Usefulness of Measurement of End-tidal CO₂ Using a Portable Capnometer in Patients with Chronic Respiratory Failure Receiving Long-term Oxygen Therapy

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Abstract:
Objective Patients with chronic respiratory failure requiring long-term oxygen therapy (LTOT) are at a risk of CO₂ retention because of excessive oxygen administration. The CapnoEye™ is a novel portable capnometer that can measure end-tidal CO₂ (EtCO₂) noninvasively. This retrospective study evaluated the usefulness of this device.
Methods EtCO₂ was measured using the CapnoEye. The EtCO₂ and partial pressure of venous carbon dioxide (PvCO₂) were analyzed, and other clinical data were assessed.
Patients Sixty-one consecutive patients with chronic respiratory failure receiving LTOT in the outpatient department at the Japanese Red Cross Medical Center between July 2017 and March 2018 were retrospectively reviewed.
Results There was a significant correlation between EtCO₂ and PvCO₂ (r=0.63) in the total study population as well as in the COPD group (r=0.65) and ILD group (r=0.67). The PvCO₂ and EtCO₂ gradient was correlated with only the body mass index in a multivariate analysis (p=0.0235). The EtCO₂ levels on the day of admission were significantly higher than those in the same patients when they were in a stable condition (p=0.0049). There was a significant correlation between ΔEtCO₂ and ΔPvCO₂ (r=0.4). A receiver-operating characteristic curve analysis revealed the optimal cut-off EtCO₂ value for identifying hypercapnia to be 34 mmHg (p=0.0005).
Conclusion The evaluation of EtCO₂ by the CapnoEye was useful for predicting PvCO₂. The body mass index was identified as a possible predictor of the PvCO₂ and EtCO₂ gradient. An increase in EtCO₂ may indicate deterioration of the respiratory status in patients with chronic respiratory failure receiving LTOT.

Key words: CapnoEye, long-term oxygen therapy, end-tidal CO₂, portable capnometer, chronic obstructive pulmonary disease, interstitial lung disease

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Introduction
Supplemental long-term oxygen therapy (LTOT) improves the survival, exercise capacity, and quality of life in patients with chronic obstructive pulmonary disease (COPD) and hypoxemia (1) as well as in those with sequelae of tuberculosis (2). LTOT has also been reported to improve the quality of life in patients with chronic interstitial lung disease (ILD) (3). The number of patients receiving LTOT has increased in Japan (4) and is likely to continue to increase because of the aging population. According to the Global Initiative for Chronic Obstructive Lung Disease guideline, LTOT is indicated in patients who have a PaO₂ ≤55 Torr or an SaO₂ ≤88% with or without hypcapnia and in those with a PaO₂ of 55-60 Torr or an SaO₂ of 88% if there is evidence of pulmonary hypertension suggesting congestive heart failure (1).
After oxygen therapy is started, blood gases should be checked to ensure that oxygenation is satisfactory without retention of CO₂ and/or worsening acidosis. An American Thoracic Society/European Respiratory Society position paper reported that an arterial blood gas (ABG) analysis was the preferred method for determining the need for oxygen, as it includes acid-base information (5). Patients with chronic respiratory failure who need LTOT are at risk of CO₂ retention as a result of the administration of excessive oxygen; therefore, it is important to monitor the blood CO₂ level regularly. However, the evaluation of the blood CO₂ level every time a patient visits the outpatient department is difficult because blood gas sampling is invasive and painful.

End-tidal CO₂ (EtCO₂), which is measured using a capnometer, is positively correlated with blood CO₂ (6) and is now part of the standard of care for all mechanically ventilated patients receiving general anesthesia and routine monitoring in intensive-care settings (7). In July 2018, the CapnoEye™ MC600 (Nissei Co., Ltd., Osaka, Japan), a novel capnometer that measures the EtCO₂ level correctly in patients who are breathing spontaneously (Fig. 1), was approved for use in Japan, but its clinical value in patients receiving LTOT remains unclear.

The blood CO₂ levels need to be measured noninvasively in outpatients with chronic respiratory failure because of the difficulties inherent in routine measurement of blood arterial CO₂. The aim of this study was to evaluate the ability of the CapnoEye MC600 to measure EtCO₂ and to assess the relationship between EtCO₂ and the PCO₂ level in patients receiving LTOT.

**Materials and Methods**

The study protocol was approved on June 1, 2018, by our institutional review board (approval number 680). The requirement for written informed consent was waived due to the use of an opt-out method (8). The study population consisted of 61 consecutive outpatients with chronic respiratory failure who received LTOT and underwent blood sampling between July 2017 and March 2018.

**EtCO₂ measurements**

The mainstream EtCO₂ level was measured using the CapnoEye. Patients performed a tidal volume (TV) maneuver with the mouthpiece at a constant flow rate and in a relaxed position six times while holding the EtCO₂ sensor with the hand opposite to the one with the SpO₂ sensor attached. The EtCO₂ was analyzed automatically as the average of the readings obtained during the six TV maneuvers and displayed on the monitor. The measurements were supported by experienced technicians in all cases.

**Data collection**

The flow of the enrolled patients throughout the study is shown in Fig. 2. Between July 2017 and March 2018, 89 patients who visited our outpatient department and received LTOT were considered for enrollment. Twenty-eight patients were excluded because a lack of either EtCO₂ or PvCO₂ data, thus leaving 61 patients for inclusion in the study. The correlations between EtCO₂, PvCO₂, and pulmonary function tests were analyzed in these 61 patients (method 1). Forty of these patients were excluded because they were not admitted for an observation period, thereby leaving 21 patients who had been admitted for additional analysis. The baseline data for these 21 patients were collected when they were in a stable condition, i.e., with stable vital signs, a normal level of consciousness, and an assessment of at least one month before the most recent admission. The EtCO₂ data at baseline were compared with those obtained during the admission period and correlations between ΔEtCO₂, ΔPvCO₂, and pulmonary function tests were sought (Method 2).

Pulmonary function tests were performed using a rolling seal-type spirometer (Fudac-77; Fukuda Denshi Co., Ltd., Tokyo, Japan). The medical records of each patient were also reviewed.

**Statistical analyses**

Correlations were analyzed using the Spearman’s rank correlation coefficient. The change in the EtCO₂ level according to the respiratory status in the same patients was analyzed using Wilcoxon’s signed rank test. A multiple regression analysis was used to predict the values of dependent and independent variables. Logistic regression and receiver-operating characteristic curve analyses were used to evaluate the diagnostic performance of EtCO₂. The descriptive data are shown as the median, frequency, and percentage. All reported p-values are two-sided. The data were analyzed using the JMP 9 software program, version 9.0.3 (SAS Institute Inc., Cary, NC, USA). A p-value <0.05 was considered statistically significant.
**Results**

The characteristics of the 61 patients [36 men, 25 women; median age 74 (34-96) years old] who received LTOT at our hospital during the study period are shown in Table. All patients had a Glasgow Coma Scale score >13, indicating a clear consciousness level. None of the patients were ventilated via tracheostomy. Eight patients required noninvasive positive pressure ventilation for COPD, ILD, or sequelae of tuberculosis. Fifty-four patients required oxygen therapy for 24 hour, and 7 required it only when sleeping or on exertion.

The underlying diseases were COPD in 31 patients, ILD in 17, sequelae of tuberculosis in 6, and other lung disease in 7. No patient had chronic kidney disease. The median EtCO₂ was 31 (18-41) mmHg and the median PvCO₂ was 49 (25-75) mmHg. On pulmonary function testing, the patients had a median FEV₁ of 1.32 (0.43-3.01) L, a %FEV₁ of 54% (25-132%), an FVC of 2.14 (0.6-4.7) L, and a %FVC of 77% (31-134%). The patient characteristics are shown according to sex in Table. There were significant differences in the smoking history, FVC, FEV₁%, and underlying diseases between the study groups.

There were significant correlations between EtCO₂ and PvCO₂, %FEV₁, and %FVC. A multivariate linear regression analysis was performed to predict the EtCO₂ and %FVC. The findings were statistically significant for EtCO₂ (regression coefficient beta, 0.63; 95% confidence interval [CI] 0.58-1.48, p <0.001) and %FEV₁ (regression coefficient beta, -0.3; 95% CI -0.22- -0.02, p=0.0189) but not for %FVC (regression coefficient beta, -0.11; 95% CI -0.07-0.16, p=0.458). There was a significant correlation between EtCO₂ and PvCO₂ in patients with COPD (r=0.5) and in those with ILD (r=0.63; Fig. 4A, 4B).

There were significant correlations between the PvCO₂ and EtCO₂ gradient and the body mass index (BMI; r=-0.35) and %FEV₁ (r=-0.33); however, there was no significant correlation with the TV (r=-0.14) or %FVC (r=-0.08; Fig. 5A-D). A multivariate linear regression analysis was performed to predict the PvCO₂ and EtCO₂ gradient based on the BMI and %FEV₁. The results were statistically significant for the BMI (regression coefficient beta, -0.34; 95% CI -1.16, -0.09, p=0.0235) but not for %FEV₁ (regression coefficient beta, -0.021; 95% CI -0.15, 0.02, p=0.1476).

The median time interval between the first visit and the day of admission was 2 (1-24) months. The EtCO₂ levels on the day of admission were significantly higher than those in the same patients when they were in a stable condition (p=0.0049; Fig. 6). Furthermore, there were significant correlations between ΔEtCO₂ and ΔPvCO₂ (r=0.4), TV (r=0.43), %FEV₁ (r=-0.4), and %FVC (r=0.45; Fig. 7A-D) in the study population overall. However, there was no statistically significant difference between the EtCO₂ level on the day of admission and that in a stable condition in the COPD and ILD groups.

The receiver-operating characteristic curve for EtCO₂ predicting hypercapnia as PvCO₂ >45 mmHg is shown in Fig. 8A. The area under the curve was 0.849 for EtCO₂. The
optimum \text{EtCO}_2 cut-off point for identifying hypercapnia was 34 mmHg (sensitivity 79.1\%, specificity 88.9\%). The receiver-operating characteristic curve for \text{EtCO}_2 predicting hypercapnia as \text{PvCO}_2 >70 \text{mmHg} is shown in Fig. 8B. The area under the curve was 0.806, and the optimum cut-off point was 38 mmHg for \text{EtCO}_2 (sensitivity 100\%, specificity 69.1\%).

**Discussion**

This is the first report on the value of \text{EtCO}_2 as measured by the CapnoEye in patients with chronic respiratory failure receiving LTOT. There was a significant correlation of \text{EtCO}_2 with \text{PvCO}_2 and an association of the \text{PvCO}_2 and \text{EtCO}_2 gradient with BMI. The \text{EtCO}_2 cut-off level of 34 mmHg was useful for predicting \text{CO}_2 retention and deterioration of respiratory status in the outpatient department.

\text{EtCO}_2 measurements obtained by a capnometer have been widely accepted as a sensitive method for reflecting the \text{PaCO}_2 level in intubated and mechanically ventilated patients. However, few studies have investigated the usefulness of \text{EtCO}_2 in patients who are breathing spontaneously (9-11). One of the reported advantages of capnometry is its ability to obtain a reliable estimate of \text{EtCO}_2 during a vital capacity maneuver in patients with chronic respiratory disease who are breathing spontaneously (9). In the present study, the \text{EtCO}_2 value was measured using the CapnoEye during a TV maneuver and compared with that obtained during a vital capacity maneuver; the TV maneuver is easy for patients with respiratory failure to perform because it needs only spontaneous breathing.

It is well known that \text{PaCO}_2 is the gold standard for the evaluation of hypercapnia; however, \text{PvCO}_2 has also been reported to have good concordance with \text{PaCO}_2 and to be a reliable, feasible, and safe alternative to repeated ABG analyses in patients with severe hypoxemic and/or hypercapnic respiratory failure (12). Therefore, \text{PvCO}_2 was thought to be a useful surrogate marker of \text{PaCO}_2 for the evaluation of hypercapnia in the present study.

The correlation of \text{EtCO}_2 and \text{PaCO}_2 has been reported to be unreliable in some clinical situations, and no correlation was found between \text{EtCO}_2 and \text{PaCO}_2 when the physiologic dead space was substantially elevated (13-19). Physiologic dead space ventilation is the sum of the anatomic dead space from the conducting airways and the alveolar dead space arising from a disease process and/or therapy.

The \text{EtCO}_2 level is normally 5 mmHg lower than that of \text{PaCO}_2 because of the mixing of \text{CO}_2 containing alveolar gas

| Table 1. Demographic and Clinical Characteristics of the 61 Patients in the Study at Baseline. |
|-----------------|-----------------|-----------------|
| Age, years      | Male (n=36)     | Female (n=25)   | p value |
| 74 (34-96)      | 75.5 (54-90)    | 72 (34-96)      | 0.7579  |
| Smoking history, pack years | 0 (0-160) | 0 (0-88.5) | <0.0001 |
| Body mass index | 19 (12-39)      | 20.5 (14-32.6)  | 0.1164  |
| \text{EtCO}_2, mmHg | 31 (18-41) | 34.5 (18-48) | 0.2013  |
| \text{PvCO}_2, mmHg | 49 (25-75) | 50 (25-75) | 0.0184  |
| \text{PvCO}_2 - \text{EtCO}_2 | 15 (-1.4, 34) | 15 (-1.4, 34) | 0.3589  |
| \text{FEV}_1, L | 1.32 (0.43-3.01) | 1.15 (0.43-3.01) | 1.4 (0.55-1.99) | 0.2674 |
| \%\text{FEV}_1, \% | 54 (25-132) | 53.9 (25-131) | 66.5 (34.9-132) | 0.1964 |
| \text{FVC}, L  | 2.14 (0.6-4.7)  | 2.58 (0.6-4.7)  | 1.56 (0.79-2.96) | 0.0057 |
| \%\text{FVC}, \% | 77 (31-134) | 79 (31.2-134) | 64.5 (39-129) | 0.2184 |
| \text{FEV}_1/\text{FVC}, \% | 66.1 (23-97) | 62 (23-88) | 73.1 (61-97) | 0.0084 |
| \text{TV}, L   | 0.66 (0.21-1.4) | 0.72 (0.21-1.4) | 0.48 (0.37-1.17) | 0.176 |
| Oxygen flow rate at rest | 2 (0-5) | 2 (0-5) | 2 (0-4) | 0.8577 |
| NPPV, n (%)     | 8               | 6               | 2       | 0.6363 |
| \text{IPAP}, cmH}_2O | 9 (0-12) | 8 (0-12) | 11 (8-11) | 0.4478 |
| \text{EPAP}, cmH}_2O | 4 (4-8) | 4 (4-8) | 4 | 0.3291 |
| Admission, n (%) | 21              | 14              | 7       | 0.3606 |
| \Delta\text{EtCO}_2, mmHg | 4 (-8, 16) | 0 (-8, 16) | 7.5 (-3, 13) | 0.0543 |
| \Delta\text{PvCO}_2, mmHg | 5 (-5, 21) | 4 (-5, 21) | 7 (-1.7, 12) | 0.6926 |
| Underlying diseases, n (%) | 31 (50.8) | 23 (37.7) | 8 (13.1) | 0.0143 |
| COPD            | 17 (27.9)      | 18 (31.1)      | 9 (14.8) | 0.2379 |
| ILD             | 6 (9.8)        | 5 (8.2)        | 1 (1.6)  | 0.0201 |
| TBsq            | 7 (11.5)       | 0              | 7 (11.5) | 0.0007 |

The data are presented as the median (range) or number (percentage). COPD: chronic obstructive pulmonary disease, EPAP: expiratory positive airway pressure, \text{EtCO}_2: end-tidal carbon dioxide, \text{FEV}_1: forced expiratory volume in one second, \text{FVC}: forced vital capacity, ILD: interstitial lung disease, IPAP: inspiratory positive airway pressure, NPPV: noninvasive positive pressure ventilation, \text{PvCO}_2: partial pressure of venous carbon dioxide, TBsq: sequelae of tuberculosis, TV: tidal volume.
and gas devoid of CO\(_2\) from the anatomic dead space (20). In patients with lung disease, the additional alveolar dead space further dilutes the EtCO\(_2\) relative to the PaCO\(_2\) (20).

In patients with lung disease, the additional alveolar dead space (22). For example, the normal ratio of the physiologic dead space to TV (VD/VT) is 0.2-0.35 (21) but has been found to be 0.4-0.55 in patients with acute lung injury as a result of the limitations and emphysematous destruction were considered to increase the alveolar dead space, which might have caused the inequality in the ventilation/perfusion (V/Q) ratio. However, Sandek et al. found no significant correlation between the air flow obstruction measured by spirometry and the V/Q ratio (24). In the present study, %FEV\(_1\) was not a significant independent predictor of the PvCO\(_2\) and EtCO\(_2\) gradient. This finding is consistent with a previous speculation that inequality in the V/Q ratio might be buffered by underlying pathophysiological processes, including hypoxic vasoconstriction and active collateral ventilation (24, 25).

The positive mechanical pressure used when measuring EtCO\(_2\) in intubated and mechanically ventilated patients might increase the ventilation of the atelectatic lobe and reduce intravascular pulmonary fluid iatrogenically, leading to a V/Q mismatch and additional alveolar dead space (26). The mechanical dead space added by the endotracheal tube might further increase the PvCO\(_2\) and EtCO\(_2\) gradient. In our study, the exclusion of mechanically ventilated patients resulted in a reduction in dead space ventilation and might explain the strong correlation found between PvCO\(_2\) and EtCO\(_2\) even in patients with chronic respiratory failure.

EtCO\(_2\) was correlated with both FEV\(_1\) and FVC in this study. There has been a similar report of a significant correlation of FEV\(_1\) with EtCO\(_2\) measured using a capnometer (11, 12); however, to our knowledge, this is the first report of a correlation between EtCO\(_2\) and FVC. Although the mechanism underlying the elevation of EtCO\(_2\) in response to decreases in FEV\(_1\) remains unclear, a reduced FEV\(_1\) value is associated with the severity of obstructive lung disease, and obstruction of the terminal bronchi has been cited as a reason for hypventilation of the alveoli and a cause of CO\(_2\) retention (27, 28). In the present study, FVC was strongly correlated with FEV\(_1\), so FEV\(_1\) may be a confounding factor that influenced the correlation between EtCO\(_2\) and FVC.

EtCO\(_2\) has previously been reported to be correlated with PCO\(_2\) in patients with COPD (9); however, there has been

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**Table 2. Baseline Characteristics of Patients with COPD, ILD and Other Diseases.**

|                          | COPD (n=31) | ILD (n=17) | Other diseases (n=13) | p value |
|--------------------------|-------------|------------|-----------------------|---------|
| Age, years               | 75 (41-96)  | 72 (54-87) | 74 (34-90)            | 0.4985  |
| Sex, n (%)               | 23          | 8          | 5                     | 0.0444  |
| Male                     | 8           | 9          | 8                     |         |
| Female                   | 23          | 8          | 8                     |         |
| Smoking history, pack years | 50 (0-150) | 0 (0-160)  | 0                     | <0.0001 |
| Body mass index          | 21 (14-28.2)| 18.9 (12-39)| 16.2 (14.1-19.5)     | 0.0079  |
| EtCO\(_2\), mmHg         | 34 (18-46)  | 36 (27-50) | 42 (30-53)            | 0.0083  |
| PvCO\(_2\), mmHg         | 47 (25-75)  | 46 (37-72) | 62 (44-73)            | 0.0064  |
| PVCO\(_2\)-EtCO\(_2\)    | 13 (-1.4, 34)| 8.5 (8-28) | 19.5 (14-26)          | 0.075   |
| FV\(_1\), L              | 1.14 (0.43-2.84)| 1.81 (0.65-3.01)| 0.77 (0.43-1.99) | 0.0128  |
| %FEV\(_1\), %            | 54 (25-132) | 100 (34.9-131)| 46.9 (37.7-73)     | 0.0026  |
| FVC, L                   | 2.6 (0.82-4.7)| 2.08 (0.98-3.39)| 0.93 (0.6-3.06)    | 0.0015  |
| %FVC, %                  | 80.4 (40-134)| 85.4 (41-111)| 41.2 (31.2-65)     | 0.0006  |
| FEV\(_1\)/FVC, %         | 60.5 (23-84)| 78.5 (64.3-97)| 74.7 (53.2-88.9) | <0.0001 |
| TV, L                    | 0.72 (0.37-1.4)| 0.81 (0.28-1.18)| 0.45 (0.21-0.81)  | 0.0052  |
| Oxygen flow rate at rest | 2 (0-5)     | 2 (0-4)    | 2 (1-4)               | 0.8754  |
| NPPV, n (%)              | 3           | 1          | 4                     | 0.013   |
| IPAP                     | 10 (0-12)   | 0          | 9.5 (8-11)            | 0.2336  |
| EPAP                     | 4 (4-8)     | 7          | 4                     | 0.2401  |
| Admission, n (%)         | 10          | 3          | 8                     | 0.1815  |
| ΔEtCO\(_2\), mmHg        | 1 (-8, -14) | -4 (-6, -4) | 7.5 (-2, -16)       | 0.0755  |
| ΔPvCO\(_2\), mmHg        | 6 (0-12)    | -1.7 (-5,-3)| 7 (-1,-21)          | 0.0716  |

The data are presented as the median (range) or number (percentage). COPD: chronic obstructive pulmonary disease, EPAP: expiratory positive airway pressure, EtCO\(_2\): end-tidal carbon dioxide, FEV\(_1\): forced expiratory volume in one second, FVC: forced vital capacity, ILD: interstitial lung disease, IPAP: inspiratory positive airway pressure, NPPV: noninvasive positive pressure ventilation, PvCO\(_2\): partial pressure of venous carbon dioxide, TV: tidal volume.
Figure 3. Correlations of EtCO2 with pulmonary function test results. EtCO2 was measured in outpatients with chronic respiratory failure who were receiving long-term oxygen therapy. (A) There was a significant positive correlation of EtCO2 with PvCO2 (r=0.63) and (B) a significant negative correlation of EtCO2 with FEV1 (r=-0.44), (C) %FEV1 (r=-0.36), (D) FVC (r=-0.54), and (E) %FVC (r=-0.64). (F) There was a significant positive correlation of %FEV1 with %FVC (r=0.52). COPD: chronic obstructive pulmonary disease, EtCO2: end-tidal carbon dioxide, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, ILD: interstitial lung disease, PvCO2: partial pressure of venous carbon dioxide.

Figure 4. Correlations of EtCO2 with PvCO2 in outpatients with COPD or ILD. There was a significant positive correlation of EtCO2 with PvCO2 in (A) outpatients with COPD (r=0.5) and (B) with ILD (r=0.63). COPD: chronic obstructive pulmonary disease, EtCO2: end-tidal carbon dioxide, ILD: interstitial lung disease, PvCO2: partial pressure of venous carbon dioxide.

no study of the correlation between EtCO2 and PCO2 in patients with ILD. In this study, EtCO2 was confirmed to be correlated with PvCO2 not only in patients with COPD but also in those with ILD. This finding highlights the value of EtCO2 for predicting hypercapnia in both obstructive and restrictive lung disease. EtCO2 on the day of admission was significantly higher than that recorded when the patients were in a stable condi-
Figure 5. Correlations of the \( P_{\text{vCO}_2} \) and \( E_{\text{tCO}_2} \) gradient with the BMI and pulmonary function test results. (A) There was a significant negative correlation of the \( P_{\text{vCO}_2} \) and \( E_{\text{tCO}_2} \) gradient with the BMI \((r=-0.35)\) and (B) \%FEV\(_1\) \((r=-0.33)\) and (C) no significant correlation of the \( P_{\text{vCO}_2} \) and \( E_{\text{tCO}_2} \) gradient with the TV \((r=-0.14)\) or (D) \%FVC \((r=-0.08)\). \( E_{\text{tCO}_2} \): end-tidal carbon dioxide, \( \text{FEV}_1 \): forced expiratory volume in one second, \( \text{FVC} \): forced vital capacity, \( P_{\text{vCO}_2} \): partial pressure of venous carbon dioxide, TV: tidal volume.

Figure 6. A comparison of \( E_{\text{tCO}_2} \) between patients who were admitted to the hospital according to their respiratory status. The \( E_{\text{tCO}_2} \) was significantly higher in patients with respiratory failure who were admitted immediately after measurement of \( E_{\text{tCO}_2} \) than in the same patients when they were in a stable condition \((p=0.0049)\). \( E_{\text{tCO}_2} \): end-tidal carbon dioxide.

It is well known that \( \text{CO}_2 \) retention depresses awareness, even to the point of total loss of consciousness, so monitoring the blood \( \text{CO}_2 \) level is an important component of the patient assessment. Previous studies that used \( P_{\text{vCO}_2} \) to
Figure 7. Correlations of ΔEtCO2 with ΔPvCO2 and pulmonary function test results. (A) There was a significant positive correlation of ΔEtCO2 with ΔPvCO2 \((r=-0.4)\) and a significant negative correlation of ΔEtCO2 with the (B) TV \((r=-0.43)\), (C) %FEV1 \((r=-0.4)\), and (D) %FVC \((r=-0.45)\). EtCO2: end-tidal carbon dioxide, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, PvCO2: partial pressure of venous carbon dioxide, TV: tidal volume.

Figure 8. Ability of the receiver-operating characteristic curve of EtCO2 to predict hypercapnia. (A) A plot of the EtCO2 curve for the prediction of hypercapnia defined as PvCO2 >45 mmHg with an area under the curve of 0.849. (B) A plot of the EtCO2 curve for the prediction of hypercapnia defined as a PvCO2 of >70 mmHg with an area under the curve of 0.806.

screen for potential hypercapnia found that it had a sensitivity of 79% when a cut-off point of >45 mmHg was used (29). Therefore, the screening cut-off in the present study was defined as a PvCO2 of >45 mmHg, and the optimum cut-off point for hypercapnia was set at an EtCO2 of >34 mmHg. Furthermore, the elevation of PaCO2 to >70-75 mmHg has been reported to reduce the level of awareness (30). An EtCO2 of >38 mmHg was shown to be a possible biomarker of a PvCO2 >70 mmHg. By determining the cut-off point for EtCO2, the evaluation of the increase in
EtCO₂ over time may be able to predict the exacerbation of respiratory failure, thereby allowing for the early treatment and avoidance of admission.

Several limitations associated with the present study warrant mention, including its retrospective design, single-institution setting, small sample size, and inclusion of patients who needed differing oxygen flow rates. Furthermore, PvCO₂ was measured instead of PaCO₂, and the difference between the venous and arterial CO₂ levels may be influenced by the cardiac output and tissue consumption; therefore, our ability to evaluate the correlation between EtCO₂ and PaCO₂ accurately was limited. Other limitations that restricted our ability to evaluate the usefulness of EtCO₂ in patients with a deteriorating respiratory status included the lack of clinical data besides EtCO₂ and PvCO₂ in patients who required hospital admission. Finally, the CapnoEye can only evaluate EtCO₂ in patients who are alert and breathing spontaneously and is thus unsuitable for use with patients who are unconscious.

**Conclusions**

This is the first study to demonstrate the correlation of EtCO₂ and PvCO₂ with the pulmonary function in spontaneously breathing patients with chronic respiratory failure. Repeated EtCO₂ measurements were obtained noninvasively by the CapnoEye. The CapnoEye was convenient and useful for estimating PvCO₂. The BMI was identified as a possible predictor of the PvCO₂ and EtCO₂ gradient. An increase in EtCO₂ to >34 mmHg may indicate the deterioration of the respiratory status in patients with chronic respiratory failure receiving LTOT.

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