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ORIGINAL PAPER

Correlation of the end-tidal CO_2 value with arterial blood gas parameters – evaluation of the treatment efficacy of COPD exacerbation in the emergency department

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ABSTRACT

Introduction and aim. Painful, invasive, and expensive arterial blood gas (ABG) analysis is required in the diagnosis, follow-up, treatment, and even discharge of patients with chronic obstructive pulmonary disease (COPD). This study aimed to compare the end-tidal carbon dioxide ($ETCO_2$) value, which allows non-invasive, painless, low-cost, and continuous monitoring, with ABG parameters, in the evaluation of the treatment efficacy of COPD exacerbation.

Material and methods. The study was prospectively conducted with patients who presented to the emergency department with COPD exacerbation. ABG analysis and $ETCO_2$ measurement were simultaneously performed in patients with COPD exacerbation at the time of arrival and after treatment, and were statistically compared.

Results. The study included a total of 216 patients, of whom 57.4% were male. The mean age of the patients was 67.3±13.9 years. The $ETCO_2$ values of the patients at arrival and after COPD exacerbation treatment were 39.2±10 and 37.3±9, respectively, and a statistically significant difference was determined (p=0.001). The partial pressure of pCO_2 values measured at arrival and after treatment were 40.85±10.54 and 38.74±9.25, respectively, and it was statistically significant (p=0.001). A strong positive and statistically significant correlation was found between the $ETCO_2$ and pCO_2 values both at arrival and after COPD exacerbation treatment (r=0.840; p<0.001 and r=0.872; p<0.001, respectively). The Bland-Altman plot was constructed for the agreement between $ETCO_2$ and pCO_2 at both evaluation times.

Conclusion. $ETCO_2$ measurement could accurately predict the pCO_2 of patients with COPD at arrival and after COPD exacerbation treatment. Also, ETCO2 may be useful in cases where pCO_2 cannot be used.

Keywords. arterial blood gas, capnograph, chronic obstructive pulmonary disease, end tidal carbon dioxide, partial pressure of carbon dioxide

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading public health problem worldwide. Although COPD is a slowly progressive, irreversible disease, it is important because of its preventable nature and the possibility of stopping of the progression.[1-3] However, COPD exacerbations adversely affect the patient's health status, hospitalization, and length of stay.[4] In these patients, arterial blood gas (ABG) measurement is one of the valuable tests used to determine the patient's oxygenation, ventilation, and acid-base status during and after an exacerbation. However, ABG is an invasive and

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painful procedure and may need to be repeated in certain cases. Therefore, alternative methods have been used in the evaluation of diagnosis, and follow-up of these patients.[5,6] One of these alternative methods is the measurement of end–tidal carbon dioxide ($ETCO_2$).

$ETCO_2$ is determined by non-invasively with a capnometer by measuring the partial pressure of expiratory carbon dioxide from the air inhaled and exhaled during respiration.[7] This parameter is generally used in the emergency department (ED) to confirm the location of the endotracheal tube, monitor spontaneous return during cardiopulmonary resuscitation in patients with cardiac arrest, and monitor ventilation status in procedural sedoanalgesia.[8,9] In addition, it can provide instant information concerning the metabolic status, perfusion, and most importantly ventilation of critically ill patients in the ED.[4] Studies have emphasized that $ETCO_2$ can be used to evaluate the severity of obstructive airway disease in the ED.[7,10]

Aim

In this study, we aimed to compare the $ETCO_2$ value measured simultaneously with the ABG in patients who came to the ED with COPD exacerbation, at the time of admission and after COPD exacerbation treatment was applied.

Material and methods

Study design

This single-center, prospective clinical study was conducted with patients who presented to the ED with COPD exacerbation, between June 27th, 2019 and December 27th, 2019. The tertiary university hospital, where the study was carried out, provides health services to approximately 4.5 million people in 12 neighboring provinces. The study protocol was in accordance with the Declaration of Helsinki and Good Clinical Practices. Informed consent was obtained from all patients participating in the study. Local ethics committee approval was obtained for the study (decision number: 27.06.2019/05-28).

Patient selection

The eligible participants and sample population were the patients who were admitted to the ED with COPD exacerbations during the study period. Patients with shortness of breath due to reasons other than COPD exacerbation, those younger than 18 years, those with contraindications to ABG sampling (such as coagulopathy, local infection, and thrombus), those that did not provide consent for participation in the study, pregnant patients, intubated patients or patients that required intubation during their follow-up, patients who could not tolerate capnometry for the $ETCO_2$ measurement, those with anatomical disabilities, and non-compliant patients were excluded from the study.

ABG sampling

In the ABG sampling procedure, after the radial artery pulse of the patient was palpated, the most suitable site for the intervention was determined and cleaned with 10% povidone iodine. Then, arterial puncture was performed by the blood gas determination set containing lithium heparin. All interventions in the ED were undertaken by the same physician. The ADL 800 Flex device was used for the ABG analyses. The blood gas analyzer was calibrated according to the manufacturer's recommendations.

Study protocol

Patients presenting to the ED and included in the study were asked to breathe through a nasal cannula connected to a capnometer for at least 30 seconds, during which ABG samples were obtained. The $ETCO_2$ value was simultaneously recorded with ABG parameters. The $ETCO_2$ measurement was performed non-invasively by the same physician using a capnograph/pulse oximeter device, Capnostream®20p portable bedside monitor. To make an accurate measurement, the patient was monitored for at least 6 minutes (240 seconds) with a capnograph/pulse oximeter.[11] During the procedure, SpO_2, rhythm (rate and rhythm) and $ETCO_2$ were monitored and respiratory rate were recorded. Then, COPD exacerbation treatment was applied to the patients in line with the guidelines of the Global Initiative on Chronic Obstructive Pulmonary Disease.[12] After the initial evaluation and exacerbation treatment, the patients were asked to breathe again with a capnometer, and the $ETCO_2$ value, respiratory rate, body temperature, heart rate, arterial blood pressure, and oxygen saturation values were recorded again simultaneously with the ABG parameters.

Treatment efficacy

The efficacy of treatment was evaluated by comparing vital signs, ABG parameters, and $ETCO_2$ measured at the time of arrival at the ED and after COPD exacerbation treatment.

Outcome measures

The primary outcome of the study was the correlation between ABG parameters and $ETCO_2$, which were obtained at the time of arrival at the ED and after COPD exacerbation treatment. The secondary outcome was the treatment efficacy evaluated by comparing the pre-treatment and post-treatment vital signs, ABG parameters, and $ETCO_2$.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Science (SPSS), Version 20.0 (IBM Corp., Armonk, New York, USA). Data were presented as mean, standard deviation, percentage and frequency. The normality of the distribution of continuous variables was analyzed by using the Shapiro-Wilk test. In the comparisons of two dependent groups, the paired-samples t-test was used for the normally distributed data, and the Wilcoxon test for data without a normal distribution. In the comparison of two continuous variables, the Pearson correlation test was conducted if the normal distribution was determined, and the Spearman correlation test otherwise. The agreement between the $ETCO_2$ value and ABG parameters was evaluated by using the Bland-Altman method. The statistical significance level was taken as $p<0.05$.

Results

Patient population and characteristics

During the study, a total of 556 patients were presented to the ED due to COPD exacerbation. After applying the inclusion and exclusion criteria, a total of 216 patients were included in the study. The flow chart of the study is given in Figure 1.

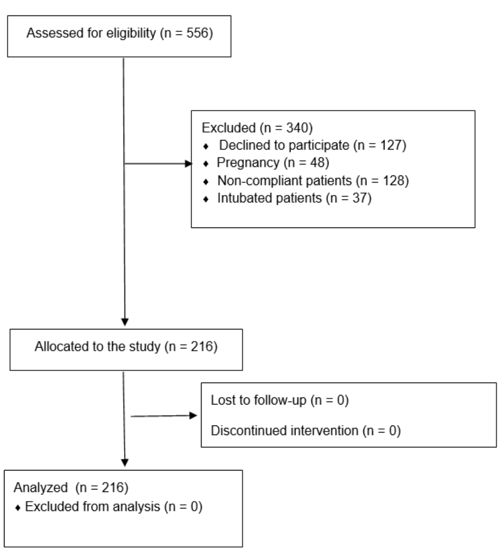

Fig. 1. Flow diagram of the study

Table 1 presents the demographic and clinical features of the patients. The mean age of the patients was 67.3±13.9 years, and 124 (57.4%) were male. All of the patients included in the study were COPD patients. The second most common disease detected in the participants was hypertension (n=107, 49.5%).

Comparison of pre-treatment and post-treatment evaluations

Figure 2 presents the comparison of the clinical features, $ETCO_2$ values and ABG parameters of the patients at the time of arrival and after COPD exacerbation treatment. There was a statistical significance between the pre- and post-treatment vital signs, $ETCO_2$ values and ABG parameters ($p<0.05$).

Table 1. Demographic and clinical characteristics of the patients (n=216) [a]

Variable	Value
Mean age (years)	67.3 ± 13.9
Gender	
Male, n (%)	124 (57.4%)
Female, n (%)	92 (42.6%)
Condenser use, n (%)	110 (50.9%)
Smokers, n (%)	191 (88.4%)
Smoking, pack-day	1.2 ± 0.1
Clinical characteristics	
Respiratory rate (breaths/min)	25.1 ± 7.2
Body temperature (°C)	36.9 ± 0.3
Heart rate (beats/min)	99.8 ± 19.9
Systolic arterial blood pressure (mmHg)	139.9 ± 19.9
Diastolic arterial blood pressure (mmHg)	84.2 ± 12.3
Oxygen saturation (%)	80.1 ± 10.6
$ETCO_2$	39.2 ± 10
Chronic diseases other than COPD	
Hypertension, n (%)	107 (49.5%)
Diabetes mellitus, n (%)	69 (31.9%)
Congestive heart failure, n (%)	56 (25.9%)
Other, n (%)	43 (19.9%)

[a] COPD – chronic obstructive pulmonary disease, $ETCO_2$ – end-tidal carbon dioxide

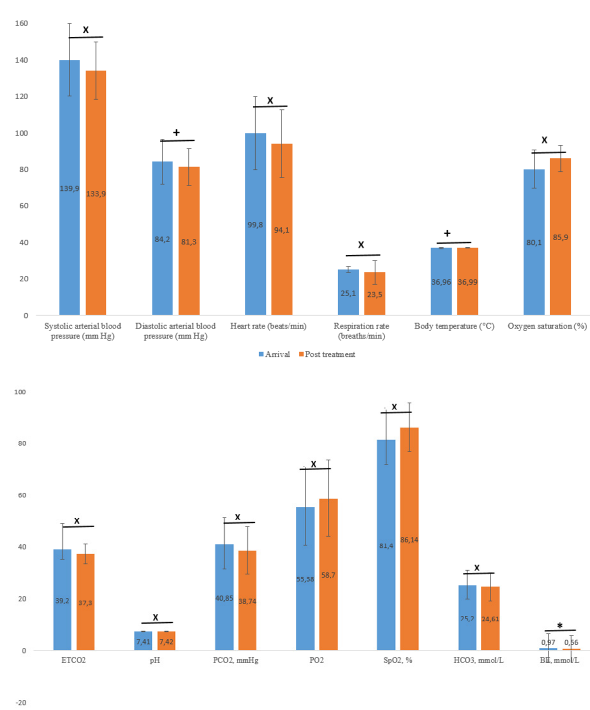

Fig. 2. Comparison of the patients' vital signs, $ETCO_2$ values and ABG parameters measured at arrival and after treatment (X: p=0.001, +: p=0.002, ++: p=0.042, *: p=0.015)

The relationship between the $ETCO_2$ value and ABG parameters measured at arrival is shown in Figure 3. There was a positive, strong and statistically significant correlation between $ETCO_2$ and pCO_2 (r=0.840, $p<0.001$).

Figure 4 shows the relationship between the $ETCO_2$ values and ABG parameters measured after COPD exacerbation treatment. Likewise, a positive, strong and statistically significant correlation was found between $ETCO_2$ and pCO_2 (r=0.872, p<0.001).
According to the Bland-Altman analysis, the mean ± standard deviation of the difference between the pCO_2 and $ETCO_2$ values measured at the time of arrival was 1.64±5.73 [95% confidence interval (CI): 0.87-2.41], and the upper and lower limits were determined as 12.87 and -9.59, respectively (Figure 5a). In the Bland-Altman analysis of the difference between the post-treatment pCO_2 and $ETCO_2$, the mean ± standard deviation was found to be 1.45±4.41 (95% CI: 0.86–2.04), and the upper and lower limits were 10.09 and -7.19, respectively (Figure 5b).

Discussion

In this study, the $ETCO_2$ value was compared with ABG parameters in patients applied with COPD exacerbation, at the time of arrival and after the treatment. In order to determine the efficacy of COPD exacerbation treatment, the vital signs and ABG parameters of the patients were examined before and after treatment, and the differences were found to be statistically significant. When the correlation of the $ETCO_2$ value with the ABG parameters was evaluated, $ETCO_2$ had a strong correlation with pCO_2 both at arrival and after treatment, and had a moderately positive and statistically significant correlation with HCO_3. In addition, there was a clear agreement between $ETCO_2$ and pCO_2 both before and after treatment according to the Bland-Altman graph.

ABG evaluation is of great importance in the hospitalization and discharge decisions after the treatment of patients with COPD exacerbation. The ABG analysis is an invasive and painful procedure that may be accompanied by possible complications.[13] Therefore, the analysis of ABG is difficult in some cases.[14] During the study, it was also observed that patients did not want to give an ABG sample for the second time.

Capnography, which is a non-invasive, painless and uncomplicated method, provides instant information concerning the patient's status by measuring the $ETCO_2$ value and respiratory rate in patients with acute respiratory problems, such as COPD exacerbations.[15] In the literature, comparisons have been made between $ETCO_2$ and pCO_2 in the evaluation of respiratory status of the patients who have undergone sedation and general anesthesia, except for COPD cases, and the results have been reported to be statistically significantly.[8,16-18] In the current study, it was shown that the $ETCO_2$ value could be used in the follow-up of patients with COPD and in the evaluation of the efficacy of COPD exacerbation treatment. Dogan et al., who investigated the accuracy of the $ETCO_2$ level in the prediction of the severity of COPD exacerbation in the ED, found the presence of a relationship between $ETCO_2$ and pCO_2, and pO_2, similar to the results of our study.[10]

Cinar et al. investigated whether there was a difference between the ABG pCO_2 value and the $ETCO_2$ value in patients applied to the ED due to acute dyspnea, and reported a positive, strong and statistically significant correlation between these two parameters (r=0.911; p<0.001).[19] The authors also emphasized that

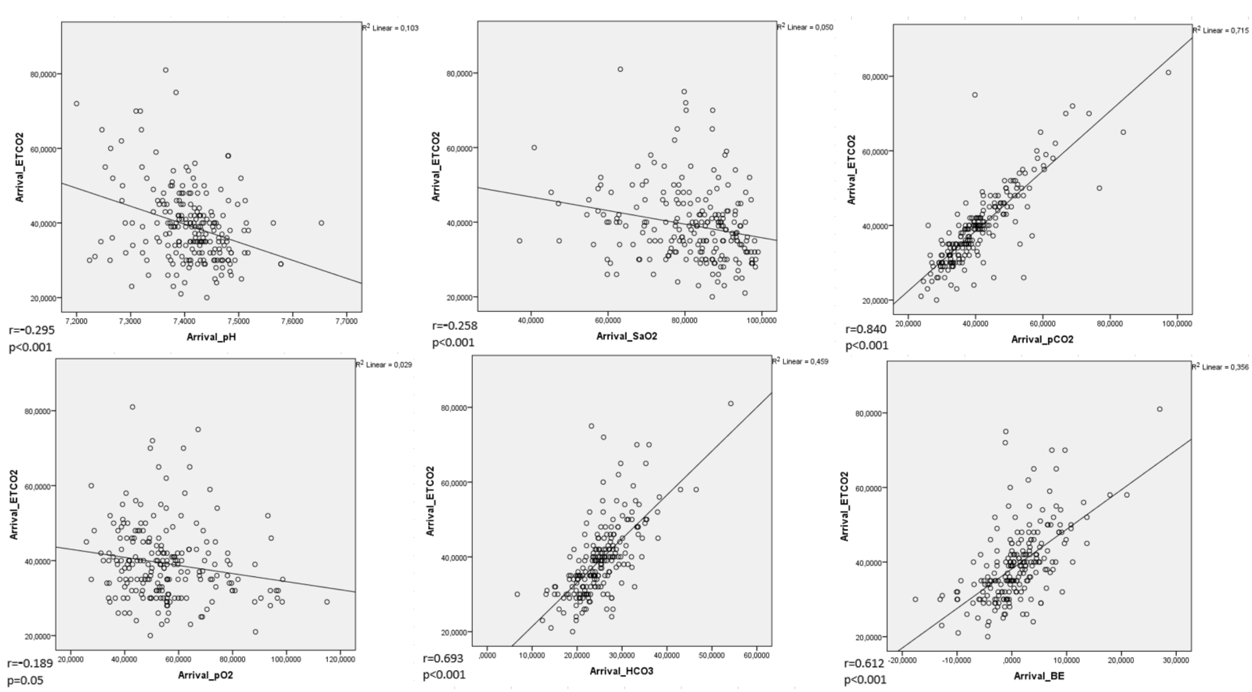

Fig. 3. Correlation of the patients' $ETCO_2$ values with arterial blood gas parameters at arrival

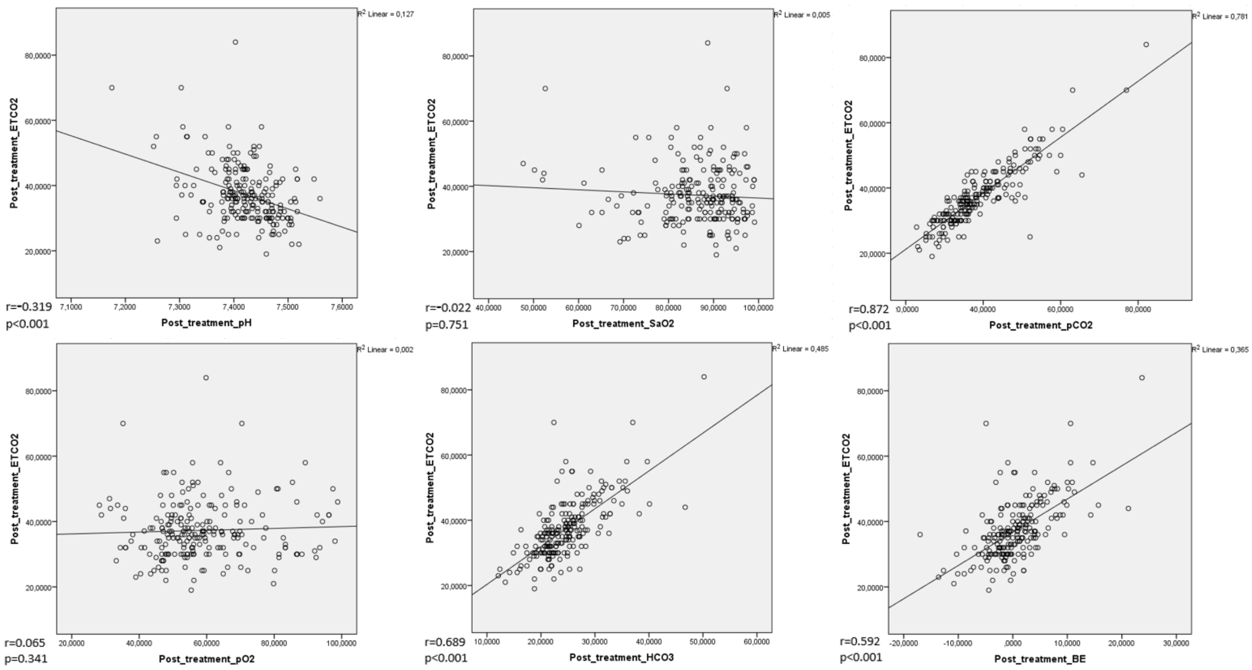

Fig. 4. Correlation of the patients' post-treatment $ETCO_2$ values with arterial blood gas parameters

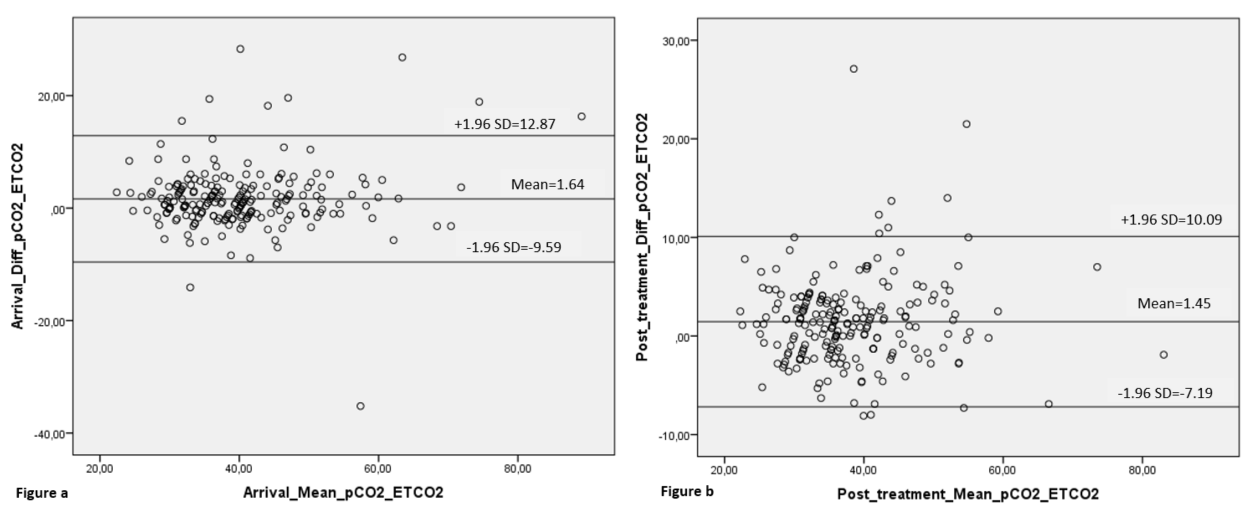

Fig. 5. Bland-Altman graph (a. agreement between $ETCO_2$ and pCO_2 at arrival, b. agreement between $ETCO_2$ and pCO_2 after COPD exacerbation treatment)

$ETCO_2$ could accurately predict the pCO_2 value of patients presenting to the ED with acute dyspnea. In another study conducted with adult asthmatic patients with acute exacerbation, Corbo et al. found a significant correlation between pCO_2 in blood gas and $ETCO_2$ measured by capnography.[20] Kartal et al. investigated the value of $ETCO_2$ measurement for patients with COPD in the ED and concluded that there was a moderate correlation between the $ETCO_2$ and pCO_2 levels, but unlike other studies, $ETCO_2$ measurement was not sufficient to predict the pCO_2 level in this patient group.[4] Similarly, Pekdemir et al. reported that the $ETCO_2$ value was significantly lower than the pCO_2 value and that there was a weak correlation between these two parameters.[21] In a review of $ETCO_2$, it was emphasized that, $ETCO_2$ was an important tool in evaluating the severity of obstructive airway disease.[7] In acute respiratory problems, ETCO2 can detect airway obstruction and hypoventilation at an early stage. Thus, they are able to provide earlier medical intervention to these patients.

Taghizadieh et al. compared $ETCO_2$ with bicarbonate (HCO_3), an ABG parameter, and emphasized that, although $ETCO_2$ could be used in the primary diagnosis of metabolic acidosis, ABG was still the gold standard for guiding diagnosis and treatment.[22] However, Kartal et al. suggested that the $ETCO_2$ level could indicate the severity of metabolic acidosis and mortality.[4] In another study comparing $ETCO_2$ with HCO_3 in patients with COPD exacerbation, Taghizadieh et al. detected no statistically significant difference between the $ETCO_2$ and HCO_3 levels (r=0.04; p=0.136).[23] In the same study, the authors found a low negative correlation between $ETCO_2$ and pH (r=-0.249; p<0.001), and a moderate positive correlation between $ETCO_2$ and pCO_2 (r=0.611; p<0.001). In the current study, the $ETCO_2$ and HCO_3 levels of the patients were positively correlated both at arrival and after treatment, and this correlation was statistically significant. In addition, we observed a low level of negative correlation between $ETCO_2$ and pH both at arrival and after treatment. According to the data obtained from our study, there was a strong positive correlation, similar distribution and agreement between the values of $ETCO_2$ and PCO_2 measured at the time of arrival. More importantly, this correlation was even stronger in the post-treatment $ETCO_2$ and PCO_2 measurements of the patients, showing less bias and lower difference, and a much better agreement.

Limitations

The first limitation of the study was that it was conducted in a single center. Secondly, patients with concomitant metabolic diseases, including diabetes mellitus and acute renal failure, which affect metabolic parameters, such as pH and HCO_3, were not excluded from the sample. Since real-world COPD patients may have some other comorbidities, and our study aimed to study all COPD patients, patients with or without certain concomitant metabolic diseases, such as diabetes or acute renal failure, were not excluded. Subsequently, factors such as cardiomegaly and elevated pulmonary artery pressure that could affect the correlation between pCO_2 and $ETCO_2$ were not evaluated. Also, body temperature, which may affect the pCO_2 level, was not taken into consideration. Lastly, the cigarette consumption of the patients was calculated as package per day. This, in turn, does not report how much COPD patients actually consume package cigarettes per year.

Conclusion

It was determined that $ETCO_2$ measurement which was non-invasive, painless, repeatable and low-cost capnography procedure may provide information about the ventilation, circulation and metabolism of patients during COPD exacerbation at the time of arrival and after treatment. Considering the similar and strongly related properties of $ETCO_2$ to PCO_2 and HCO_3, we believe that it may be used during the follow-up of patients.

Declarations

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Author contributions

Conceptualization, F.Ç. and E.T.; Methodology, F.Ç. and E.T.; Software, F.Ç.; Validation, F.Ç. and E.T.; Formal Analysis, F.Ç. and E.T.; Investigation, F.Ç.; Resources, F.Ç.; Data Curation, F.Ç. and E.T.; Writing – Original Draft Preparation, F.Ç. and E.T.; Writing – Review & Editing, F.Ç. and E.T.; Visualization, F.Ç.; Supervision, E.T.

Conflicts of interest

The authors have no conflict of interest to declare.

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Ethics approval

Local ethics committee approval was obtained from the Ethics Committee of Faculty of Medicine, University of Ataturk, Erzurum, Turkey, with the decision number of 27.06.2019/05-28.

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