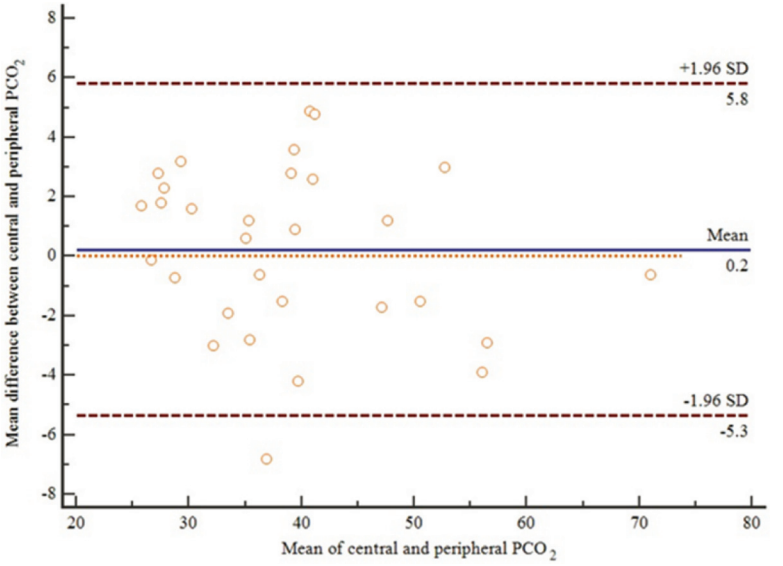

Figure 1. Bland-Altman plot.

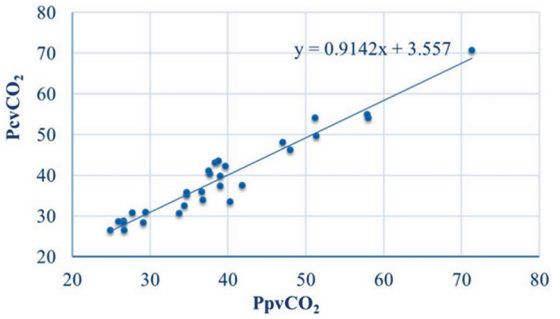

Figure 2. Relationship between peripheral and central partial pressure of carbon dioxide.

calculated and shown to be 0.98 (95% CI 0.96 to 0.99, p<0.001). The power analysis of ICC resulted in 100% power to detect an ICC of 0.98 under the alternative hypothesis when the ICC under the null hypothesis was 0.60 using an F-test with a significance level of 0.05. With satisfactory power from initial sample size, the study was concluded. The result was reported as completed. The Bland-Altman plot demonstrated a mean bias of 0.2 and limited of agreement of –5.3 to 5.8 mmHg (see Figure 1). The linear regression was performed, and prediction equation was determined as $PcvCO_2$ (in mmHg) = 0.9142 × $PpvCO_2$ (in mmHg) + 3.557 with coefficient of determination, R^2=0.93 (see Figure 2).

Discussion

In the present study, a strong correlation between $PpvCO_2$ and $PcvCO_2$ was observed. An ICC of 0.98 underscores the high consistency between the two measurements, suggesting that $PpvCO_2$ may serve as a potential surrogate for $PcvCO_2$.

Central venous pressure once recommended as a component of early sepsis resuscitation goals, now became less apparent[12]. Moreover, thoroughly selected peripheral venous catheter and well-designed leakage management protocol made peripheral venous route a considered safe alternative for initial vasoactive or inotropic drug administration in patients[13]. With all the aforementioned, less patients would have superior vena cava central venous catheter in place.

Considering installing a central venous catheter for only inotropic and vasoactive drugs can be postponed. On the other hand, assessing the adequacy of cardiac output should not be delayed. The CO_2 gap, with less interference from microcirculation dysfunction, became a familiar tool for intensivists as a surrogate for adequacy of cardiac output. With less need to install a central venous catheter, installing the catheter only for the initial central venous blood sampling in patients with no other indication is time-consuming and may pose additional and unnecessary risks to the patient. Peripheral venous blood, with less complication from blood sampling and much easier to access, was shown to have various level of correlation in chemical components and may be a potential surrogate for central venous blood for partial pressure of carbon dioxide.

Using $PpvCO_2$ as surrogate for $PcvCO_2$ may be tempting. However, with a wide range of limits of

agreement (–5.3 to 5.8 mmHg), its usage for CO_2 gap interpretation, with the narrow common cutoff of 6 mmHg, may be limited. This may indicate that upper extremities are still too upstream from the superior vena cava, and venous blood from more downstream site may better reflect the central venous blood, or the location of peripheral blood sampling should be more specific to narrow the limits of agreement.

Limitation

Limitations should be considered when interpreting the results. First, since one patient could have more than one pair of blood samples, the effect of the subject might affect the results of the present study. To limit the influence of this variation, all patients were limited to giving a maximum of three pairs of samples. Second, to avoid patient discomfort, the patients with expected difficult peripheral venous blood sampling, which were common in critically ill patients, were excluded. This group of patients that may have severe edema, severe peripheral vasoconstriction, and high dose of vasopressor, were more likely to represent more serious conditions. Moreover, defining expected difficult peripheral venous blood sampling was according to subjective judgment of the performer with no standardized criteria. The present study included all vasopressors and inotropes; however, all the samples were from patients receiving norepinephrine, which was the most commonly used vasopressor in institutional practice. Although, this was not unexpected, it may limit the generalizability of the findings. Finally, long tourniquet time or long sampling process might have changed chemical components in the sample. Limiting tourniquet time and sampling process to 10 minutes should have minimized the effects.

Conclusion

The present study revealed excellent correlation between $PpvCO_2$ and $PcvCO_2$ in critically ill patients with shock.

What is already known about this topic?

Carbon dioxide gap is one of resuscitation goals. To calculate the gap, central venous catheter for central venous blood sampling is needed. The correlation of various chemical components of venous blood between central and peripheral compartment had been demonstrated.

What does this study add?

This study demonstrates excellent correlation between $PpvCO_2$ and $PcvCO_2$ in critically ill patients with shock but with wide limits of agreement range.

Acknowledgement

Departmental and institutional funding.

Conflict of interest

The authors have no conflict of interest to declare.

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