ORIGINAL ARTICLE

Concordance of CO_2 gaps measured using peripheral and central venous blood in patients diagnosed with septic shock

Concordancia de las brechas de CO_2 medidas en sangre venosa periférica y central en pacientes diagnosticados de choque séptico

Erdem Yalcinkaya[1], Umut Sabri Kasapoglu[1], Huseyin Arikan[1], Nazım Onur Sahin[1], Betul Yildiz[1], Esra Tekin[2], Aybuke Selcuk[1], Emel Eryuksel[1], and Sait Karakurt[1]*

[1]Department of Pulmonary and Critical Care Medicine, Marmara University School of Medicine; [2]Department of Critical Care Medicine, Marmara University Hospital. Istanbul, Turkiye

Abstract

Objective: *This study evaluates the venous-arterial CO_2 difference ($Pv\text{-}aCO_2$) from peripheral venous blood ($Pv\text{-}aCO_2p$) as a less invasive alternative to central venous $Pv\text{-}aCO_2$ for assessing tissue perfusion in septic shock.* **Methods:** *A prospective, single-center study included 54 septic shock patients with central venous catheters placed within 24 h of intensive care unit admission. Blood samples from arterial, central venous, and peripheral venous sources were analyzed. Correlation analyses and Bland-Altman plots were used to assess agreement between $Pv\text{-}aCO_2p$ and central $Pv\text{-}aCO_2$.* **Results:** *Patients had a mean age of 70 years, and 51.9% were male. The median SOFA score was 8.5, and the mean APACHE-II score was 22.7. The $Pv\text{-}aCO_2p$ gap was 8 mmHg, whereas the central $Pv\text{-}aCO_2$ gap was 6 mmHg. A moderate correlation was found between $Pv\text{-}aCO_2p$ and central $Pv\text{-}aCO_2$ ($r = 0.593$, $p < 0.001$), with stronger correlations observed in patients with arterial lactate ≥2 mmol/L ($r = 0.673$) and hemoglobin <8 g/dL ($r = 0.625$). Bland-Altman analysis revealed a mean difference of 8.278 mmHg between arterial and peripheral pCO_2.* **Conclusions:** *Peripheral $Pv\text{-}aCO_2p$ correlates well with central $Pv\text{-}aCO_2$ and can serve as a less invasive alternative for assessing tissue perfusion in septic shock patients. It offers practical utility when central venous access is not available, aiding in early clinical decisions.*

Keywords: *$Pv\text{-}aCO_2$. Tissue perfusion. Septic shock. Veno-arterial CO_2 difference. Hemodynamic monitoring.*

Resumen

Objetivo: *Evaluar la diferencia venosa-arterial de CO_2 ($Pv\text{-}aCO_2$) medida en sangre venosa periférica ($Pv\text{-}aCO_2p$) como una alternativa menos invasiva a la $Pv\text{-}aCO_2$ venosa central para evaluar la perfusión tisular en el choque séptico.* **Métodos:** *Estudio prospectivo, unicéntrico, que incluyó 54 pacientes con choque séptico y catéter venoso central colocado dentro de las primeras 24 horas de ingreso a la UCI. Se analizaron muestras de sangre arterial, venosa central y venosa periférica. Se realizaron análisis de correlación y gráficos de Bland-Altman para evaluar la concordancia entre la $Pv\text{-}aCO_2p$ y la $Pv\text{-}aCO_2$ central.* **Resultados:** *Los pacientes tenían una edad promedio de 70 años y el 51.9% eran hombres. La mediana del puntaje SOFA fue de 8.5 y el puntaje APACHE-II promedio fue de 22.7. La brecha de $Pv\text{-}aCO_2p$ fue de 8 mmHg, mientras que la brecha de $Pv\text{-}aCO_2$ central fue de 6 mmHg. Se encontró una correlación moderada entre la $Pv\text{-}aCO_2p$ y la $Pv\text{-}aCO_2$ central ($r = 0.593$; $p < 0.001$), con correlaciones más fuertes en los pacientes con lactato en sangre arterial ≥ 2 mmol/l ($r = 0.673$) y hemoglobina < 8 g/dl ($r = 0.625$). El análisis de Bland-Altman reveló una diferencia promedio de 8.278 mmHg entre la pCO_2*

***Correspondence:**
Erdem Yalcinkaya
E-mail: drerdemyalcinkaya@gmail.com

Date of reception: 25-11-2024
Date of acceptance: 07-04-2025
DOI: 10.24875/CIRU.24000617

Cir Cir. 2025;93(6):613-619
Contents available at PubMed
www.cirugiaycirujanos.com

en sangre arterial y en sangre periférica. **Conclusiones:** *La Pv-aCO$_2$p se correlaciona bien con la Pv-aCO$_2$ central y puede servir como una alternativa menos invasiva para evaluar la perfusión tisular en pacientes con choque séptico. Es de utilidad práctica cuando no se dispone de acceso venoso central, ayudando en las decisiones clínicas tempranas.*

Palabras clave: *Pv-aCO$_2$. Perfusión tisular. Choque séptico. Diferencia venosa-arterial de CO$_2$. Monitoreo hemodinámico.*

Introduction

Early identification of tissue hypoperfusion and prompt, effective resuscitation are crucial for the successful management of patients with septic shock[1]. The latest guidelines from the Surviving Sepsis Campaign (SSC) for managing patients with septic shock emphasize hemodynamic support using a structured protocol of fluid administration and vasopressor therapy. The objective is to enhance tissue perfusion and fulfill tissue oxygen requirements[2]. The veno-arterial partial pressure of carbon dioxide difference (Pv-aCO$_2$ or ΔpCO_2) has been suggested as a marker for tissue hypoperfusion[3]. These findings have immediate clinical relevance, as they can alter the treatment strategy at the patient's bedside. Under physiological conditions, the Pv-aCO$_2$ typically does not exceed 0.8 kPa (6 mmHg) and reflects the adequacy of venous blood flow and cardiac output (CO)[4].

Several researchers have emphasized a linear relationship between Pv-aCO$_2$ determined from mixed or central venous blood[5,6]. However, the studies conducted so far have been performed in an intensive care setting using central venous catheters. Evaluating the CO$_2$ gap using peripheral venous blood samples outside/inside the intensive care environment is important for its potential to aid daily practice as well. The objective of this study was to determine whether a linear correlation exists between Pv-aCO$_2$ measured from peripheral venous blood (Pv-aCO$_2$p) and Pv-aCO$_2$ measured from central venous blood.

Methods

We conducted a prospective, observational single-center study at Level-3 medical ıntensive care unit (ICU) of Marmara University Hospital, focusing on patients diagnosed with septic shock according to SSC: International Guidelines for Management of Sepsis and Septic Shock 2021 recommendations (e.g., for patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 h of resuscitation) who were admitted between December 2023 and June 2024[7].

The study specifically targeted patients who had a central venous catheter inserted within the first 24 h following their diagnosis and with at least one site of peripheral venous access. Patients were excluded if they were under 18 years of age, or if they presented with trauma, burns, thrombosis, or other contraindications to jugular vein catheterization, were undergoing extracorporeal membrane oxygenation, continous renal replacement therapy, or extracorporeal CO$_2$ removal therapy, or had a prior diagnosis of congestive heart failure and patients with < 24 h of ICU stay (Fig. 1).

Patient management

All evaluations were performed within 24 h of identifying septic shock in eligible ICU patients. Peripheral blood samples were obtained using a needle cannula in one of the upper extremities, typically in the ICU, with a tourniquet applied. Simultaneously, central venous blood samples were collected under ultrasound guidance following the placement of an internal jugular vein catheter. Patients were thoroughly assessed, with blood samples taken for complete blood count, arterial blood gas analysis, venous blood gas analysis, metabolic panel, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and calculation of Acute Physiology and Chronic Health Evaluation-II (APACHE-II) and the Sequential Organ Failure Assessment (SOFA) scores.

Consent for the hospital's clinical management was requested from each patient, ensuring alignment with their clinical condition. Data were anonymously collected and stored in secure databases accessible solely to investigators specified in the protocol.

Calculation of the venous-to-arterial CO$_2$ tension difference

Blood samples were collected from central and peripheral veins, as well as arterial blood, to determine CO$_2$ values in a cohort of 54 patients. The v-a CO$_2$ gap was calculated by subtracting the arterial pCO$_2$

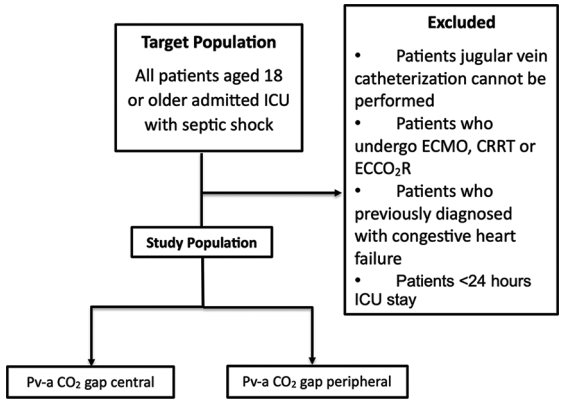

Figure 1. *Flowchart of the study.*

values from the pCO_2 values obtained from the central and peripheral venous blood samples.

Outcomes

The primary aim was the evaluation of the linear correlation and agreement between the Pv-aCO_2 measured with peripheral venous and central venous blood. The secondary objective of the study was to identify patient subgroups or specific laboratory parameters associated with a potentially stronger correlation. To accomplish this, we aimed to stratify patients based on their mean arterial pressures, heart rates, mottling scores, capillary refilling times (CRT), arterial lactate levels, APACHE-II scores, SOFA scores, NT-proBNP values, as well as the type and dosage of vasopressors initiated at the time of septic shock diagnosis.

Statistical analysis

To determine the sample size for this study, literature data were utilized (with a significance level of $\alpha = 0.05$ and power = 90%), leading to the inclusion of a total of 50 patients, with calculations performed using G-Power version 3.1.9.7.8.

The data analysis was conducted using IBM Statistical Package for the Social Sciences Statistics Version 23. Normality of the data distribution was assessed using the Shapiro–Wilk test. Analysis results were presented as mean ± standard deviation or median (minimum–maximum). The paired samples t-test was employed for normally distributed data in two dependent groups, whereas the Wilcoxon test was used for data that did not follow a normal distribution. Pearson correlation coefficient was used to examine the relationship between normally distributed continuous parameters, whereas Spearman's ρ correlation coefficient was employed for non-normally distributed continuous parameters.

In the comparative analysis of methods, the robust Bland-Altman analysis was utilized, renowned for its effectiveness in assessing agreement between two measurement techniques or observers. This method offers insights into the agreement and potential biases between two quantitative measurements, contributing valuable information on the degree of agreement and any systematic differences.

Furthermore, the intra-class correlation coefficient (ICC) was utilized to assess the concordance of pCO_2 differences across regions. The ICC is a widely used statistical measure for evaluating the agreement or consistency between multiple measurements or observations. Specifically, in the context of regional PCO_2 differences, ICC sheds light on the overall consistency of measurements across different regions.

By employing these rigorous statistical methods and adhering to established significance levels, the study ensures robustness and reliability in its findings, thereby contributing to the advancement of knowledge in the field and facilitating informed decision-making in clinical practice.

The significance level of $p < 0.050$ was established to determine statistical significance, aligning with conventional practices in hypothesis testing. This threshold ensures that findings with a p-value below 0.050 are considered statistically significant, indicating a high likelihood of rejecting the null hypothesis.

Results

Among the participants, 28 (51.9%) were male. Diabetes mellitus was present in 12 (22.2%) individuals, whereas 22 (40.7%) had hypertension. Coronary arterial disease was found in 9 (16.7%) participants, and chronic renal failure was reported in 12 (22.2%) individuals. The mean age of the participants was 70 ± 15 years. The mean SOFA score was 8.52 ± 3.65, and the mean APACHE score was 22.7 ± 5.89. The median CRT was determined to be 3 (1-8) s. The median mottling score was 0 (0-5). Patients' characteristics and baseline laboratory findings are shown in table 1.

Out of 54 determinations, the mean difference in PCO_2 values obtained from arterial and central regions (Pv-aCO_2) was found to be 6.81, with this difference being statistically significant from zero ($p < 0.001$). The lower limit of agreement was −0.848, whereas the upper limit was 14,478. In addition, a statistically significant

Table 1. Main characteristics, laboratory results, and clinical scores of the study population on ICU admission

Characteristics	Patients
Male sex, n (%)	28 (51.9)
Age (mean value ± SD)	70 ± 15
Comorbid diseases	
DM, n (%)	12 (22.2)
HT, n (%)	22 (40.7)
CAD, n (%)	9 (16.7)
CKD, n (%)	12 (22.2)
COPD, n (%)	4 (7.4)
Hematologic malignancy, n (%)	4 (7.4)
Solid tumor, n (%)	16 (29.6%)
Mean arterial pressure (mmHg), (mean value ± SD)	71.15 ± 10.54
Heart rate (bpm), (mean value ± SD)	96.11 ± 20.88
SOFA score, (median [25-75])	8.5 (1-17)
APACHE-II score, (mean value ± SD)	22.7 ± 5.89
NT-ProBNP (pg/mL), (median [25-75])	4034 (10-35000)
Hgb (g/dL), (mean value ± SD)	9.06 ± 2.05
Htc (%), (mean value ± SD)	27.7 ± 6.36
Noradrenaline dose (mcg/kg/min), (median [25-75])	0.18 (0.02-1)
Capillary refilling time (seconds), (median [25-75])	3 (1-8)
Mottling score, (median [25-75])	0 (0-5)

ICU: intensive care unit; SD: standard deviation; DM: diabetes mellitus; HT: hypertension; CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; SOFA: the sequential organ failure assessment; APACHE-II: acute physiology and chronic health evaluation-II; Hgb: hemoglobin; Htc: hematocrit; NT-ProBNP: n-terminal pro-B-type natriuretic peptide.

Table 2. Blood gas analysis of the study population

Parameter	Arterial	Central	Peripheral
pH, (min-max)	7.45 (7.06-7.74)	7.4 (6.98-7.65)	7.38 (7.02-7.58)
pO_2, mmHg, (min-max)	92.5 (51-289)	41 (24-137)	36 (15-104)
pCO_2, mmHg, (min-max)	36 (14-73)	43.5 (20-84)	46 (23-81)
HCO_3, mEq/L, (min-max)	25.1 (8.5-38.8)	25.05 (9.9-39.2)	24.45 (9-38.1)
BE, (min-max)	0.6 (−22.5-15.5)	1.15 (−18.9-16.5)	1.65 (−19.3-13.9)
Lactate, mmol/L, (min-max)	1.9 (0.3-8.6)	2.05 (0.1-14.8)	2.2 (0.2-13.7)
sO_2, %, (min-max)	98 (80-100)	70.72 ± 11.98	60 (24-95)
Pv-aCO_2 (mmHg), (Median [25-75])		6.81 ± 3.91	
Pv-aCO_2p (mmHg), (Median [25-75])		8.27 ± 4.60	

Table 3. Analysis results of Bland-Altman and examination of agreement between Pv-aCO_2 and Pv-aCO_2p

Variable	Median difference (95% CI)	SD	ICC (95% CI)	p
Pv-aCO_2	6.815 (5.75-7.882)	3.910	0.942 (0.902-0.966)	< 0.001
Pv-aCO_2p	8.278 (7.02-9.53)	4.595	0.914 (0.856-0.949)	< 0.001

CI: confidence interval; SD: standard deviation; ICC: intra-class correlation coefficient.

strong agreement was observed between arterial and central regions (ICC = 0.942; p < 0.001). Similarly, the mean difference in pCO_2 values obtained from arterial and peripheral regions (Pv-aCO_2p) was 8.27, with this difference being statistically significant from zero (p < 0.001) (Table 2). The lower limit of agreement was -0.728, whereas the upper limit was 17,283. Furthermore, a statistically significant strong agreement was observed between arterial and peripheral regions (ICC = 0.914; p < 0.001) (Table 3). These findings indicate a consistent and reliable agreement between pCO_2 measurements taken from arterial and central regions, as well as between arterial and peripheral regions. This strong agreement highlights the robustness of comparing pCO_2 values across different regions (Fig. 2).

Among individuals with arterial lactate levels of 2 or higher, there was a strong positive correlation between Pv-aCO_2 and Pv-aCO_2p (r = 0.673, p < 0.001). Similarly, individuals with NT-proBNP values < 2000, Hgb values < 8, and noradrenaline values < 0.1 exhibited high positive correlations between Pv-aCO_2 and Pv-aCO_2p values (r = 0.637, p = 0006; r = 0.625, p = 0.004; r = 0.620, p = 0.032, respectively) (Table 4).

Discussion

Our study focused on analyzing the Pv-aCO_2 gap obtained from central venous catheters and comparing it to the Pv-aCO_2p gap obtained from peripheral venous catheters. The outcomes of our study reveal useful insights into the relationship between these two types of venous access methods and their corresponding Pv-aCO_2 measurements. The research showed a statistically significant relationship between the Pv-aCO_2 gaps measured at central and peripheral venous sites, showing that measurements obtained from peripheral venous access are similarly reflective of those obtained from central venous access.

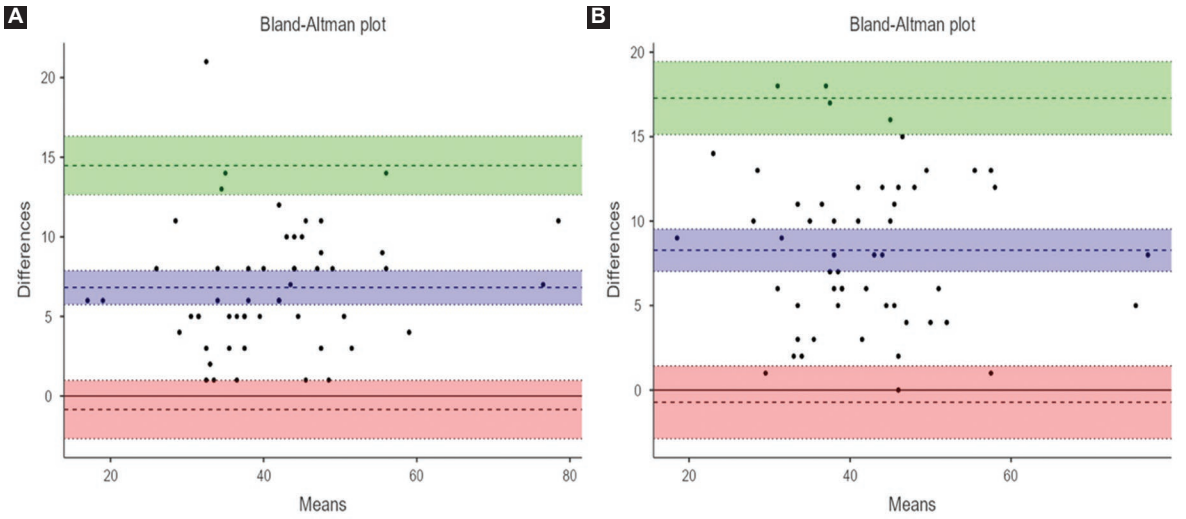

Figure 2. *The Bland-Altman plot comparison shows the agreement between two measurement methods. Each plot presents differences in measurements on the y-axis against their mean values on the x-axis, and includes limits of agreement, typically set at ± 1.96 standard deviations from the mean difference.* **A:** *the mean difference of PCO values obtained from arterial and central regions was found to be 6.815, with a statistically significant difference from 0 ($p < 0.001$). In this plot, the lower limit of agreement was approximately –0.848, and the upper limit was about 14.478. Most data points lie within these limits, indicating a strong agreement between the arterial and central regions. The shaded areas (green for the upper limit and red for the lower limit) emphasize the range within which the majority of measurements fall, with only a few outliers observed. The intraclass correlation coefficient (ICC) was 0.942, showing a statistically significant and very strong agreement ($p < 0.001$).* **B:** *which illustrates the comparison between arterial and peripheral regions, the mean difference of PCO values was calculated as 8.278, also showing a statistically significant difference from 0 ($p < 0.001$). Here, the lower limit of agreement was approximately –0.728, and the upper limit was around 17.283. While most data points again fall within the shaded limits, the wider spread indicates a slightly greater variability in measurements between the arterial and peripheral regions compared to the central region. Nevertheless, a very strong agreement was still observed between the arterial and peripheral regions, with an ICC of 0.914 ($p < 0.001$), underscoring the statistically significant agreement in this comparison as well.*

This finding has significant therapeutic effects, as central venous access, despite its frequent utilization for precise hemodynamic monitoring, is associated with risks such as infection, thrombosis, and pneumothorax, especially in critically ill individuals[8]. On the other hand, peripheral venous access is a minimally invasive treatment that is easier to perform and has a lower risk of problems. If the measurements of the peripheral Pv-aCO_2p gap show a strong correlation with those obtained via central venous access, as shown by our findings, then peripheral venous sampling could be considered a feasible option in cases where central venous access is not possible or considered risky.

The practical applications of using peripheral venous Pv-aCO_2p gap measurements as a substitute for central venous measurements are numerous. In emergency settings or resource-limited environments where central venous catheterization may not be easily accessible or feasible, peripheral venous sampling can be used to effectively monitor tissue perfusion and provide guidance for vital actions. Furthermore, this approach can be especially beneficial for patients who are unable to have central venous access due to anatomical or physiological limitations.

Another crucial factor to take into consideration is the potential impact on patient comfort and overall treatment. Peripheral venous catheterization is characterized by lower pain, better tolerance, and the ability to be performed with fewer assets and staff when compared to central venous catheterization[9]. This has the potential to improve patient outcomes by decreasing problems associated with procedures and enabling faster implementation of monitoring, particularly in urgent situations such as septic shock.

The strong correlations shown in our study have not been thoroughly investigated in previous studies, and the provided values have been isolated from statistical analysis[10,11]. Although our research provides valuable data in this relatively unexplored field, larger-scale investigations are necessary to validate our findings and identify specific clinical conditions in which peripheral venous sampling might effectively replace a central venous sample.

Various clinical settings are involved in managing septic patients, particularly in the initial stages of the syndrome, including pre-hospital medicine, emergency medicine, and hospital medicine. In these contexts, obtaining a central venous line may pose

Table 4. Comparison of pCO_2 differences in regions by groups

Clinical variable	Pv-aCO2p (mmHg)		Pv-aCO2 (mmHg)		r/p	Test statistic	p
	Mean value ± SD	Median (Min-Max)	Mean value ± SD	Median (Min-Max)			
Arterial lactate level, mmol/L							
≥ 2	8.1 ± 4.67	7 (2-18)	6.21 ± 3.34	6 (1-14)	0.433/0.019***	2.316	0.028*
< 2	8.48 ± 4.59	9 (0-18)	7.52 ± 4.45	8 (1-21)	0.673/< 0.001***	1.313	0.202*
NT-proBNP, pg/mL							
< 2000	7.18 ± 4.08	7 (1-13)	7.35 ± 4.7	6 (1-21)	0.637/0.006****	–0.032	0.975**
≥ 2000	9.22 ± 4.67	9.5 (0-18)	6.94 ± 3.51	6.5 (1-14)	0.516/0.003***	3.108	0.004*
Hgb, g/dL							
< 8	7.21 ± 3.74	7 (2-14)	5.0 ± 3.09	5 (1-12)	0.625/0.004***	3.2	0.005*
≥ 8	8.86 ± 4.95	9 (0-18)	7.8 ± 3.99	8 (1-21)	0.545/0.001****	–1.107	0.268**
HR, beats/min							
< 100/min	8.87 ± 4.76	10 (0-18)	6.71 ± 3.36	6 (1-14)	0.600/< 0.001***	3.134	0.004*
≥ 100/min	7.27 ± 4.32	6.5 (1-17)	6.82 ± 4.69	5.5 (1-21)	0.562/0.007****	–0.328	0.743**
Noradrenaline dose (mcg/kg/dak)							
< 0.1	5.75 ± 3.47	6 (1-13)	5.33 ± 3.17	5 (1-11)	0.620/0.032***	0.497	0.629*
≥ 0.1	9.18 ± 4.93	10 (0-18)	7.21 ± 4.36	6 (1-21)	0.540/0.001***	2.524	0.017*

*Paired two-sample t-test.
**Wilcoxon test.
***Pearson correlation coefficient.
****Spearman's rho correlation coefficient.
NT-proBNP: n-terminal pro-B-type natriuretic peptide; Hgb: hemoglobin; HR: heart rate; SD: standard deviation.

challenges. Early assessment of the CO_2 gap could prompt earlier initiation of inotropic medications, which have been demonstrated to be safely administered via peripheral venous access[12].

To the best of our knowledge, only two studies in the literature have explored the association between standard Pv-aCO_2 and Pv-aCO_2p. Gao et al.[11] reported a correlation of 90%, and Orso et al.8 reported a correlation of 70%.

In the present study, we observed a direct correlation between Pv-aCO_2 and Pv-aCO_2p. The ICC value of 0.914 underscores the strong consistency and reliability of these measurements, affirming their robust agreement and reliability in clinical assessment.

Beyond the primary findings regarding the correlation between Pv-aCO_2 and Pv-aCO_2p gaps, our study revealed several additional correlations that hold important clinical implications and have not been previously addressed in the literature. Among patients with arterial lactate levels of 2 mmol/L or higher, we observed a robust positive correlation between Pv-aCO_2 and Pv-aCO_2p ($r = 0.673$, $p < 0.001$). Elevated lactate is often associated with impaired tissue oxygenation and metabolic stress, yet our findings suggest that even in this physiologically challenging condition, peripheral venous measurements remain reliably reflective of central venous values[13]. This could potentially offer a safer, less invasive alternative for hemodynamic monitoring in patients where elevated lactate levels would traditionally necessitate central venous access.

In addition, in patients with NT-proBNP levels under 2000, hemoglobin values below 8 g/dL, and noradrenaline doses < 0.1 μg/kg/min, we found similarly high positive correlations between Pv-aCO_2 and Pv-aCO_2p ($r = 0.637$, $p = 0.006$; $r = 0.625$, $p = 0.004$; $r = 0.620$, $p = 0.032$, respectively). The ability of peripheral Pv-aCO_2p measurements to align with central values across these diverse clinical markers reinforces its potential role as a practical alternative, particularly in situations where central venous access may be risky or infeasible.

Furthermore, our research revealed a statistically significant moderate positive correlation between capillary refill time and mottling score ($p < 0.001$), which are both simple bedside measurements of peripheral perfusion[13,14]. The correlation between these two non-invasive indicators enhances the significance of their combined utilization in evaluating the degree of circulatory failure in critically ill patients.

The results of our study show that peripheral venous measures can be reliably accurate under a variety of clinical situations, including those marked by increased lactate levels, decreased hemoglobin levels, impaired cardiac function, and the administration of low doses of vasopressors. This emphasizes the broader relevance

of peripheral venous sampling as a less invasive, but accurate option for central venous access in critically ill patients. Our investigation offers new insights into the correlations between Pv-aCO_2 and Pv-aCO_2p in different conditions. This gives a basis for future research to assess and expand upon these findings, potentially leading to modifications in the approach to venous sampling and hemodynamic monitoring in critical care.

Our study presents several limitations. First, it is a single-center study, so the results might not universally apply. Second, we did not measure cardiac index, and we excluded patients with a prior diagnosis of heart failure from our study to avoid potential confusion with cardiac dysfunction that could develop secondary to sepsis. Finally, our patient group received only single-agent vasopressor therapy with noradrenaline. Therefore, our results should be validated in future studies with a larger sample size.

Conclusion

The significant linear correlation observed between Pv-aCO_2 levels from central and peripheral venous catheters in patients with septic shock underscores the potential benefits of using peripheral venous access. This approach offers a less invasive alternative for Pv-aCO_2 measurement, simplifying patient management while still providing valuable physiological insights. Further controlled clinical trials are necessary to explore whether Pv-aCO_2p could be utilized in broader clinical settings beyond ICUs, aiming to assess whether CO adequately meets tissue metabolic demands during early sepsis stages.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

The authors acknowledge and thank the American Thoracic Society's Methods in Epidemiologic, Clinical and Operations Research (MECOR) Program and MECOR Turkey Level 2 Faculty; Zuhal Karakurt, Sinem Gungor, Ozge Yilmaz.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study. The protocol for this study was approved by the Marmara University School of Medicine Ethics Committee (Approval No: 09.2023.566, date: 07.04.2023). The study was carried out in strict adherence to the principles outlined in the Declaration of Helsinki.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1795-815.
2. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43:304-77.
3. Bitar ZI, Maadarani OS, El-Shably AM, Elshabasy RD, Zaalouk TM. The forgotten hemodynamic (PCO_2 gap) in severe sepsis. Crit Care Res Pract. 2020;2020:9281623.
4. Johnson BA, Weil MH. Redefining ischemia due to circulatory failure as dual defects of oxygen deficits and of carbon dioxide excesses. Crit Care Med. 1991;19:1432-8.
5. Ho K, Harding R, Chamberlain J. A comparison of central venous-arterial and mixed venous-arterial carbon dioxide tension gradient in circulatory failure. Anaesth Intensive Care. 2007;35:695-701.
6. Mallat J, Lazkani A, Lemyze M, Pepy F, Meddour M, Gasan G, et al. Repeatability of blood gas parameters, PCO_2 gap, and PCO_2 gap to arterial-to-venous oxygen content difference in critically ill adult patients. Medicine (Baltimore). 2015;94:e415.
7. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47:1181-247.
8. Orso D, Molinari C, Bacchetti G, Zanini V, Montanar V, Copetti R, et al. Correlation and agreement between the CO_2 Gap obtained from peripheral venous blood and from mixed venous blood in mechanically ventilated septic patients. Semin Cardiothorac Vasc Anesth. 2024;28:18-27.
9. Chua CK, Le Guen M, Lim R, Udy A. Using central venous pressure waveform to confirm the placement of an internal jugular central venous catheter in the intensive care unit. Aust Crit Care. 2024;37:628-31.
10. Waxman MJ, Schechter-Perkins EM. Peripheral intravenous catheters are preferable for emergency department patients with septic shock. Ann Emerg Med. 2024;83:607-8.
11. Gao W, Zhang Y, Ni H, Zhang J, Zhou D, Yin L, et al. Prognostic value of difference between peripheral venous and arterial partial pressure of carbon dioxide in patients with septic shock: a pilot study. Nan Fang Yi Ke Da Xue Xue Bao. 2018;38:1312-7.
12. Tran QK, Mester G, Bzhilyanskaya V, Afridi LZ, Andhavarapu S, Alam Z, et al. Complication of vasopressor infusion through peripheral venous catheter: a systematic review and meta-analysis. Am J Emerg Med. 2020;38:2434-43.
13. Liu S, Yang T, Jiang Q, Zhang L, Shi X, Liu X, et al. Lactate and lactylation in sepsis: a comprehensive review. J Inflamm Res. 2024;17:440517.
14. Gutierrez-Zarate D, Rosas-Sanchez K, Zaragoza JJ. Clinical evaluation of peripheral tissue perfusion as a predictor of mortality in sepsis and septic shock in the intensive care unit: systematic review and meta-analysis. Med Intensiva (Engl Ed). 2023;47:697-707.