

Comparison of End-Tidal, Arterial, Venous, and Transcutaneous PCO₂

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BACKGROUND: We investigated the measurement of end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) with a capnometer in patients with respiratory failure, and we determined whether this technique could provide an alternative to measurement of P_{aCO_2} using arterial blood gas analysis in the clinical setting. **METHODS:** We measured P_{ETCO_2} in subjects with hypoxemic and hypercarbic respiratory failure using a capnometer. We simultaneously measured P_{aCO_2} , venous partial pressure of carbon dioxide (P_{vCO_2}), and transcutaneously measured partial pressure P_{CO_2} (P_{tcCO_2}). We analyzed agreements among these parameters with Bland-Altman analysis. We obtained 30 samples from subjects with hypoxemic respiratory failure and 30 samples from subjects with hypercarbic respiratory failure. **RESULTS:** Thirty subjects with hypoxemic respiratory failure and 18 subjects with hypercarbic respiratory failure participated in this study. Significant relationships were found between P_{ETCO_2} and P_{aCO_2} , between P_{tcCO_2} and P_{aCO_2} , and between P_{vCO_2} and P_{aCO_2} . Bland-Altman analysis of P_{ETCO_2} and P_{aCO_2} in all subjects revealed a bias of 6.48 mm Hg (95% CI 4.93–8.03, $P < .001$) with a precision of 6.01 mm Hg. Bland-Altman analysis of P_{ETCO_2} and P_{aCO_2} with hypoxemic respiratory failure revealed a bias of 5.14 mm Hg (95% CI 3.35–6.93, $P < .001$) with a precision of 4.80 mm Hg. Bland-Altman analysis of P_{ETCO_2} and P_{aCO_2} in subjects with hypercarbic respiratory failure revealed a bias of 7.83 mm Hg (95% CI 5.27–10.38, $P < .001$) with a precision of 6.83 mm Hg. **CONCLUSIONS:** P_{ETCO_2} can be measured simply using a capnometer, and P_{ETCO_2} measurements can estimate P_{aCO_2} . However, the limits of agreement were wide. Therefore, care providers must pay attention to the characteristics and errors of these devices. These results suggest that measurement of P_{ETCO_2} might be useful for screening for hypercarbic respiratory failure in the clinical setting. *Key words:* capnography; COPD; hypercapnia; monitoring; primary healthcare; respiratory failure. [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Hypoxemic respiratory failure is a respiratory disorder in which patients have a P_{aO_2} in room air of ≤ 60 mm Hg and a $P_{aCO_2} < 45$ mm Hg due to respiratory dysfunction. In contrast, a P_{aCO_2} of > 45 mm Hg is defined as hypercarbic respiratory failure. Evaluation of hypercapnia and

hypoxemia is essential when treating patients with respiratory disease, especially patients with hypercapnic respiratory failure. Arterial blood sampling is therefore required, sometimes repeatedly, but ideally noninvasive techniques should be used when possible to monitor the patient's respiratory condition in the hospital, as well as in outpatient clinics.¹ Oxygen saturation is thus commonly measured because pulse oximetry offers a simple and noninvasive approach.

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Air Water Medical provided the CapnoEye MC-600 device free of charge. The authors have disclosed no conflicts of interest.

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Measurement of end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) also provides a noninvasive method for estimating P_{aCO_2} ; however, it is difficult to collect pure respiratory gas in patients who are not intubated, making it difficult to measure P_{ETCO_2} accurately. We previously measured P_{ETCO_2} by attaching a monitor to the ventilator circuit, and measurement of P_{ETCO_2} has therefore usually been limited to patients in settings such as the operating room and ICU.² It is unknown whether measurement of P_{ETCO_2} using a capnometer in spontaneously breathing patients can be used as an alternative measurement of P_{aCO_2} to using arterial blood gas analysis in the clinical setting. We therefore evaluated P_{ETCO_2} measured with a capnometer and P_{aCO_2} in subjects with hypoxemic and hypercarbic respiratory failure and calculated their agreement and accuracy. We also compared these characteristics for transcutaneously measured partial pressure of carbon dioxide (P_{tcCO_2}), which is covered by insurance in Japan, and venous partial pressure of carbon dioxide (P_{vCO_2}) against P_{aCO_2} .

Methods

Ethical Consideration

This was a prospective observational cohort study of subjects who received out-patient care or were admitted to the National Center for Global Health and Medicine between February 2017 and April 2017. All subjects provided informed consent for inclusion before participation in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Clinical Investigation for the National Center for Global Health and Medicine (Approval Number: NCGM-G-002135–00).

Equipment

P_{ETCO_2} was measured using a CapnoEye MC-600 (Air Water Medical, Tokyo, Japan). This is a transportable mainstream pulse oxi-capnometer that enables measurement of P_{ETCO_2} and oxygen saturation by pulse oximetry at the patient's bedside, either in the hospital or at the patient's home (Fig. 1A, 1B). Measurements were performed using a mouthpiece from a conventional capnometer, but with the device's own analysis algorithm. Subjects held the mouthpiece in their mouth and breathed quietly 6 times. P_{ETCO_2} measurements were based on a nondispersive infrared absorption method, which utilizes the ability to absorb infrared light of a wavelength corresponding to the concentration of carbon dioxide contained in the expired gas. Infrared light is irradiated toward and absorbed by the respiratory gas, and the amount of remaining light is detected by a light receiver through 2 types of optical filters.

QUICK LOOK

Current knowledge

Evaluation of hypercapnia and hypoxemia is essential when treating patients with respiratory disease, especially in patients with hypercapnic respiratory failure. It is preferable to use the most noninvasive monitoring technique possible to monitor the patient's respiratory condition.

What this paper contributes to our knowledge

P_{ETCO_2} can be measured simply using a capnometer. Measurement of P_{ETCO_2} in spontaneously breathing patients might be useful for screening for hypercapnic respiratory failure. However, clinicians must be aware of the characteristics and potential errors of these devices.

The P_{ETCO_2} level was then obtained based on the measured value.

P_{tcCO_2} was measured with a TCM TOSCA device (Radiometer Basel AG, Basel, Switzerland) (Fig. 1C), which is an established method for obtaining P_{tcCO_2} . Several reports have described its use as a monitor,³ and it has demonstrated good correlation between P_{aCO_2} and P_{tcCO_2} when used in the operating room.⁴ The device was calibrated beforehand using carbon dioxide gas built into the TCM TOSCA. The probe was then attached to the earlobe using a dedicated clip, and P_{tcCO_2} was recorded after the value measured by the TCM TOSCA had stabilized.

Arterial blood samples were drawn from either the right or left radial artery and collected via a heparinized needle and syringe system. Venous blood samples were drawn from either the right or left antecubital vein and aspirated into a separate heparinized blood gas syringe via a needle. The samples were analyzed using a blood gas analyzer (GASTAT 602i; Techno Medica, Yokohama, Japan) as quickly as possible after collection.

Subjects and Study Design

We screened and registered subjects already known to satisfy the definitions of respiratory failure regarding P_{aO_2} measures prior to being placed on supplemental oxygen. We simultaneously measured P_{ETCO_2} , P_{aCO_2} , P_{vCO_2} , and P_{tcCO_2} , and we then analyzed the relationships among these parameters and compared the measured data between the 2 groups.

Measurements were performed while the subjects rested in a sitting position. A constant oxygen dose was administered during the measurement period, but this was inter-

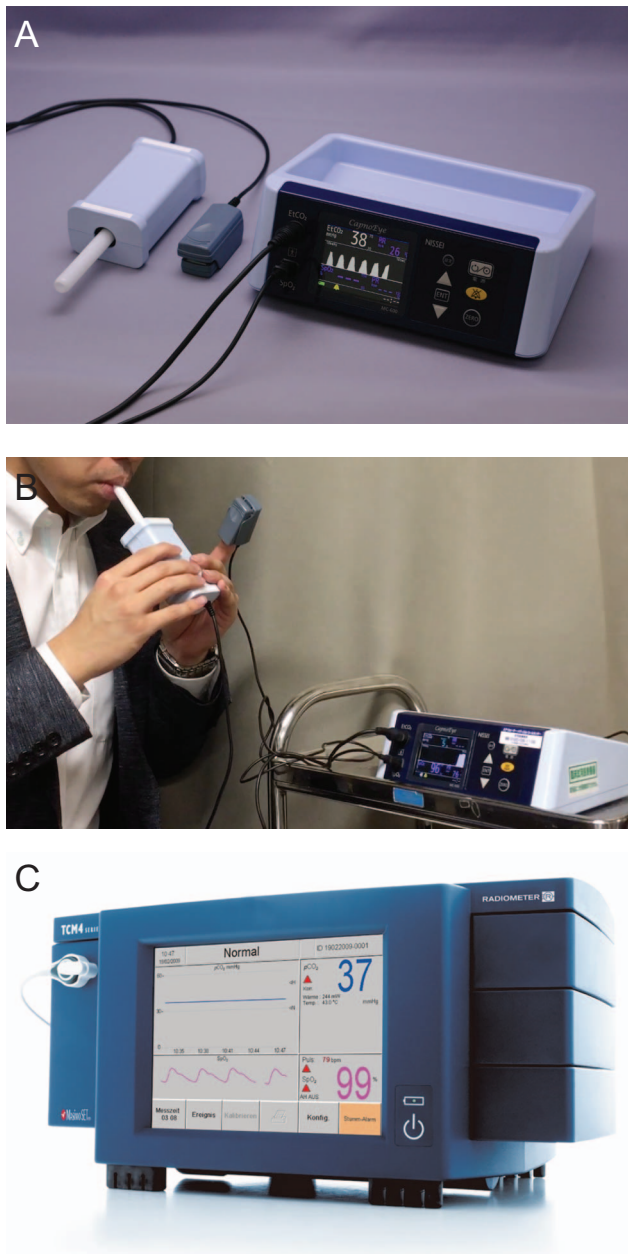
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Fig. 1. Equipment used in this study. A: CapnoEye MC-600. B: Measurement of P_{ETCO_2} using CapnoEye MC-600. C: TCM TOSCA. With permission.

rupted immediately before P_{ETCO_2} measurement to prevent the oxygen flow from affecting the value measured with the capnometer. Oxygen administration was resumed promptly upon completion of the measurement.

Statistical Analysis

We estimated the required sample size based on data provided by the manufacturer of the capnometer (Air Water Medical); 30 measurements were required for each

type of respiratory failure (ie, hypoxemic and hypercarbic).

Data are presented as mean \pm SD. We analyzed the agreements between P_{ETCO_2} and P_{aCO_2} and between P_{tCO_2} and P_{aCO_2} with Bland-Altman analysis, and we calculated the estimated bias (ie, the mean difference between 2 methods) and precision (ie, 1 SD of the differences) in subjects with hypoxemic respiratory failure, in subjects with hypercarbic respiratory failure, and in both groups as a whole. Pairwise comparison of characteristics was performed with the Fisher exact test for categorical variables and with the Wilcoxon rank-sum test for non-normally distributed numerical variables. Statistical analysis was performed using JMP 13 (SAS Institute, Cary, North Carolina).

Results

Subject Characteristics

Subjects' main characteristics are shown in Table 1; 30 subjects with hypoxemic respiratory failure and 18 subjects with hypercarbic respiratory failure participated in this study. We collected a total of 60 samples (ie, 30 samples from subjects with hypoxemic respiratory failure and 30 samples from subjects with hypercarbic respiratory failure) to confirm the accuracy of the examination in subjects with either high or low carbon dioxide measurements. Some subjects with hypercarbic respiratory failure therefore underwent more than one measurement. The mean age of the subjects was 76 ± 11 years. The subjects had various underlying diseases, of which COPD was the most common. Thoracic deformity tended to be more common in subjects with hypercarbic respiratory failure.

Relationships Among Respiratory Function Measures in All Subjects

Agreements between P_{ETCO_2} and P_{aCO_2} , between P_{tCO_2} and P_{aCO_2} , and between $P_{\bar{V}CO_2}$ and P_{aCO_2} in all subjects are shown in Figure 2. Bland-Altman analysis between P_{ETCO_2} and P_{aCO_2} revealed a bias of 6.48 mm Hg (95% CI, 4.93–8.03, $P < .001$) with a precision of 6.01 mm Hg. Bland-Altman analysis between P_{tCO_2} and P_{aCO_2} revealed a bias of 1.25 mm Hg (95% CI, -0.12 to 2.63, $P = .037$) with a precision of 5.35 mm Hg. Bland-Altman analysis between $P_{\bar{V}CO_2}$ and P_{aCO_2} revealed a bias of -7.08 mm Hg (95% CI, -9.18 to -4.97 , $P < .001$) with a precision of 8.14 mm Hg.

Relationships Among Respiratory Function Measures in Subjects With Hypoxemic Respiratory Failure

Bland-Altman analysis between P_{ETCO_2} and P_{aCO_2} in subjects with hypoxemic respiratory failure revealed a bias

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Table 1. Subject Characteristics

	Subjects	Hypoxemic Respiratory Failure	Hypercarbic Respiratory Failure	<i>P</i>
Male gender	41 (68)	25 (83)	16 (53)	.03
Age, y	76 ± 11	75 ± 11	78 ± 10	.29
P_{aCO_2} , mm Hg	48 ± 13	39 ± 5	56 ± 10	<.001
P_{vCO_2} , mm Hg	55 ± 14	46 ± 6	63 ± 14	<.001
P_{ETCO_2} , mm Hg	41 ± 11	33 ± 5	49 ± 8	<.001
P_{tcCO_2} , mm Hg	47 ± 12	38 ± 5	55 ± 9	<.001
COPD	29 (48)	16 (53)	13 (43)	.61
Interstitial pneumonia	15 (25)	10 (33)	5 (16)	.23
Previous tuberculosis	13 (22)	6 (20)	7 (23)	>.99
Bronchiectasis	4 (7)	2 (7)	2 (7)	>.99
Asthma	13 (22)	5 (17)	8 (27)	.53
Lung cancer	4 (7)	3 (10)	1 (3)	.61
Thoracic deformity	11 (18)	2 (7)	9 (30)	.041
Pneumonia	11 (18)	5 (17)	6 (20)	>.99
Chronic pulmonary aspergillosis	1 (2)	1 (3)	0 (0)	>.99
Non-tuberculous mycobacterium	2 (4)	0 (0)	2 (7)	.49
Pulmonary thromboembolism	2 (3)	2 (7)	0 (0)	.49
Chronic heart failure	9 (15)	4 (13)	5 (17)	>.99

There were 60 total samples, 30 samples from each respiratory failure group. Data are presented as mean ± SD or *n* (%). If a subject had multiple diseases, we counted each disease as a separate case. The Fisher exact test was used for categorical variables, and the Wilcoxon rank-sum was used for numerical variables.

P_{vCO_2} = mixed venous partial pressure of carbon dioxide

P_{tcCO_2} = transcutaneously measured partial pressure of carbon dioxide

of 5.14 mm Hg (95% CI, 3.35–6.93, $P < .001$) with a precision of 4.80 mm Hg. Bland-Altman analysis between P_{tcCO_2} and P_{aCO_2} revealed a bias of 0.97 mm Hg (95% CI, −0.59 to 2.54, $P = .10$) with a precision of 4.19 mm Hg. Bland-Altman analysis between P_{vCO_2} and P_{aCO_2} revealed a bias of −7.79 mm Hg (95% CI −9.80 to −5.77, $P < .001$) with a precision of 5.51 mm Hg.

Relationships Among Respiratory Function Measures in Subjects With Hypercarbic Respiratory Failure

Bland-Altman analysis between P_{ETCO_2} and P_{aCO_2} in subjects with hypercarbic respiratory failure revealed a bias of 7.83 mm Hg (95% CI 5.27–10.38, $P < .001$) with a precision of 6.83 mm Hg. Bland-Altman analysis between P_{tcCO_2} and P_{aCO_2} revealed a bias of 1.53 mm Hg (95% CI −0.84 to 3.90, $P = .09$) with a precision of 6.36 mm Hg. Bland-Altman analysis between P_{vCO_2} and P_{aCO_2} revealed a bias of −6.37 mm Hg (95% CI, −10.0 to −2.65, $P < .001$) with a precision of 10.2 mm Hg.

Discussion

Our findings showed that simple and noninvasive measurements of P_{ETCO_2} with a capnometer estimated P_{aCO_2} . However, the limits of agreement were wide. Therefore, care providers must pay attention to the characteristics and errors of these devices.

P_{ETCO_2} is often measured in closed circuits in patients undergoing mechanical ventilation. In the absence of significant changes in cardiac output or the ventilation/perfusion ratio, P_{aCO_2} can then be estimated with clinically acceptable sensitivity and specificity in comparison with P_{ETCO_2} .^{5,6} However, accurate measurement of P_{ETCO_2} has been problematic in patients who are not intubated because it is difficult to collect pure respiratory gas. Several recently developed transportable capnometers can measure P_{ETCO_2} easily and noninvasively in patients who are not intubated, and a recent study showed that they could provide reliable P_{ETCO_2} values compared with P_{aCO_2} .⁷ We therefore examined the usefulness of this approach in terms of the principle, experience of use, and measured values. A previous study showed that P_{ETCO_2} was 2–5 mm Hg lower than P_{aCO_2} during general anesthesia in subjects without lung disease,⁸ and we observed that P_{ETCO_2} was 6 ± 6 mm Hg lower than P_{aCO_2} . This study revealed wide limits of agreement in each group, which suggests that the measurement of P_{ETCO_2} with a capnometer requires attention to the characteristics and errors of these devices.

P_{tcCO_2} is more accurate than other measurements in any patient group. However, P_{tcCO_2} is complicated to measure and the required equipment is expensive, and therefore this technique is less widely used than pulse oximetry. There is thus a need to develop devices that can easily estimate P_{aCO_2} .

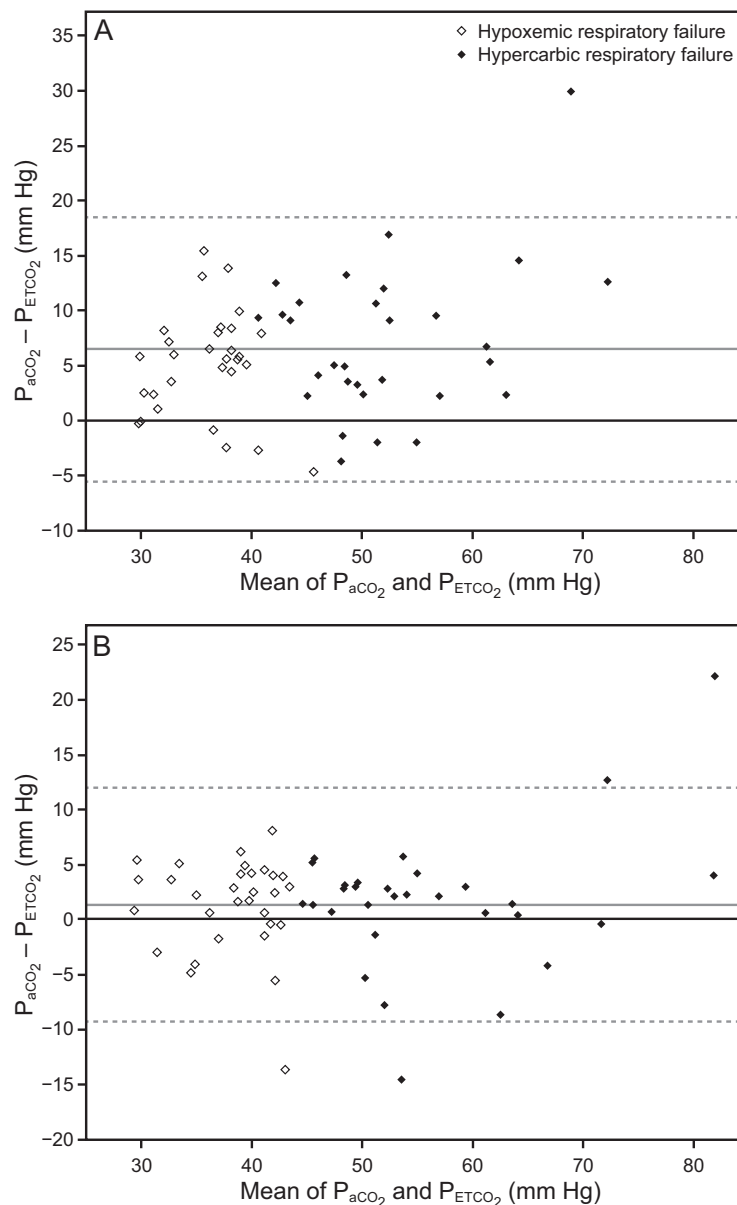
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Fig. 2. Bland-Altman analysis of respiratory gas parameters in all subjects. A: Comparison of P_{ETCO_2} and P_{aCO_2} in all subjects, with mean bias and limits of agreement. The solid line indicates bias = 6.48; dotted lines indicate upper and lower limits of agreement (± 1.96 SD). B: Comparison of P_{tCO_2} and P_{aCO_2} in all subjects, with mean bias and limits of agreement. The solid line indicates bias = 1.25; dotted lines indicate upper and lower limits of agreement (± 1.96 SD).

A previous study reported that P_{aCO_2} measurements at the time of COPD exacerbation could be replaced with P_{vCO_2} measurements.⁹ However, although P_{vCO_2} may be a useful measure, venous blood sampling is mildly invasive. Our results indicate that P_{ETCO_2} agreed with P_{aCO_2} as well as or better than P_{vCO_2} in any subject group, suggesting that P_{ETCO_2} may be a more useful measure than P_{vCO_2} .

The relative advantages and disadvantages of the capnometer and the transcutaneous carbon dioxide monitor are shown in Table 2. The capnometer is small and easy to carry, allowing it to be used regardless of location. In

addition, measurements can be performed within a few minutes, allowing its use even during out-patient clinical practice. It can also be used in settings outside of the hospital or out-patient clinic where blood gas analysis is not an option, such as during house calls. We observed no measurement-related complications in this study, and the patient burden was very small. Furthermore, the only equipment required is disposable mouthpieces, allowing the capnometer to measure P_{ETCO_2} at low cost. The capnometer has a disadvantage, however, in that the measured value changes depending on the patient's breathing pattern, and

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Table 2. Advantages and Disadvantages of CapnoEye and TCM TOSCA

	CapnoEye	TCM TOSCA
Advantages	<ul style="list-style-type: none"> • Easy to use • Portable • Inexpensive • Can measure in a few minutes • Can be used in primary care • No complications in measurement 	<ul style="list-style-type: none"> • More precise value • Objective value • Can measure continuously • Can be used for unconscious patients • Can record
Disadvantages	<ul style="list-style-type: none"> • Measurement values depend on the breathing pattern and oxygen flow • Can't measure continuously • Can't be used for unconscious patients • Can't record 	<ul style="list-style-type: none"> • Complicated to use • Expensive • Need a long time to measure • Complications of low-temperature burns

measured values of inhaled oxygen may be affected by oxygen flow. The developer of the device states that supplemental O_2 does not significantly affect the examination value at a flow ≤ 2 L of nasal oxygen. However, administration must be interrupted in cases of higher oxygen flows. In our study, we interrupted oxygen delivery at the time of measurement, and we therefore did not consider the relationship between oxygen flow rate and the measured value. Further studies are needed to clarify the effect of oxygen administration.

Another disadvantage of the capnometer is its inability to continuously monitor and record measurement values inside the equipment. Transcutaneous carbon dioxide monitors provide such measurements, and our results indicate that P_{tcCO_2} is more accurate than P_{ETCO_2} . Transcutaneous carbon dioxide monitors also measure P_{tcCO_2} continuously, and they can be used in patients with altered mental status, making them useful in ICUs and operating rooms. However, the measurement method is complicated and lengthy, and errors are caused by mixing of air. Furthermore, low-temperature burns have also been reported,¹¹ and the device must therefore be moved periodically to avoid this complication. This technique is limited further by the relative expense of the equipment and accessories. In addition, measurements obtained with transcutaneous carbon dioxide monitors tend to be higher than the P_{aCO_2} when the measured value is ≥ 50 mm Hg.⁴ We confirmed that measurement of P_{ETCO_2} with a capnometer could provide a simpler approach than measurement of P_{tcCO_2} .

This study had several limitations. First, the capnometer measurement depends on the subject's breathing pattern, thus the examiner must be familiar with the measurement method. Furthermore, caution is needed because expired air may leak from the corners of the patient's nose and mouth. Although P_{ETCO_2} was measured only once in this study, it may be possible to reduce error by measuring P_{ETCO_2} several times and using the average value. Second, numerous factors reportedly weaken the correlation be-

tween P_{ETCO_2} and P_{aCO_2} in mechanically ventilated patients,^{11,12} including severe respiratory failure, obesity, pregnancy, breathing frequency at the time of measurement, and posture,¹³⁻¹⁵ and these factors should also be taken into consideration when measuring P_{ETCO_2} with a capnometer. Third, some patients with hypercarbic respiratory failure underwent repeated measurements, which may be a source of bias. Finally, although we drew from either the right or left antecubital vein and took the tourniquet time as the minimum necessary time, we attempted to reduce the bias as much as possible by having the same researcher draw blood in the same way for all samples. In contrast, $P_{\bar{v}CO_2}$ is affected by local conditions, such as muscle conditions, and does not represent the partial pressure of central venous carbon dioxide, which may partly explain why $P_{\bar{v}CO_2}$ had a poor agreement with P_{aCO_2} . P_{ETCO_2} and P_{tcCO_2} have shown agreements with P_{aCO_2} commensurate with the increasing accuracy of the measuring instruments, and these measurements have become clinically applied as a substitute for P_{aCO_2} . However, caution is required for its application, and use without knowing the advantages and disadvantages of this method may result in erroneous results and improper clinical interpretation. Further studies are needed to assess their suitability in different diseases and clinical situations.

Conclusions

In this study, P_{ETCO_2} can be measured simply and non-invasively with a capnometer, and P_{ETCO_2} measurements can estimate P_{aCO_2} . However, the limits of agreement were wide. Therefore, care providers must pay attention to the characteristics and potential errors of these devices. Our results suggest that measurement of P_{ETCO_2} might be useful for screening for hypercarbic respiratory failure in the clinical setting, although further studies are needed to confirm the usefulness of these measurements.

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