

# Correlation of PaCO<sub>2</sub> and ETCO<sub>2</sub> in COPD Patients with Exacerbation on Mechanical Ventilation

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## ABSTRACT

**Introduction:** Chronic obstructive pulmonary disease (COPD) patients in hypercapnic respiratory failure require multiple arterial blood gas (ABG) analysis for monitoring. It is a painful, invasive, and expensive investigation. This study was aimed at finding an agreement between end-tidal carbon dioxide (ETCO<sub>2</sub>, a noninvasive modality) and arterial carbon dioxide (PaCO<sub>2</sub>) in COPD patients with acute exacerbation on mechanical ventilation.

**Materials and methods:** A prospective observational study was conducted in COPD patients who required mechanical ventilation. ETCO<sub>2</sub> was recorded by mainstream capnography along with ABG analysis. An agreement between PaCO<sub>2</sub> and ETCO<sub>2</sub> was assessed. The effect of various factors on correlation was also studied.

**Results:** A total of 100 patients with COPD in hypercapnic respiratory failure were included. Seventy-three percentage of patients were managed on invasive mechanical ventilation (IMV). The mean ETCO<sub>2</sub> and PaCO<sub>2</sub> were 48.66 ± 15.57 mm Hg and 75.52 ± 21.9 mm Hg, respectively. There was a significant correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> values ( $r = 0.82$ , 95% confidence interval of  $r = 0.78-0.86$ ,  $p < 0.0001$ ). The Bland-Altman analysis shows the mean bias as -19.4 (95% limits of agreement = -40.0 to 1.1). Pearson's correlation coefficient was 0.84 in intubated patients and 0.58 in patients on noninvasive ventilation (NIV). Pearson's correlation coefficient between PaCO<sub>2</sub> and ETCO<sub>2</sub> in subjects with consolidation, cardiomegaly, hypotension, and raised pulmonary artery pressures was 0.78, 0.86, 0.85, and 0.86, respectively.

**Conclusion:** Mainstream ETCO<sub>2</sub> measurement accurately predicts the PaCO<sub>2</sub> in COPD patients on IMV. However, for patients on NIV, ETCO<sub>2</sub> is insufficient in monitoring PaCO<sub>2</sub> levels due to weak correlation.

**Clinical significance:** ETCO<sub>2</sub> can be used as a noninvasive modality in intensive care unit for monitoring the PaCO<sub>2</sub> in COPD patients on IMV. This can reduce the requirement of arterial blood sampling to a minimum number, in turn reducing the cost of the treatment and discomfort to the patients.

**Keywords:** Arterial carbon dioxide, Chronic obstructive pulmonary disease, End-tidal carbon dioxide, Mechanical ventilation.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) exacerbations are defined as acute worsening of symptoms beyond the day-to-day variability that result in additional therapy.<sup>1</sup> The frequency of hypercapnic respiratory failure in patients with COPD is around 20% with an overall mortality of 12% during index admission and may increase to 33% if respiratory acidosis develops after hospitalization.<sup>2,3</sup> COPD patients presenting in respiratory failure are managed with mechanical ventilation either through a noninvasive ventilation (NIV) mask or through an endotracheal tube. Multiple arterial blood gases (ABG) are recommended in all COPD patients with acute exacerbation, for monitoring oxygenation, ventilation, and acid-base status. As arterial puncture is painful, there is less patient acceptability for this procedure. An arterial puncture may predispose the patient to develop complications like arterial injury, thrombosis with distal ischemia, hemorrhage, aneurysm formation, median nerve damage, and rarely reflex sympathetic dystrophy. Although venous blood gas analysis has replaced ABG in patients with metabolic disorders, it cannot assess the carbon dioxide (CO<sub>2</sub>) levels (ventilation status) correctly in pulmonary disorders. The use of less-invasive techniques to assess the ventilation status of the COPD patients has been a topic of interest.

End-tidal carbon dioxide (ETCO<sub>2</sub>, measured by capnography) is the noninvasive measurement of the partial pressure of CO<sub>2</sub> in the expiratory gases at the end of exhalation. The ETCO<sub>2</sub> value

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approximates the PaCO<sub>2</sub> level and is displayed on the monitor in mm Hg. The ETCO<sub>2</sub> values are expected to be 3 to 8 mm Hg lower than the normal ABG values of 35 to 45 mm Hg. The importance of ETCO<sub>2</sub> in diagnosing metabolic acid-base disorders in adult patients has been well established.<sup>4-8</sup> The purpose of this study is to find an agreement between ETCO<sub>2</sub> and PaCO<sub>2</sub> in COPD patients presenting with acute exacerbation and to determine whether ETCO<sub>2</sub>, a noninvasive method, can replace ABG for the assessment of ventilation status of COPD patients. Such a correlation would help in minimizing the cost of management and the need of frequent arterial punctures for the collection of blood.

## METHODS

COPD patients with acute exacerbation who were admitted for invasive mechanical ventilation (IMV) and NIV in an intensive care unit (ICU) and high dependency unit (HDU) of Pulmonary and Critical Care Medicine Department, PGIMS, Rohtak, India, from March 2017 to February 2018 were considered for this prospective observational study. A written informed consent was obtained. Patients with coexistent interstitial lung disease, tuberculosis in the present or past, pulmonary embolism, chest deformity (e.g., kyphoscoliosis), neurological disease, or history of chest trauma were excluded. Then, 0.5 to 1 mL of blood from radial arteries was collected in preheparinized plastic syringe with 24G needle. A minimum of three samples were analyzed per patient. The first sample was taken immediately at the time of admission to ICU on mechanical ventilation, and the next two samples were taken at the point of 2 hours and 4 hours from the time of admission. The samples were analyzed immediately after collection using the blood gas analyzer (COMBILINE Eschweilers, CL-2022). The blood gas analyzer was calibrated as per the manufacturer's recommendations.

ETCO<sub>2</sub> was measured by Nihon Kohden LifeScope VS BSM-3000 series bedside monitors, using mainstream adaptors. TG-920P CO<sub>2</sub> sensor kit has two types of adapters (airway or nasal) that can be connected to the patient's respiratory circuit (intubated patients) or directly to the patient's nostrils (in nonintubated patients). CO<sub>2</sub> sensor kit is then connected to the monitor. Using TG-920P CO<sub>2</sub> sensor kit, measurements assumed that no CO<sub>2</sub> gas was present during the inspiration. ETCO<sub>2</sub> was measured at the same time of taking arterial blood samples.

## Statistical Analysis

Continuous variables were represented as mean and standard deviations, whereas the categorical variables were represented in percentages. The linear correlation between ETCO<sub>2</sub> and PaCO<sub>2</sub> was performed by Pearson's correlation coefficient. An agreement between ETCO<sub>2</sub> and PaCO<sub>2</sub> was assessed using the Bland-Altman method. A *p* value <0.05 was considered as statistically significant.

## RESULTS

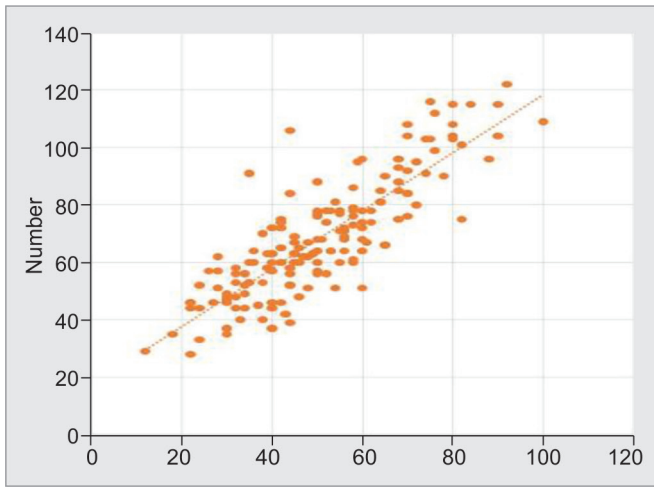
A total of 125 cases of COPD with acute exacerbation requiring IMV or NIV were enrolled. Twenty-five cases were excluded as per exclusion criteria (18 patients had a history of tuberculosis, three had kyphoscoliosis, two presented with chest trauma, one had pulmonary embolism). Demographic characteristics of the patients are described in Table 1. The patient population consisted of 70% males and 30% females. The mean age of the subjects was 60.51 ± 9.2 years with a range between 40 and 85 years. Forty-five percentage of patients were active tobacco smokers, 29% of patients were ex-smokers, 52.7% of patients were heavy smokers, 33.7% of patients were moderate smokers, and 13.5% of patients were light smokers. Among the patients with biomass smoke exposure, 14 (46.7%) patients had severe exposure, 10 (33.3%) patients had moderate exposure, and 6 patients (20%) had mild exposure. The mean ETCO<sub>2</sub> and PaCO<sub>2</sub> were 48.66 ± 15.57 mm Hg and 75.52 ± 21.9 mm Hg, respectively. There was a significant correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> values (*r* = 0.82, 95% confidence interval of *r* = 0.78–0.86, *p* <0.0001) (Fig. 1). The Bland-Altman analysis showed the mean bias as -19.4 (95% limits of agreement = -40.0 to 1.1) (Fig. 2).

The total number of patients managed through IMV was 73 (73%). Mean PaCO<sub>2</sub> and ETCO<sub>2</sub> in patients on IMV were

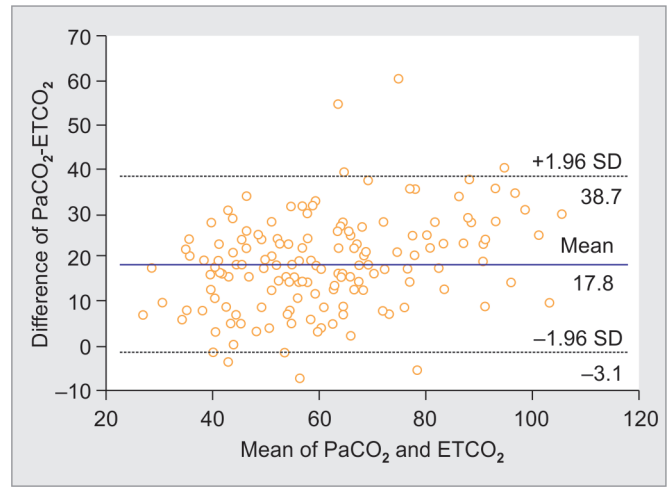
**Table 1:** Demographics and patient characteristics

1.	Age, mean (years ± SD)	60.51 ± 9.2	
	Age-groups, no (%)	≤40	1 (1)
		41–50	15 (15)
		51–60	39 (39)
		61–70	34 (34)
		71–80	9 (9)
		>80	2 (2)
2.	Gender, no. (%)	Males	70 (70)
		Females	30 (30)
3.	Comorbidities, no (%)	47 (47)	
		Hypertension	20 (42.6)
		Ischemic heart disease	12 (25.5)
		Diabetes mellitus	12 (25.5)
		Hypothyroidism	9 (19.1)
		Obstructive sleep apnea	4 (8.5)
		History of cerebrovascular accident	3 (6.4)
		Alcoholic liver disease	1 (2.1)
4.	Smoking status, no (%)	100 (100)	
		Current tobacco smokers	45 (45)
		Ex-smokers	29 (29)
		Biomass smoke exposure	30 (30)
5.	Severity of smoking in tobacco smokers.	Light smokers (SI ≤100)	10 (13.5)
		Moderate smokers (SI = 101–300)	25 (33.7)
		Heavy smokers (SI ≥300)	39 (52.7)
6.	Severity of biomass smoke exposure	Mild (<30)	6 (20)
		Moderate (31–60)	10 (33.3)
		Heavy (>60)	14 (46.7)
7.	Occupation	Farmer	29 (29)
		Housewife	29 (29)
		Desk job	20 (20)
		Laborer	10 (10)
		Shopkeeper	5 (5)
		Retired army personnel	3 (3)
		Teacher	1 (1)
		Tailor	1 (1)
		Electrician	1 (1)
		Driver	1 (1)
8.	Mode of ventilation	Invasive	73 (73)
		Noninvasive	27 (27)
9.	Chest radiology	Bilateral hyperinflation	100 (100)
		Consolidation	13 (13)
		Cardiomegaly	11 (11)
		Pleural effusion	1 (1)
10.	Blood pressure	Normotensive	83 (83)
		Hypotensive	17 (17)
11.	Pulmonary hypertension	Present	32 (32)
		Absent	68 (68)

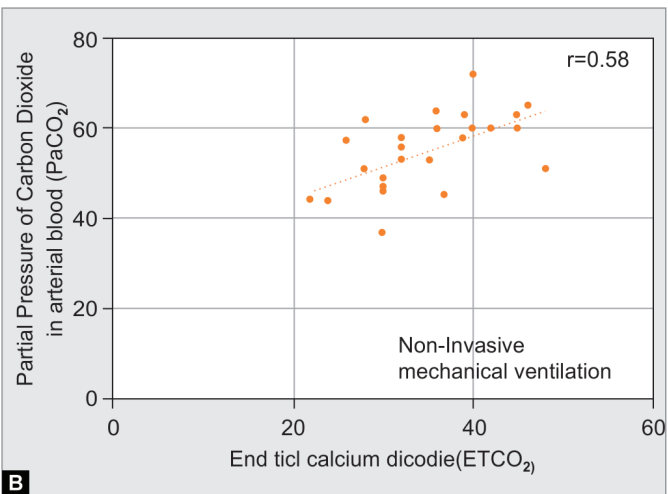
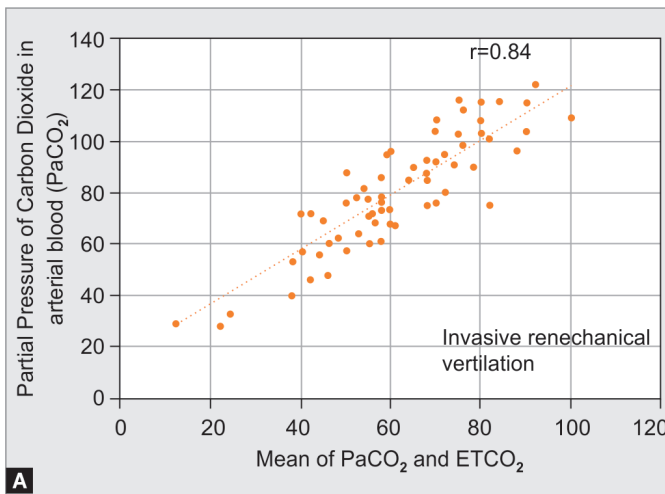
80.38 ± 38 mm Hg and 61.16 ± 16.92 mm Hg, whereas the mean PaCO<sub>2</sub> and ETCO<sub>2</sub> in patients on NIV were 54.96 ± 8.23 mm Hg and 34.96 ± 7.06 mm Hg. Pearson's correlation coefficient was



**Fig. 1:** Scatter plot showing a strong correlation between arterial and end-tidal carbon dioxide ( $r = 0.82$ )



**Fig. 2:** Bland-Altman plot for arterial and end-tidal carbon dioxide showing good agreement (mean bias =  $-19.4$ , 95% limits of agreement =  $-40.0$  to  $1.1$ )



**Fig. 3:** Effect of type of mechanical ventilation (invasive vs noninvasive) on correlation of arterial and end-tidal carbon dioxide

0.84 (strong and statistically significant) in intubated patients and 0.58 (weak correlation) in patients on NIV (Fig. 3). On radiological evaluation, bilateral hyperinflation was present in 100% of patients followed by consolidation in 13% of patients. Seventeen patients (17%) were hypotensive and received vasopressors and inotropic support. Thirty-two patients (32%) had pulmonary arterial hypertension. Pearson's correlation coefficient between PaCO<sub>2</sub> and ETCO<sub>2</sub> in subjects with consolidation, cardiomegaly, hypotension, and raised pulmonary artery pressures was 0.78, 0.86, 0.85, and 0.86, respectively.

## DISCUSSION

COPD patients with respiratory failure requiring mechanical ventilation (invasive or noninvasive) have to undergo multiple ABG analysis for the assessment of oxygenation, ventilation, and acid-base status. Previous studies have found a good correlation between venous and arterial values of pH and HCO<sub>3</sub><sup>-</sup>.<sup>9</sup> Oxygenation can be easily assessed by noninvasive pulse oximetry. Ventilation status in the COPD patients is determined by the PaCO<sub>2</sub> levels.

As both ABG and VBG are invasive procedures, we explored the possibility of using a noninvasive method for blood gas analysis. Considering the fact that the value of CO<sub>2</sub> may guide the therapy and assess possible improvements, we tried to establish a correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> (a noninvasive modality) for monitoring hypercapnia.

We found a positive, strong, and statistically significant correlation of 0.82 between PaCO<sub>2</sub> and ETCO<sub>2</sub> in COPD patients with hypercapnic respiratory failure on mechanical ventilation. Bland-Altman analysis also showed a good agreement between the two variables. We also derived the linear regression equation for the calculation of PaCO<sub>2</sub> from ETCO<sub>2</sub>. Although the importance of ETCO<sub>2</sub> in diagnosing metabolic acid-base disorders has been well established, patients with pulmonary diseases having a shunt or mismatch of ventilation and perfusion showed variable results. The majority of research in this field has been done in nonintubated patients in the emergency department. Most of them have used sidestream capnography to measure ETCO<sub>2</sub>. A single study has correlated the PaCO<sub>2</sub> and ETCO<sub>2</sub> in mechanically ventilated, heterogeneous population of trauma patients and observed a

significant correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> values ( $r = 0.89$ ).<sup>10</sup> No study has compared PaCO<sub>2</sub> and ETCO<sub>2</sub> in COPD patients on mechanical ventilation (invasive or noninvasive).

In a study conducted by Yosefy et al., ETCO<sub>2</sub> was used to predict PaCO<sub>2</sub> levels in patients with respiratory distress in an emergency department.<sup>11</sup> Although the patient population was heterogeneous including both COPD (19%) and heart failure patients (75%), they found a good correlation between the two parameters ( $r = 0.75$ ). A prospective cohort study in patients with acute severe asthma showed a positive concordance between ETCO<sub>2</sub> measured by capnography and arterial PaCO<sub>2</sub>.<sup>12</sup> In a pediatric study on nonintubated, moderate-to-severe respiratory distress patients with asthma, bronchiolitis, and pneumonia but excluding chronic pulmonary disease, cardiac disease, and poor tissue perfusion, ETCO<sub>2</sub> highly correlated with venous partial CO<sub>2</sub> ( $r = 0.92$ ).<sup>13</sup> Kartel et al. measured the ETCO<sub>2</sub> using sidestream technique in COPD patients presenting in the emergency department and found only a moderate correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> levels, which possibly could be due to measurement by sidestream method.<sup>14</sup> However, in a heterogeneous group of emergency patients, Pekdemir et al. did not find any correlation between ETCO<sub>2</sub> (measured by both sidestream and mainstream method) and PaCO<sub>2</sub>. However, their study population was heterogeneous consisting of both patients with and without lung pathology, and measurement errors were noted while recording ETCO<sub>2</sub>.<sup>15</sup>

We tried to evaluate the effect of type of mechanical ventilation (invasive vs noninvasive) on the correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub>. Although NIV is currently recommended for the management of patients with acute hypercapnic respiratory failure secondary to COPD, 73% of subjects were on IMV in our study, possibly because ours is a tertiary care referral center and serves the very sick patients. Pearson's correlation coefficient was 0.84 (strong and statistically significant) in intubated patients and 0.58 (weak correlation) in patients on NIV. The reason could be leakage and dead space ventilation in patients on NIV, as the mainstream capnography adaptors are different for intubated and nonintubated patients. Therefore, we concluded that ETCO<sub>2</sub> cannot be used to monitor PaCO<sub>2</sub> levels in COPD patients on NIV.

We also studied other factors like presence of consolidation, cardiomegaly, hypotension, and raised pulmonary artery pressures, which could affect the blood gases and may affect the correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub>. None of these conditions were found to affect the correlation in a significant manner. Pearson's correlation coefficient between PaCO<sub>2</sub> and ETCO<sub>2</sub> in subjects with consolidation, cardiomegaly, hypotension, and raised pulmonary artery pressures was 0.78, 0.86, 0.85, and 0.86, respectively. Pekdemir et al. also did not find any effect of different lung pathologies on ETCO<sub>2</sub>.<sup>15</sup> We infer that ETCO<sub>2</sub> can be used for monitoring COPD patients on IMV. As not much work has been done in this field, the study requires further evaluation to confirm our findings, preferably in a multicentric blinded study to avoid detection and performance bias.

Limitations of our study were as follows: It was a single-center study and included COPD subjects with coexisting metabolic diseases like diabetes mellitus and acute kidney injury, which affect the metabolic parameters like HCO<sub>3</sub><sup>-</sup> and pH. Another factor could be errors resulting from the functioning of devices, although all the devices used during the study were calibrated by qualified technicians. Performing measurements by a single researcher minimizes the potential for variations that could be caused by many operators. Bias could not be ruled out as the investigator who measured ETCO<sub>2</sub> knew the PaCO<sub>2</sub> values, although the

technician doing ABG analysis was blinded to the PaCO<sub>2</sub> results. Lack of a control group as the study was descriptive in nature could have impacted the study results. And lastly, the fact that subgroup analysis was not planned before and was done later from the collected data. The numbers in the noninvasive group were small, which could be the reason for the difference in correlation of coefficient between the two groups, and may be considered a hypothesis-generating point requiring further validation by a larger study.

## CONCLUSION

We found a good correlation between PaCO<sub>2</sub> and ETCO<sub>2</sub> in COPD patients with acute exacerbations on mechanical ventilation. Mainstream ETCO<sub>2</sub> measurement accurately predicted the PaCO<sub>2</sub> in COPD patients on IMV and was independent of various coexisting confounding factors like consolidation, cardiomegaly, hypotension, and raised pulmonary artery pressures. ETCO<sub>2</sub> can be used as a noninvasive modality for monitoring the PaCO<sub>2</sub> in COPD patients who are on IMV. It can reduce the frequency of arterial blood sampling, minimizing the discomfort to the patients and reducing the cost of treatment. However, for patients on NIV, ETCO<sub>2</sub> is insufficient in monitoring PaCO<sub>2</sub> levels due to poor correlation between the two.

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## REFERENCES

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 report. Available at: [goldcopd.org/archived-reports/](http://goldcopd.org/archived-reports/).
2. Plant PK, Owen J, Elliott MW. One year period prevalence study of respiratory acidosis in acute exacerbation of COPD; implications for the provision of non-invasive ventilation and oxygen administration. *Thorax* 2000; 55(7):550–554. DOI: 10.1136/thorax.55.7.550.
3. Roberts CM, Stone RA, Buckingham RJ, Pursey NA, Lowe D. Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations. *Thorax* 2011;66(1):43–48. DOI: 10.1136/thx.2010.153114.
4. Garcia E, Abramo TJ, Okada P, Guzman DD, Reisch JS, Wiebe RA. Capnometry for noninvasive continuous monitoring of metabolic status in pediatric diabetic ketoacidosis. *Crit Care Med* 2003;31(10):2539–2543. DOI: 10.1097/01.CCM.0000090008.79790.A7.
5. Gilhotra Y, Porter P. Predicting diabetic ketoacidosis in children by measuring end-tidal CO<sub>2</sub> via non-invasive nasal capnography. *J Paediatr Child Health* 2007;43(10):677–680. DOI: 10.1111/j.1440-1754.2007.01186.x.
6. Fearon DM, Steele DW. End-tidal carbon dioxide predicts the presence and severity of acidosis in children with diabetes. *Acad Emerg Med* 2002;9(12):1373–1378. DOI: 10.1111/j.1553-2712.2002.tb01605.x.
7. Agus MS, Alexander JL, Mantell PA. Continuous non-invasive end-tidal CO<sub>2</sub> monitoring in pediatric in patients with diabetic ketoacidosis. *Pediatr Diabetes* 2006;7(4):196–200. DOI: 10.1111/j.1399-5448.2006.00186.x.
8. Pishbin E, Ahmadi GD, Sharifi MD, Deloei MT, Shamloo AS, Reihani H. The correlation between end-tidal carbon dioxide and arterial blood gas parameters in patients evaluated for metabolic acid-base disorders. *Electron Physician* 2015;7(3):1095–1101. DOI: 10.14661/2015.1095-1101.

9. Bingheng L, Jianxin C, Yu C, Yu Y. Comparison of peripheral venous and arterial blood gas in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD): a meta-analysis. *Notfall Rettungsmed* 2019;22:620–627. DOI: 10.1007/s10049-018-0469-9.
10. Razi E, Moosavi GA, Omid K, Saebi AK, Razi A. Correlation of end tidal CO<sub>2</sub> and arterial CO<sub>2</sub> in mechanically ventilated patients. *Arch Trauma Res* 2012;1(2):58–62. DOI: 10.5812/atr.6444.
11. Yosefy C, Hay E, Nasri Y, Magen E, Reisin L. End tidal carbon dioxide as a predictor of the arterial PCO<sub>2</sub> in the emergency department setting. *Emerg Med J* 2004;21(5):557–559. DOI: 10.1136/emj.2003.005819.
12. Corbo J, Bijur P, Lahn M, Gallagher EJ. Concordance between capnography and arterial blood gas measurements of carbon dioxide in acute asthma. *Ann Emerg Med* 2005;46(4):323–327. DOI: 10.1016/j.annemergmed.2004.12.005.
13. Moses JM, Alexander JL, Agus MS. The correlation and level of agreement between end-tidal and blood gas pCO<sub>2</sub> in children with respiratory distress: a retrospective analysis. *BMC Pediatr* 2009;9:20. DOI: 10.1186/1471-2431-9-20.
14. Kartal M, Goksu E, Eray O, Isik S, Sayrac AV, Yigit OE, et al. The value of ETCO<sub>2</sub> measurement for COPD patients in the emergency department. *Eur J Emerg Med* 2011;18(1):9–12. DOI: 10.1097/mej.0b013e328337b9b9
15. Pekdemir M, Cinar O, Yilmaz S, Yaka E, Yuksel M. Disparity between mainstream and sidestream end-tidal carbon dioxide values and arterial carbon dioxide levels. *Respir Care* 2013;58(7):1152–1156. DOI: 10.4187/respcare.02227.