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RESEARCH ARTICLE

The relation of lactate level and carbon dioxide pressure discrepancies between transcutaneous and arterial measurements

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ABSTRACT

The relation of lactate level and carbon dioxide pressure discrepancies between transcutaneous and arterial measurements

Introduction: *Partial carbondioxide pressure of the arterial blood ($PaCO_2$) is used to evaluate alveolar ventilation. Transcutaneous carbon dioxide pressure ($TcCO_2$) monitoring has been developed as a non-invasive (NIV) alternative to arterial blood gas analysis (ABG). Studies have shown that decreased tissue perfusion leads to increased carbondioxide (CO_2). The use of transcutaneous capnometry may be unreliable in patients with perfusion abnormalities. In this study, we aimed to evaluate the relation between $TcCO_2$-$PaCO_2$ and lactate level which is recognized as a marker of hypoperfusion.*

Materials and Methods: *In this prospective cohort study in critical care patients with hypercapnic respiratory failure ($PaCO_2$ ≥45 mmHg) who received NIV between April 2019 and January 2020 in the intensive care unit were enrolled in the study. Patients' simultaneously measured $TcCO_2$ and $PaCO_2$ values of hypercapnic patients were recorded. Each paired measurement was categorized into two groups; normal lactate (<2 mmol/L) and increased lactate (≥2 mmol/L).*

Results: *A total of 116 paired $TcCO_2$ and $PaCO_2$ measurements of 29 patients were recorded. Bland-Altman analysis showed the mean bias between the $TcCO_2$ and $PaCO_2$ and 95% limits of agreement (LOA) in all measurements (1.75 mmHg 95% LOA -3.67 to 7.17); in the normal lactate group (0.66 mmHg 95% LOA -1.71 to 3.03); and in the increased lactate group (5.17 mmHg 95% LOA -1.63 to 11.97). The analysis showed a correlation between lactate level and the difference between $TcCO_2$ and $PaCO_2$ (r= 0.79, p< 0.001) and a negative correlation between mean blood pressure and the difference between $TcCO_2$ and $PaCO_2$ (r= -0.54, p= 0.001). Multiple regression analysis results showed that lactate level was independently associated with increased differences between $TcCO_2$ and $PaCO_2$ (Beta= 0.875, p< 0.001)*

Conclusion: *$TcCO_2$ monitoring may not be reliable in patients with increased lactate levels. $TcCO_2$ levels should be checked by ABG analysis in these patients.*

Key words: *Transcutaneous carbondioxide; lactate; arterial blood gases; hypercapnia*

ÖZ

Transkütanöz ve arteriyel ölçümler arasındaki laktat düzeyi ile karbondioksit basıncı ilişkisi

Giriş: *Alveoler ventilasyonun değerlendirilmesinde arteriyel kanın kısmi karbondioksit basıncı ($PaCO_2$) kullanılır. Transkütanöz karbondioksit basıncı ($TcCO_2$) izlemesi, arteriyel kan gazı analizine (ABG) non-invaziv (NİV) bir alternatif olarak geliştirilmiştir. Çalışmalar azalan doku perfüzyonunun karbondioksitin (CO_2) artmasına yol açtığını göstermiştir. Perfüzyon anormallikleri olan hastalarda transkütanöz kapnometrinin kullanımı güvenilmez olabilir. Çalışmamızda hipoperfüzyonun belirteci olarak kabul edilen laktat düzeyi ile $TcCO_2$-$PaCO_2$ arasındaki ilişkiyi değerlendirmeyi amaçladık.*

Materyal ve Metod: *Bu prospektif kohort çalışmada yoğun bakım ünitesinde Nisan 2019 ile Ocak 2020 arasında NİV alan hiperkapnik solunum yetmezliği olan ($PaCO_2$ ≥45 mmHg) yoğun bakım hastaları çalışmaya dahil edildi. Hastaların eş zamanlı ölçülen $TcCO_2$ ve $PaCO_2$ değerleri kaydedildi. Her eşleştirilmiş ölçüm normal laktat (<2 mmol/L) ve artmış laktat (≥2 mmol/L) olmak üzere iki gruba ayrıldı.*

Bulgular: *Toplam 29 hastanın 116 eşleştirilmiş $TcCO_2$ ve $PaCO_2$ ölçümü kaydedildi. Bland-Altman analizi, tüm ölçümlerde $TcCO_2$ ve $PaCO_2$ arasındaki ortalama sapmayı ve %95 uyum limitlerini (LOA) gösterdi (1,75 mmHg %95 LOA -3,67 ile 7,17); normal laktat grubunda (0,66 mmHg %95 LOA -1,71 ile 3,03); ve laktat artışı olan grupta (5,17 mmHg %95 LOA -1,63 ile 11,97). Analiz, laktat düzeyi ile $TcCO_2$ ve $PaCO_2$ arasındaki fark (r= 0,79, p< 0,001) arasında pozitif bir korelasyon ve ortalama kan basıncı ile $TcCO_2$ ve $PaCO_2$ arasındaki fark (r= -0,54, p= 0,001) arasında negatif bir korelasyon gösterdi. Çoklu regresyon analizi sonuçları, laktat seviyesinin bağımsız olarak $TcCO_2$ ve $PaCO_2$ arasındaki artan farklarla ilişkili olduğunu gösterdi (Beta= 0,875, p< 0,001).*

Sonuç: *Laktat düzeyi yüksek olan hastalarda $TcCO_2$ takibi güvenilir olmayabilir. Bu hastalarda ABG analizi ile $TcCO_2$ düzeylerine bakılmalıdır.*

Anahtar kelimeler: *Transkütan karbondioksit; laktat; arter kan gazı; hiperkapni*

INTRODUCTION

Partial carbon dioxide pressure ($PaCO_2$) is used as an essential parameter in evaluating the adequacy of alveolar ventilation. Different pathophysiological conditions such as increased dead space, reduced respiratory drive, and increased work of breathing promote increased $PaCO_2$ (1,2). Arterial blood gas (ABG) is considered the gold standard for assessing $PaCO_2$ level. Patients with the conditions described above, especially those receiving non-invasive (NIV) or invasive mechanical ventilation support, need frequent ABG monitoring. However, it is a painful procedure and carries a potential risk for bleeding, hematoma and thrombosis (3,4). These conditions have led to the search for non-invasive alternative methods for measuring $PaCO_2$, and thus, the end-tidal the partial CO_2 pressure ($EtCO_2$) and the transcutaneous partial pressure of CO_2 ($TcCO_2$) have been developed (1). Transcutaneous carbon dioxide monitoring was first described in the 1960s and has been continually improved in the following years (5). Good agreement between $TcCO_2$ and $PaCO_2$ has been shown in studies in children and adult populations (6-10). On the contrary, several studies suggest that transcutaneous measurement of CO_2 may not be reliable in patients with increased $PaCO_2$ (11,12).

$TcCO_2$ is dependent on the local and systemic perfusion of the patient. Particularly in the presence of circulatory failure, decoupling occurs between arterial $PaCO_2$ and $TcCO_2$, and an increase in $TcCO_2$ occurs independently from arterial $PaCO_2$. In accordance with this, it was demonstrated that altered tissue perfusion leads to elevated tissue CO_2 and the difference between $TcCO_2$ and $PaCO_2$ levels (4). Lactate is a widely used marker for the indirect assessment of tissue perfusion and/or hypoxia (4,13). In this paper, we hypothesized that transcutaneous capnometry may be unreliable in patients with tissue perfusion impairment/hypoxia, which can be represented by hyperlactatemia. To our knowledge, there are no studies focusing on the relationship of lactate level on measurements of $TcCO_2$.

The purpose of this study was to evaluate the effect of lactate levels on the agreement of $TcCO_2$ and $PaCO_2$ in hypercapnic patients who receive NIV.

MATERIALS and METHODS

Study Population

We conducted a prospective cohort study in critical care patients with hypercapnic respiratory failure ($PaCO_2$ ≥45 mmHg) who received NIV between April 2019 and January 2020 in the intensive care unit of Ankara University Faculty of Medicine department of chest disease. Patients aged ≥18 years, patients receiving NIV as initial ventilation support due to hypercapnic respiratory failure, and those whose $TcCO_2$ measurement could be recorded continuously during the first 24 hours were enrolled in the study exclusion criteria were defined as follows: Requiring emergency intubation at critical care admission;

requiring invasive mechanical ventilation within the first 24 hours of NIV therapy; low systemic blood pressure (mean arterial pressure <60 mmHg); requiring vasopressor treatment during ICU stay; acute or chronic renal/hepatic failure, drug intoxication and the presence of a skin lesion that prevents placement of the transcutaneous capnometry probe; or the inability of monitoring transcutaneous measurements for any reason. The presence of mechanisms such as multiple organ dysfunctions, sepsis, vasopressor use, barbiturates and propofol, which often cause an increase in lactate levels in different ways, were more common in patients who required invasive mechanical ventilation, so patients receiving invasive mechanical ventilation were not enrolled in the study to maintain the clarity of findings.

Data for the sample size was taken from a study by Endo et al. (14). Considering the four repeated measurements (0^{th}, 1^{st}, 4^{th} and 24^{th} hours) of $TcCO_2$ and arterial $PaCO_2$ for each patient, with an effect size of 0.41 and with a setting correlation of 0.29 for repeated measures, we calculated that 28 patients were needed to reach the power of 85% with an alfa level of 5%. The G*POWER 3.1.9.6 program was used to calculate the sample size.

The study was approved by the Institutional Ethics Review Committee (05-305-18). Informed consent was obtained from all study patients.

Study Protocol, Measurements and Data Collection

The demographic features, comorbid conditions, and baseline laboratory parameters, including complete blood count data and renal/liver function tests were recorded at the time of critical care admission. ABG parameters including pH, $PaCO_2$, PaO_2, SaO_2, HCO_3 and lactate level, arterial blood pressure and body temperature of the study patients were recorded at 0, 1, 4 and 24 hours of NIV application. All the ABG samples were analyzed within five minutes of blood collection using the ABL800 blood gas analyzers (Radiometer Medical ApS, Denmark). The $TcCO_2$ levels were monitored using the TOSCA TCM4 (Radiometer Ltd., Crawley, United Kingdom). The transcutaneous electrode includes a heating piece, temperature sensor, and an H+ measuring electrode. Heating the skin provokes regional vasodilation and increased CO_2 permeability. CO_2 that diffuses through the membrane reacts with water to form carbonic acid, which then dissociates into hydrogen and bicarbonate ions. This results in a change in pH that causes a potential difference between the two electrodes. Based on the linear relationship between pH and Log PCO_2, $TcCO_2$ is recorded. $TcCO_2$ represents a mixture of venous, capillary, and arterial CO_2 pressures (4). According to the manufacturer's instructions, we performed the following steps for the transcutaneous measurements: A sensor fixation ring was placed on the previously cleaned upper anterior chest wall, and the conductive gel was dropped on the ring. Besides, sensor calibration was automatically done after each monitoring, and the membrane was changed every 14 days. $TcCO_2$ values were recorded simultaneously with the ABG sampling. Measurement method diagram is given in Figure 1.

The same clinicians performed all measurements to prevent interobserver reliability. Also, the clinicians and all staff are regularly trained and controlled. To ensure quality assurance of all measurements, the transcutaneous carbon dioxide monitor, arterial blood gases analyzers and the ventilator devices used for NIV have a program of periodic equipment maintenance and ongoing monitoring established according to the manufacturer's instructions.

As hyperlactatemia is defined as increased serum lactate level ≥2 mmol/L, all paired measurements are categorized into two different groups to evaluate the differences of CO_2 measurements as normal lactate group (<2 mmol/L) and increased lactate group (≥2 mmol/L) (15).

Primary Endpoint

The primary endpoint was to assess the effect of lactate levels on the agreement in measurement between $TcCO_2$ and $PaCO_2$ in hypercapnic patients receiving NIV therapy.

Statistical Analysis

Data were analyzed using SPSS 22.0 software (SPSS, Inc, Chicago, IL, United States of America). Continuous variables with normal distribution were presented as mean ± standard deviation (mean ± SD) and median [25^{th}-75^{th} percentiles, interquartile range (IQR)] for non-normal distributed variables. Kolmogorov-Smirnov test was used to analyze the distribution of variables and a Levene test to assess the equality of variances. The Bland-Altman method was performed to display bias (systematic error-mean the difference between $TcCO_2$ and $PaCO_2$) and precision (random error-standard deviation of mean difference) and were calculated. Mean difference

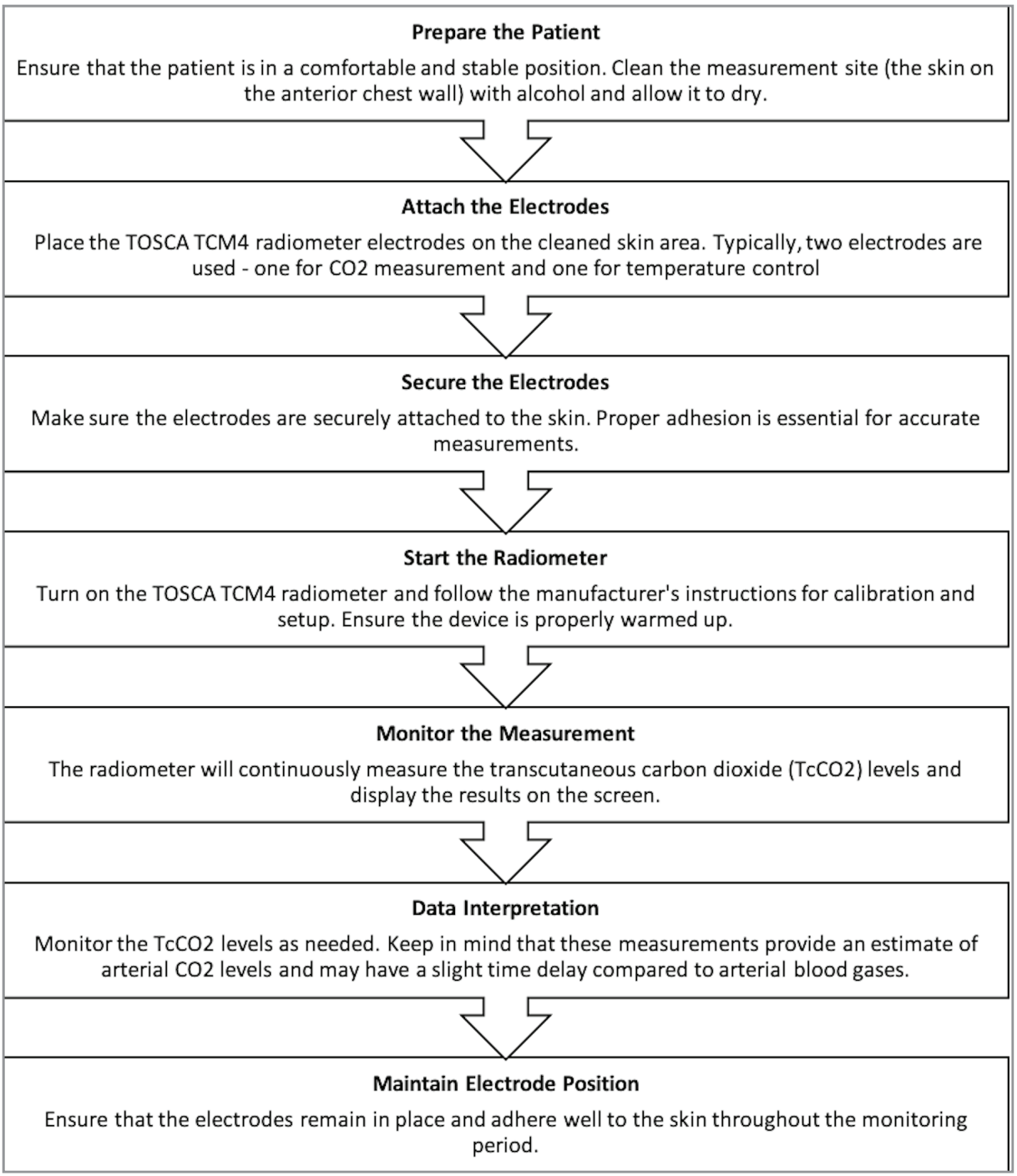


Figure 1. Measurement of transcutaneous carbon dioxide method diagram.

between $TcCO_2$ and $PaCO_2$ were given with 95% limits of agreement (± 1.96 SD). Repeated measures analysis of variance was used to determine changes of $PaCO_2$, $TcCO_2$ and differences of $TcCO_2$ and $PaCO_2$ over time. A Pearson's correlation analysis was calculated to assess the strength of the associations between any two variables. A multiple linear regression model was performed with enter method to identify independent predictors of the difference between $TcCO_2$ and $PaCO_2$. The model fit was assessed using appropriate residual and goodness-of-fit statistics. Tolerance and variance

inflation factor were used to determine the collinearity between independent variables. Statistical significance level was set as $p< 0.05$ for all tests.

RESULTS

A total of 116 paired $TcCO_2$ and $PaCO_2$ measurements of 29 patients were enrolled for the study. Flow chart of the study patients is presented in Figure 2. Mean age of the study patients was 69.44 ± 10.62 years. The characteristics of the 29 study subjects are given in Table 1. The 116 paired mesaurements were categorized into increased lactate level (n= 28) and normal lactate level (n= 88).

The following clinical data were collected at the time of each $TcCO_2$-$PaCO_2$ measurement: Mean temperature 36.54 ± 0.35 °C, oxygen saturations 90.84 ± 5.18 %, and mean arterial blood pressure 82.19 ± 13.27 mmHg.

Mean $TcCO_2$ and $PaCO_2$ levels were 58.30 ± 10.68 and 56.54 ± 10.86, respectively. Mean bias between $TcCO_2$ and $PaCO_2$ was 1.75 mmHg with 95% limits of agreement from -3.67 to 7.17 mmHg (Figure 3).

Paired measurements tested in 29 patients during 24 hours (analysed for 0, 1, 4 and 24 hours of NIV support) did not show any significant change in $TcCO_2$, $PaCO_2$ and differences of $TcCO_2$ and $PaCO_2$ over the time ($p= 0.09$; $p= 0.09$; $p= 0.64$ respectively, Figure 4).

When the measurements were grouped according to lactate levels, in the normal lactate level group (<2 mmol/L), the mean bias between $TcCO_2$ and $PaCO_2$ was 0.66 mmHg with 95% limits of agreement from -1.71 to 3.03 mmHg (Figure 5A), and $TcCO_2$ levels showed high correlation with the $PaCO_2$ levels ($r= 0.99$, $p< 0.001$, Figure 5B).

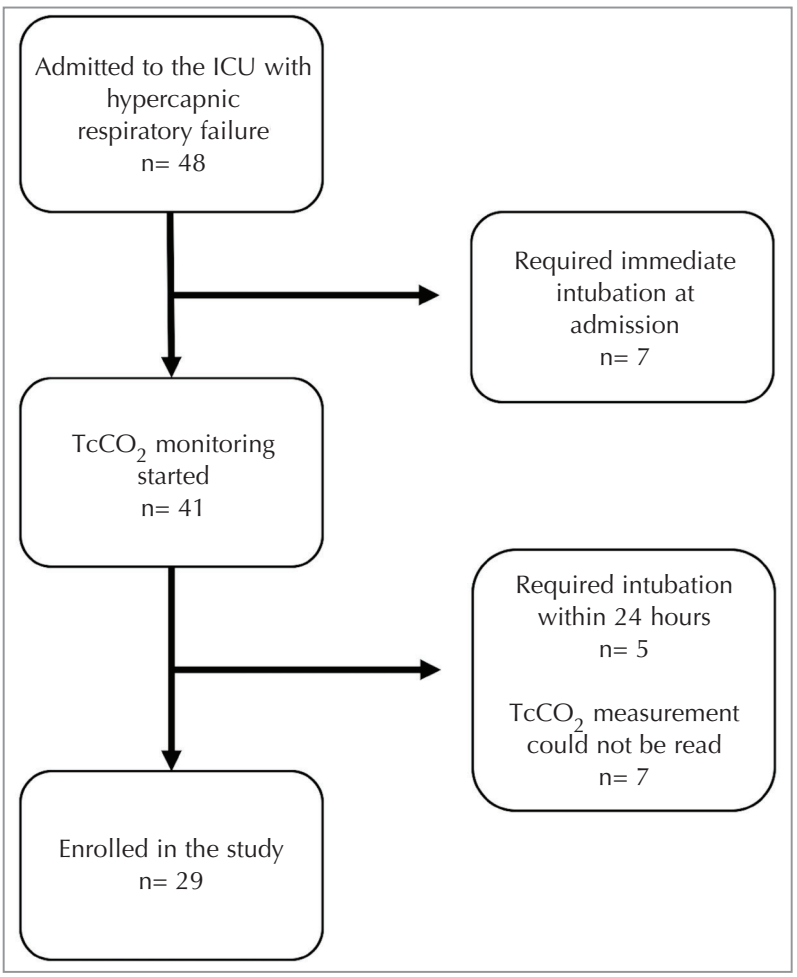


Figure 2. Flow diagram of the study.

Table 1. General characteristics of the study patients

	n= 29 mean ± SD median (IQR25-75) n (%)
Age (year)	69.44 ± 10.62
Sex (male)	17 (58.6)
Reason for hypercapnic respiratory failure	
COPD exacerbation	18 (62)
Pulmonary edema	4 (13.8)
Pneumonia	3 (10.3)
Interstitial lung disease	2 (6.9)
Neuromuscular disease	2 (6.9)
Laboratory parameters	
Hb (g/dL)	11.81 ± 2.24
Leucocyte (10^9/L)	9.15 ± 2.68
Thrombocyte (10^9/L)	216.0 (172.5-295.0)
BUN (mg/dL)	29.0 (22.5-34.8)
Creatinin (mg/dL)	0.93 ± 0.31
ALT (U/L)	27.0 (17.5-37.0)
AST (U/L)	29 (16.5-39)

COPD: Chronic obstructive lung disease, Hb: Haemoglobin, BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase.

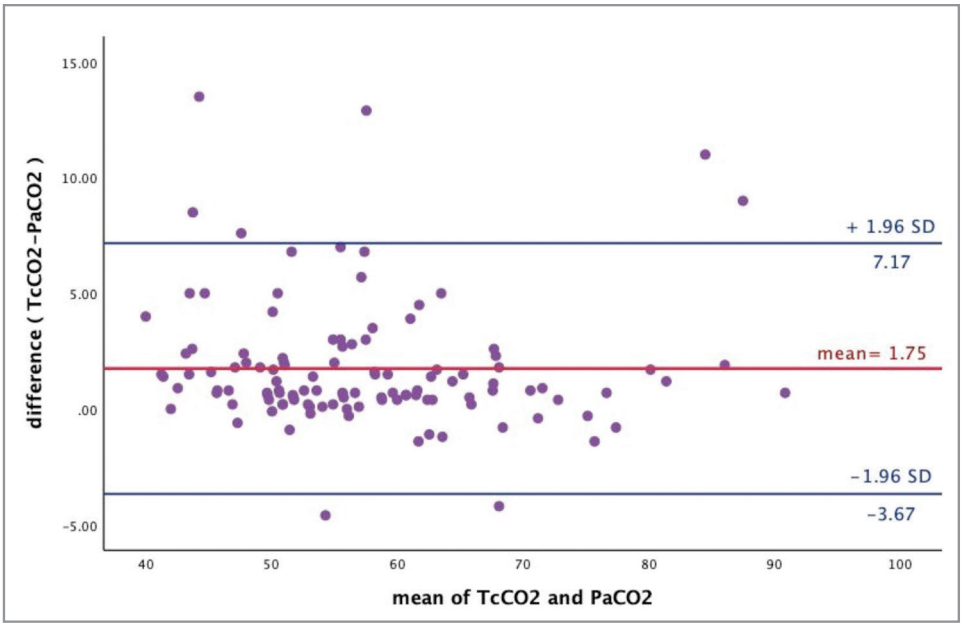


Figure 3. Bland-Altman plots for comparing $TcCO_2$ with $PaCO_2$ within the total study group. The X-axis represents the mean of $TcCO_2$ with $PaCO_2$ [($TcCO_2$+ $PaCO_2$)/2] in mmHg and the Y-axis represents the difference between $TcCO_2$ with $PaCO_2$ ($TcCO_2$-$PaCO_2$) in mmHg. Red line shows the mean bias. Blue lines represent upper and lower limits of agreement at ± 1.96 SD.

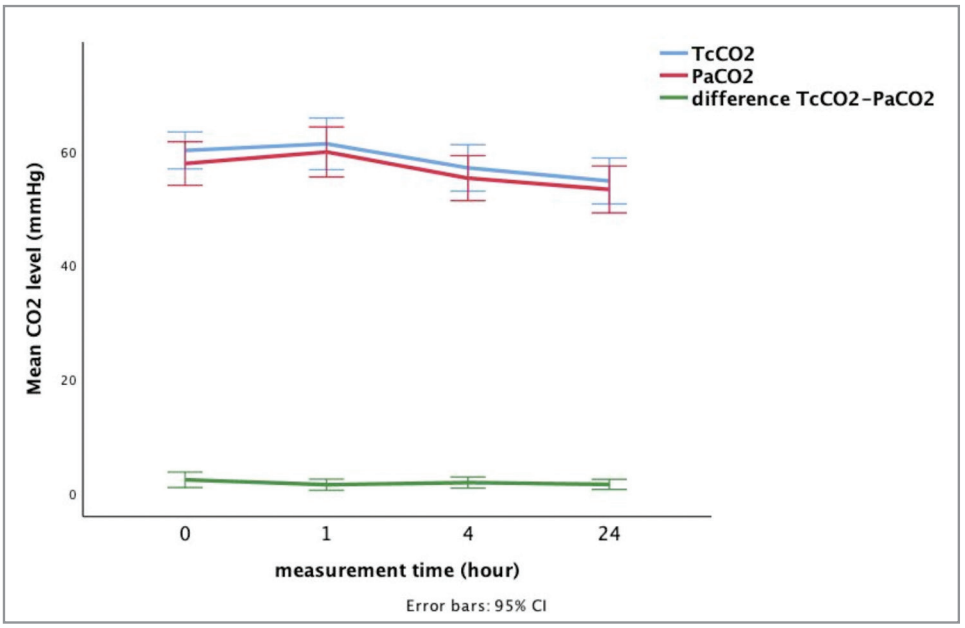


Figure 4. Graph represents the changes of $TcCO_2$ (blue line), $PaCO_2$ (red line) and difference between $TcCO_2$ and $PaCO_2$ (green line) over the 24 hours with the 95% CI.

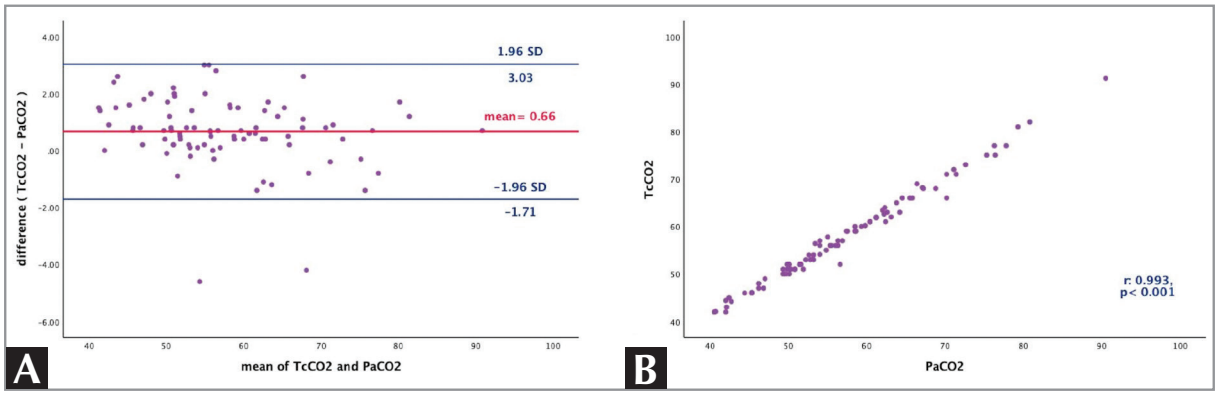


Figure 5. Bland-Altman plots for comparing $TcCO_2$ with $PaCO_2$ within the normal lactate group. The X-axis represents the mean of $TcCO_2$ with $PaCO_2$ [($TcCO_2$+ $PaCO_2$)/2] in mmHg and the Y-axis represents the difference between $TcCO_2$ with $PaCO_2$ ($TcCO_2$-$PaCO_2$) in mmHg. Red line shows the mean bias. Blue lines represent upper and lower limits of agreement at ±1.96 SD **(A)**. Association between $TcCO_2$ and $PaCO_2$ for normal lactate group **(B)**.

Besides this, within the high lactate group, mean bias between $TcCO_2$ and $PaCO_2$ was calculated as 5.17 mmHg with 95% limits of agreement from -1.63 to 11.97 mmHg (Figure 6A). $TcCO_2$ levels still showed high correlation with the $PaCO_2$ levels (r= 0.96, p< 0.001, Figure 6B).

Our findings showed a positive correlation of lactate level and with difference between $TcCO_2$ and $PaCO_2$ (r= 0.79, p< 0.001) (Figure 7A) and a negative correlation between mean blood pressure and the difference between $TcCO_2$ and $PaCO_2$ (r= -0.54, p= 0.001, Figure 7B). No other correlations were found with the difference between $TcCO_2$ and $PaCO_2$. After multiple regression analyses, the relation between lactate level and the difference between $TcCO_2$ and $PaCO_2$ remained, while the association of mean blood pressure became insignificant. Multiple regression analysis of possible variables affecting the increase of difference between $TcCO_2$ and $PaCO_2$ values is given in Table 2.

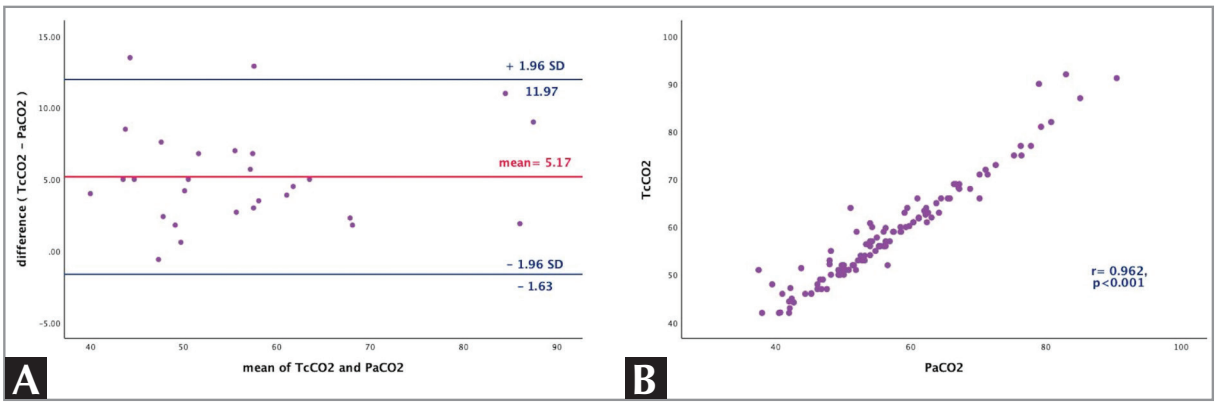


Figure 6. Bland-Altman plots for comparing $TcCO_2$ with $PaCO_2$ within increased lactate group. The X-axis represents the mean of $TcCO_2$ with $PaCO_2$ [($TcCO_2$+ $PaCO_2$)/2] in mmHg and the Y-axis represents the difference between $TcCO_2$ with $PaCO_2$ ($TcCO_2$-$PaCO_2$) in mmHg. Red line shows the mean bias. Blue lines represent upper and lower limits of agreement at ±1.96 SD **(A)**. Association between $TcCO_2$ and $PaCO_2$ for increased lactate group **(B)**.

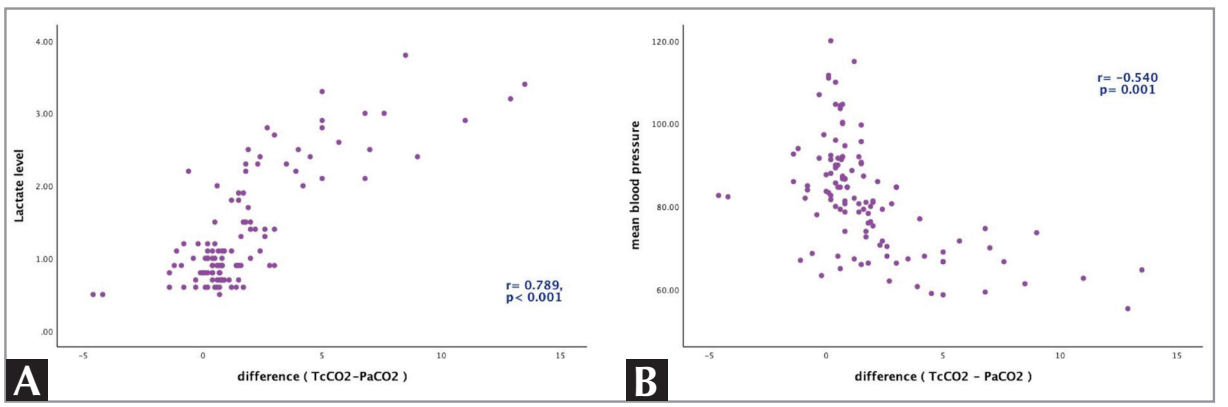


Figure 7. Association of difference between $TcCO_2$ and $PaCO_2$ with lactate level for all paired measurements **(A)**. Association of difference between $TcCO_2$ and $PaCO_2$ with mean arterial blood pressure for all paired measurements **(B)**.

Table 2. Multiple linear regression analysis: Association between the variables and the difference between $TcCO_2$ and $PaCO_2$

	B	95% CI	Beta	t	p
pH	2.599	-5.559-10.757	0.048	0.631	0.529
PaO_2 (mmHg)	0.007	-0.13-0.27	0.042	0.701	0.485
$PaCO_2$ (mmHg)	-0.003	-0.038-0.034	-0.010	-0.139	0.890
Mean blood pressure (mmHg)	0.019	-0.018-0.055	0.089	1.012	0.314
Lactate level (mmol/L)	3.080	2.446-3.713	0.875	9.632	**<0.001**
Temperature	0.110	-0.819-1.038	0.014	0.234	0.815

R^2= 0.630, Adj R^2= 0.610, F-value: 30.96, p< 0.001.
PaO_2= Arterial partial oxygen pressure, $PaCO_2$= Arterial partial carbon dioxide oxygen pressure.
B= Unstandardized co-efficients, Beta= Standardized co-efficients, CI= Confidence interval.
p< 0.05 is considered as the significant level.

DISCUSSION

The findings of our study revealed a positive correlation between serum lactate level and the difference of $TcCO_2$ and $PaCO_2$. Among all paired measurements, the mean bias between $TcCO_2$ and $PaCO_2$ was 1.75 mmHg with 95% limits of agreement from -3.67 to 7.17 mmHg. Besides that, the bias

between $TcCO_2$ and $PaCO_2$ increased as 5.17 mmHg with 95% limits of agreement from -1.63 to 11.97 mmHg, within the measurements with increased lactate (≥2 mmol/L). To the best of our knowledge, this is the first study targeting to investigate the effect of serum lactate level on transcutaneous CO_2 measurement in critical care patients.

In clinical practice, $PaCO_2$ is one of the main monitoring markers, especially in intensive care units, and ABG analysis is accepted as the gold standard technique for measuring it. In line with this, arterial blood sampling is the most extensive procedure for CO_2 monitoring worldwide (1). Since arterial blood gas sampling is painful and carries risks such as thrombosis and hematoma, alternative methods are searched for CO_2 monitoring (4). Arterial lines are sometimes placed to avoid repeated punctures, but it is also associated with significant risks, including infection and ischemia (16). Although the development of transcutaneous capnography for this purpose dates back a few decades, its usage is still quite limited, and data on its reliability in spesific patients group is insufficient.

Serum lactate level has been a widely used biomarker for assessing hemodynamic conditions of the patients (13,17). The association between tissue hypoxia and elevated lactate level is known as the result of decreasing perfusion and reducing the components of systemic oxygen distribution due to low levels of haemoglobin, oxygen saturation, or cardiac output (13). Parallel to this, lactate level is used surrogate of tissue perfusion as it is influenced by macrocirculation, microcirculation (including arterioles, capillaries, and venules network), and mitochondrial function. The cutaneous CO_2 represents the CO_2 value of the mixture of venous, capillary, and arterial networks. The level of tissue CO_2 is based on the production of CO_2 by tissues, the wash-out capacity of CO_2 from the tissue through enough perfusion, and arterial CO_2 content (3). Previous studies have clearly shown that tissue CO_2 is increased in shock states, which is closely related to tissue perfusion impairment (18-20).

Regarding $TcCO_2$ measurements in circulatory alterations, a prospective observational study has suggested that $TcCO_2$ monitoring could be used in patients with acutely developed hypotension (9). In a pig-model study by Endo et al., it has been reported the $TcCO_2$-$PaCO_2$ level markedly negatively correlated with cardiac output (CO) measured by both pulmonary arterial catheterization (PAC) and the pulse index continuous cardiac output (PiCCO) (CO by PAC: r= -0.79 p< 0.001; CO by PiCCO: r= -0.74; p< 0.001) (14).

Moreover, several studies advocate the monitoring of $TcCO_2$ to predict the status of hypoperfusion (4,14,21). The decoupling of $TcCO_2$ and $PaCO_2$ explains this condition in cases of circulatory failure in a famous study examining the kinetics of tissue CO_2 during shock status (22). Notably, monitoring the difference between tissue and arterial PCO_2 is more beneficial than the absolute value of $TcPCO_2$ in detecting perfusion alterations (4). In our study group, mean arterial blood pressure was negatively correlated with the difference between $TcCO_2$ and $PaCO_2$. However, after multiple regression analyses, the association became insignificant. Nonetheless, the association between lactate level and increased $TcCO_2$ and $PaCO_2$ remained even after multiple analyses. We believe that lactate level may be a stronger indicator of tissue perfusion than arterial blood pressure since it is also affected by microcirculatory dysfunciton.

Previous studies have suggested 7.5 mmHg as the clinically acceptable limit for the maximum mean bias between CO_2 measurement methods (6,23,24). A study conducted in the emergency department by McVicar and Eager has reported a bias of 0.15 mmHg and limits of agreement of -6.6 to -6.9 mmHg (25). In another study, the bias has been found as 0.1 mmHg and limits of agreement of as -6 to 6.2 mmHg within a similar patient population (26). Mummary et al. have performed a study with patients requiring acute medical settings and reported $TcCO_2$ tended to be -0.16 kPa [~1.20 mmHg (95% CI ± 1.54 kPa (~11.55 mmHg)] lower than $PaCO_2$ (27). Another study examining the agreement of $TcCO_2$ and $PaCO_2$ during chronic obstructive pulmonary disease (COPD) exacerbation has found the bias for $TcCO_2$ and $PaCO_2$ to be 2.3 mmHg (-3.8 to 8.3 mmHg) (28). Our results of total measurements seem to concur reasonably with previous studies in terms of agreement of $TcCO_2$ and $PaCO_2$ with slight bias and acceptable limits of agreement for all measurements. In contrast, the mean $TcCO_2$-$PaCO_2$ difference (bias) increased from 0.66 mmHg in the normal lactate group to 5.17 mmHg in the increased lactate group. Furthermore, the limits of agreement got wider from normal lactate group to increased lactate group (from -1.71 to 3.03 mmHg; to -1.63 to 11.97 mmHg).

Beyond that, an acceptable clinical range of agreement has been recommended by The American Association for Respiratory Care, between $TcCO_2$ and $PaCO_2$ ± 1.96 SD= ± 7.5 mmHg or narrower (29). Considering these data, we think transcutaneous CO_2 monitoring may not be reliable in cases with hyperlactatemia.

Our study had some limitations. It was carried out in a single centre. We used only one type of sensor device, and transcutaneous measurements were only performed on the anterior chest wall. Furthermore, the absence of measurements related to macrocirculation indicators, such as cardiac output and left ventricle ejection fraction, as well as the lack of data concerning microcirculatory status, including microcirculatory blood flow and postcapillary venous oxygen saturation, might have influenced the findings regarding the relation between lactate levels and $TcCO_2$.

To conclude, $TcCO_2$ monitoring may be a beneficial tool for estimating $PaCO_2$ in critical care patients with hypercapnic respiratory failure receiving NIV. But, it may not be reliable in monitoring patients with increased lactate levels. For this reason, patients with known high lactate levels should be followed up with ABG as $TcCO_2$ monitoring may provide doubtful results. In addition, $TcCO_2$ measurements should be confirmed with ABG in cases with suspected hyperlactatemia in their follow-up. Further carefully designed studies taking into account different causes of hyperlactatemia and possible confounders are necessary to demonstrate the relationship between lactate levels and transcutaneous carbon dioxide measurements.

Ethical Committee Approval: This study was approved by the Ankara University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 05-305-18, Date: 12.03.2018).

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AGK, ŞNÖ, AK

Analysis/Interpretation: AGK

Data acqusition: AGK, MÖ, ŞNÖ, SE, FA

Writing: AGK, MÖ, SE, FA

Clinical Revision: All of authors

Final Approval: AGK, AK

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