Use of maximum end-tidal CO(2) values to improve end-tidal CO(2) monitoring accuracy.

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Use of Maximum End-Tidal CO_2 Values to Improve End-Tidal CO_2 Monitoring Accuracy

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BACKGROUND: The arterial partial pressure of CO_2 (P_{aCO_2}) can be grossly estimated by the end-tidal partial pressure of CO_2 (P_{ETCO_2}). This principle is used in SmartCare (Dräger, Lübeck, Germany), which is an automated closed-loop system that uses P_{ETCO_2} to estimate alveolar ventilation during mechanical ventilation. OBJECTIVE: To assess whether the maximum P_{ETCO_2} value (instead of the averaged P_{ETCO_2} value) over 2-min or 5-min periods improves P_{aCO_2} estimation, and determine the consequences for the SmartCare system. METHODS: We continuously monitored breath-by-breath P_{ETCO_2} during ventilation with SmartCare in 36 patients mechanically ventilated for various disorders, including 14 patients with COPD. Data were collected simultaneously from SmartCare recordings, every 2 min or 5 min, and through a dedicated software that recorded ventilation data every 10 s. We compared the maximum and averaged P_{ETCO_2} values over 2-min and 5-min periods to the P_{aCO_2} measured from 80 arterial blood samples clinically indicated in 26 patients. We also compared SmartCare's classifications of patient ventilatory status based on averaged P_{ETCO_2} values to what the classifications would have been with the maximum P_{ETCO_2} values. RESULTS: Mean P_{aCO_2} was 44 ± 11 mm Hg. P_{aCO_2} was higher than averaged P_{ETCO_2} by 10 ± 6 mm Hg, and this difference was reduced to 6 ± 6 mm Hg with maximum P_{ETCO_2}. The results were similar whether patients had COPD or not. Very few aberrant values ($< 0.01\%$) needed to be discarded. Among the 3,137 classifications made by the SmartCare system, 1.6% were changed by using the maximum P_{ETCO_2} value instead of the averaged P_{ETCO_2} value. CONCLUSIONS: Use of maximum P_{ETCO_2} reduces the difference between P_{aCO_2} and P_{ETCO_2} and improves SmartCare's classification of patient ventilatory status. *Key words: alveolar ventilation; capnometry; monitoring; mechanical ventilation; closed loop systems; weaning.* [Respir Care 2011;56(3):278–283. © 2011 Daedalus Enterprises]

Introduction

Monitoring of end-tidal partial pressure of CO_2 (P_{ETCO_2}) has applications in emergency medicine, anesthesia, and intensive care.[1,2] Although P_{ETCO_2} does not perfectly reflect arterial CO_2 measured from an arterial blood sample (P_{aCO_2}),[3,4] capnometry allows continuous monitoring of alveolar ventilation in intubated patients. The SmartCare automated ventilation and weaning system (Dräger, Lübeck,

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Germany) uses P_{ETCO_2} as a safety parameter, in addition to respiratory rate and tidal volume (V_T), to automatically control the pressure-support level.[5,6] SmartCare averages

P_{ETCO_2}, respiratory rate, and V_T over 2-min or 5-min periods, classifies the patient's ventilatory status, and adjusts the pressure-support level accordingly. P_{ETCO_2} is not a main control parameter in SmartCare, but can be used in situations such as a low respiratory rate to help differentiate between, for instance, central hypoventilation leading to hypercapnia versus hyperventilation with hypocapnia. P_{ETCO_2} is known to frequently underestimate P_{aCO_2} because of ventilation-perfusion mismatching and dead-space effect.[7,8] A spontaneously breathing patient may intermittently have higher P_{ETCO_2} values than the averaged value during prolonged exhalations.[9] Such a value may better reflect alveolar P_{CO_2} and may thus be closer to P_{aCO_2}. We assessed the use of the maximum P_{ETCO_2} value instead of the averaged P_{ETCO_2} value over 2 min or 5 min. On the one hand, this could improve the

accuracy of P$_{ETCO_2}$ as a proxy for P$_{aCO_2}$, and on the other hand it could improve SmartCare's classifications of the patient's ventilatory status by using a more reliable P$_{ETCO_2}$ value.

Methods

This study was purely observational, and the protocol was approved by the ethics committee of Erasme Hospital, Brussels, Belgium. The study was performed in the Erasme Hospital and Henri Mondor Hospital intensive care units.

Patients

The main inclusion criteria were hemodynamic stability, acceptable neurological status (Glasgow coma score $\geq$ 8), PEEP not higher than 10 cm H$_2$O, and pressure-support ventilation with pressure support of $\leq$ 20 cm H$_2$O. Patients were excluded if a clinical procedure was going to be performed within the next few hours.

Data Collection

Arterial blood samples were drawn for clinical indications and analyzed (ABL700, Radiometer, Copenhagen, Denmark, and GEM Premier 4000, Instrumentation Laboratory, Lexington, Kentucky) within a few minutes. Patients were ventilated with an Evita XL ventilator (Dräger, Lübeck, Germany) provided with the SmartCare system and an infrared P$_{ETCO_2}$ mainstream sensor (product number 6871500, Dräger, Lübeck, Germany) connected to a CO$_2$ cuvette for measurement. During pressure-support

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ventilation with SmartCare, a dedicated software (VentView, Dräger, Lübeck, Germany) recorded ventilatory data, including P$_{ETCO_2}$, every 10 s. SmartCare averages P$_{ETCO_2}$ values over 2 min or 5 min to classify the patient's ventilatory status, and we downloaded these data from the ventilator to the computer.

Procedure

SmartCare averages respiratory rate, V$_T$, and P$_{ETCO_2}$ over 2 min or 5 min, from values taken at a sampling period of 10 s. The VentView software records the respiratory data at the same sampling period. Recorded data correspond to the last breath of each 10-s data period. In a preliminary study, we compared VentView's P$_{ETCO_2}$ data averaged along SmartCare periods to SmartCare's own data, and the difference between VentView and SmartCare's averaged data was always less than 0.5 mm Hg. For each considered period, the averaged and maximum P$_{ETCO_2}$ were thus determined from the VentView data. Our study of P$_{aCO_2}$, P$_{ETCO_2}$, and SmartCare concerned 80 SmartCare periods of 2 min or 5 min, during which we took arterial blood samples. We compared SmartCare's classifications to the maximum P$_{ETCO_2}$ values instead of the averaged P$_{ETCO_2}$ values.

Statistics

We analyzed the relationship between P$_{aCO_2}$ and the averaged and maximum P$_{ETCO_2}$ with linear regression. We used the Pearson test to evaluate the correlation. Quantitative data are expressed as mean $\pm$ SD or median and interquartile range.

Results

The sample consisted of 36 mechanically ventilated patients, between March 2006 and July 2007. There were 14 females and 22 males, with a mean age of 63 $\pm$ 14 y. The patients' respiratory mechanics, as determined by the ventilator, were: dynamic compliance 44 mL/cm H$_2$O (IQR 31–63 mL/cm H$_2$O) and resistance 10 cm H$_2$O/L/s (IQR 7–13 cm H$_2$O/L/s). At inclusion, the mean PEEP was 5 (IQR 5–8) cm H$_2$O, the mean pressure-support level was 14 cm H$_2$O (IQR 12–16 cm H$_2$O), and the mean F$_{IO_2}$ was 0.40 (IQR 0.31–0.4). Fourteen patients had COPD. Three patients were tracheotomized; the others were orotracheally intubated. All ventilation was with a heated humidifier.

The mean duration of ventilation recordings with SmartCare was 3 hours 36 min per patient (IQR 3 hours 9 min to 4 hours 57 min). Of the 36 subjects, 26 had arterial blood gas measurements contemporaneous with the VentView and SmartCare data.

Table 1. Difference Between Averaged and Maximum P$_{ETCO_2}$ and P$_{aCO_2}$ During Ventilation With SmartCare*

	Difference (mm Hg) mean ± SD
P$_{aCO_2}$–averaged P$_{ETCO_2}$	10 ± 6
P$_{aCO_2}$–maximum P$_{ETCO_2}$	6 ± 6
Maximum P$_{ETCO_2}$–averaged P$_{ETCO_2}$	4 ± 3

* 26 patients. 80 pairs of values. P$_{aCO_2}$ = 43 ± 10 mm Hg. Averaged end-tidal partial pressure of CO2 (P$_{ETCO_2}$) = 33 ± 7 mm Hg. Maximum P$_{ETCO_2}$ = 37 ± 8 mm Hg.
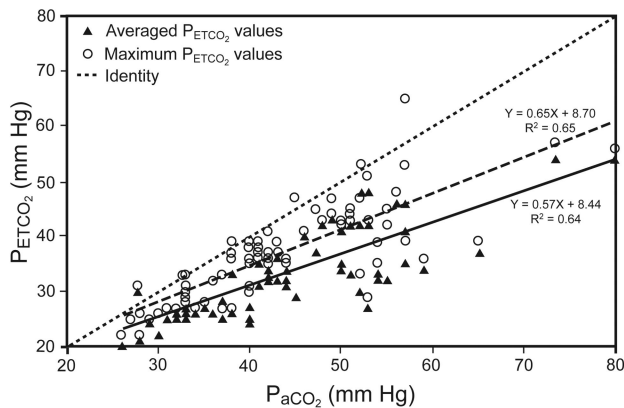

Fig. 1. Linear regression analysis of 80 pairs of maximum (dashed line) and averaged (solid line) end-tidal partial pressure of carbon dioxide (P$_{ETCO_2}$) and P$_{aCO_2}$ values, from 26 patients.

Relationship Between P$_{ETCO_2}$ and P$_{aCO_2}$

We analyzed 80 pairs of P$_{ETCO_2}$ and P$_{aCO_2}$ values from 26 patients. The mean ± SD number of arterial blood gas measurements was 3 ± 1 per patient. Mean P$_{aCO_2}$ was 44 ± 11 mm Hg.

Table 1 shows the differences between the averaged and maximum P$_{ETCO_2}$ and P$_{aCO_2}$ values. The pairs of values were obtained during 49 2-min SmartCare periods and 31 5-min SmartCare periods. P$_{aCO_2}$ was higher than averaged P$_{ETCO_2}$ by 10 ± 6 mm Hg. Taking the maximum instead of the averaged P$_{ETCO_2}$ value reduced the difference with P$_{aCO_2}$ by 4 mm Hg. Figure 1 shows the linear regression of the averaged and the maximum P$_{ETCO_2}$ against the P$_{aCO_2}$ values. The coefficient of regression was closer to identity with the maximum P$_{ETCO_2}$ values. Figure 2 plots the maximum P$_{ETCO_2}$ against the averaged P$_{ETCO_2}$.

Relationship Between P$_{ETCO_2}$ and P$_{aCO_2}$ Relative to COPD

There were 44 values from the 14 COPD patients and 36 values from 12 the non-COPD patients (Table 2). The results were similar whether patients had COPD or not.
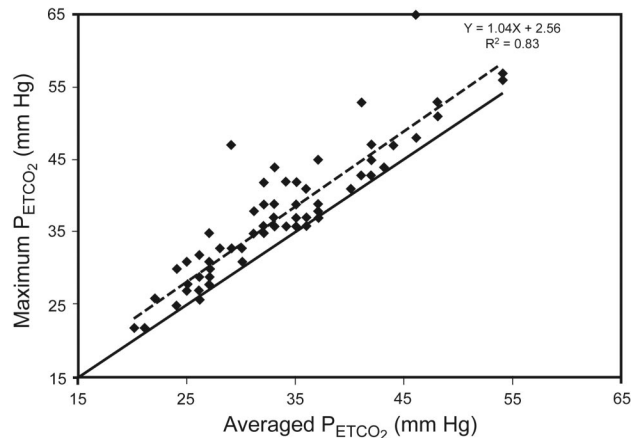

Fig. 2. Linear regression analysis of maximum end-tidal partial pressure of carbon dioxide (P$_{ETCO_2}$) versus averaged P$_{ETCO_2}$. The solid line is the identity line. The dashed line is the regression line.

Exclusion of P$_{ETCO_2}$ Aberrant Values

We defined an aberrant value as a contextually non-physiologic high P$_{ETCO_2}$ value. Aberrant values, measured via CO$_2$ infrared sensor, may be due to moisture, water, or dirt on the sensor. Because using one single maximum P$_{ETCO_2}$ value instead of averaged P$_{ETCO_2}$ values ran the risk of using aberrant values, when the difference between 2 consecutive values (separated by 10 s) was more than 40 mm Hg, the latter value was considered aberrant. We found 32 aberrant values (in the 74,777 total measurements), which came from 6 patients. Four patients had only one aberrant value, one patient had 21 aberrant values, and one patient had 7 aberrant values. The rate of aberrant values was 0.04%. We discarded all aberrant values.

SmartCare Classification

The classification of ventilation made by SmartCare for every recording using the averaged P$_{ETCO_2}$ and the maximum P$_{ETCO_2}$ values among the 3,137 SmartCare classifications for the 36 patients differed only for 49 classifications (1.6%), in 9 patients. For the pairs of data related to these classifications, the difference between maximum and averaged P$_{ETCO_2}$ was 16 ± 9 mm Hg, with a median of 13 mm Hg (IQR 13–20 mm Hg).

Discussion

The maximum P$_{ETCO_2}$ value was on average 4 mm Hg closer to P$_{aCO_2}$ than the averaged P$_{ETCO_2}$. Linear regression between P$_{ETCO_2}$ and P$_{aCO_2}$ was closer to the identity line with maximum P$_{ETCO_2}$. The use of maximum P$_{ETCO_2}$ in-

Table 2. P$_{ETCO_2}$ and P$_{aCO_2}$ in COPD Versus Non-COPD Patients During Ventilation With SmartCare

Patients	P$_{aCO_2}$ (mm Hg)	Averaged P$_{ETCO_2}$ (mm Hg)	Maximum P$_{ETCO_2}$ (mm Hg)	Comparison	Difference (mm Hg) mean $\pm$ SD	Pearson Correlation (r)
Without COPD (36 paired values, 12 patients)	40 $\pm$ 10	31 $\pm$ 7	35 $\pm$ 9	P$_{aCO_2}$ – averaged P$_{ETCO_2}$	9 $\pm$ 6	0.773
				P$_{aCO_2}$ – maximum P$_{ETCO_2}$	5 $\pm$ 6	0.813
				Maximum P$_{ETCO_2}$ – averaged P$_{ETCO_2}$	4 $\pm$ 4	0.936
With COPD (44 paired values, 14 patients)	46 $\pm$ 10	35 $\pm$ 8	39 $\pm$ 7	P$_{aCO_2}$ – averaged P$_{ETCO_2}$	11 $\pm$ 6	0.799
				P$_{aCO_2}$ – maximum P$_{ETCO_2}$	7 $\pm$ 6	0.795
				Maximum P$_{ETCO_2}$ – averaged P$_{ETCO_2}$	4 $\pm$ 3	0.903

P$_{ETCO_2}$ = end-tidal partial pressure of CO$_2$

frequently changed the classification determined by Smart-Care.

Relationship Between P$_{ETCO_2}$ and P$_{aCO_2}$

P$_{ETCO_2}$ is supposed to represent alveolar P$_{CO_2}$ (P$_{ACO_2}$), which is determined by the speeds at which CO$_2$ is filling alveoli and being emptied from alveoli. The P$_{ACO_2}$ depends on CO$_2$ production by tissues and venous blood flow content. CO$_2$ exhalation from alveoli depends on alveolar ventilation. If the alveolar ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$) is low, the P$_{ACO_2}$ will be close to venous pressure. If this ratio is normal, the P$_{ACO_2}$ will be close to P$_{aCO_2}$. If $\dot{V}_A/\dot{Q}$ is high, the P$_{ACO_2}$ will be closer to the inspired CO$_2$.[7] So P$_{aCO_2}$ tends to be higher than P$_{ACO_2}$, mainly because of ventilation-perfusion discrepancies. P$_{ACO_2}$ and P$_{ETCO_2}$ can thus be different, owing to the patient's ventilation and pulmonary condition (eg, restrictive or obstructive lung disease). Allowing a prolonged or complete exhalation (compared to a normal breath) could increase P$_{ETCO_2}$.[10] A longer exhalation may therefore better reflect P$_{ACO_2}$ among spontaneous breaths. We inferred that the use of maximum P$_{ETCO_2}$ during periods of 2 min or 5 min, as determined by the SmartCare system for averaging its parameters, could be a better indicator of alveolar ventilation than the averaged P$_{ETCO_2}$ during the same period.

We measured averaged P$_{ETCO_2}$, maximum P$_{ETCO_2}$, and P$_{aCO_2}$ contemporaneously. Table 1 shows that the difference between averaged P$_{ETCO_2}$ and P$_{aCO_2}$ was around 10 mm Hg, a value reported in several previous studies.[11-14] Our maximum P$_{ETCO_2}$ values were closer to P$_{aCO_2}$ by about 4 mm Hg, compared to the averaged P$_{ETCO_2}$. The maximum P$_{ETCO_2}$ had a higher correlation coefficient (r = 0.65 vs 0.57) in all periods (see Fig. 1), which indicates that maximum P$_{ETCO_2}$ better approximates P$_{aCO_2}$ than does averaged P$_{ETCO_2}$.

Maximum P$_{ETCO_2}$ was also found more accurate by Weinger et al.[9] They recorded P$_{aCO_2}$ and P$_{ETCO_2}$ in 25 patients after cardiotomy and being weaned with intermit-tent mandatory ventilation. P$_{ETCO_2}$ varied widely from breath to breath, and two thirds of the time the P$_{ETCO_2}$ of spontaneous breaths was greater than that of ventilator breaths. Maximum P$_{ETCO_2}$ was the most accurate indicator of P$_{aCO_2}$ (r = 0.77, P < .001), and the arterial-to-end-tidal difference was 4 $\pm$ 4 mm Hg (P < .01).

Chopin et al[10] also found a larger difference between maximum P$_{ETCO_2}$ and P$_{aCO_2}$ in patients with pulmonary embolism (12 mm Hg) versus patients without (1 mm Hg). They used a prolonged passive exhalation until maximum P$_{ETCO_2}$ was reached and found those values much closer to P$_{aCO_2}$.

Lujan et al[14] studied 120 non-ventilated patients and control subjects, classified in 4 equal groups according to COPD severity. With each subject, arterial blood was sampled, then the subject was asked to breath normally through a mouthpiece attached to a sidestream capnograph, and then to produce 3 maximal exhalations of at least 5 s each. For the entire cohort they found a better Pearson correlation between P$_{aCO_2}$ and P$_{ETCO_2}$ with maximal exhalation (r = 0.88, P < .001) than with P$_{ETCO_2}$ during normal tidal breathing (r = 0.72, P < .01). However, they also found that P$_{ETCO_2}$ during maximal expiration tended to overestimate P$_{aCO_2}$. In our study we found a similar alveolar-versus-end-tidal CO$_2$ difference (-2 mm Hg, interquartile range -3 to -1 mm Hg) in only 6 of the 80 pairs of maximum P$_{ETCO_2}$ and P$_{aCO_2}$ values. However, for the whole data the mean difference was positive (6 $\pm$ 6 mm Hg). The difference with Lujan's study,[14] which often found an overestimation of P$_{aCO_2}$, may be due to the long duration of maximal exhalation maneuvers (at least 5 s), while it was only spontaneous exhalations in our study.

P$_{ETCO_2}$ and P$_{aCO_2}$ Relative to COPD

P$_{ETCO_2}$ can be a poor proxy for P$_{aCO_2}$ in patients with parenchymal lung disease or emphysema undergoing weaning from mechanical ventilation.[15] In our clinical study we observed (see Table 2) a similar difference (4 mm Hg) between the maximum and averaged P$_{ETCO_2}$ in COPD and

Table 3. SmartCare's Classification of Ventilation Periods*

Condition	Spontaneous Respiratory Rate Condition (f)	V$_T$ Condition	P$_{ETCO_2}$ Condition	Change in Pressure Support
Hypoventilation	f < f low	V$_T$ low ≤ V$_T$	P$_{ETCO_2}$ high ≤ P$_{ETCO_2}$	Increase
Acute tachypnea	f max ≤ f	V$_T$ low ≤ V$_T$	20 mm Hg ≤ P$_{ETCO_2}$	Increase
Insufficient ventilation	f low ≤ f < f max	NA	P$_{ETCO_2}$ high ≤ P$_{ETCO_2}$	Increase
	f low ≤ f	V$_T$ < V$_T$ low	NA	Increase
Tachypnea	f high ≤ f < f max	V$_T$ low ≤ V$_T$	20 mm Hg ≤ P$_{ETCO_2}$ < P$_{ETCO_2}$ high	Increase
Central hypoventilation	f < f low	V$_T$ < V$_T$ low	P$_{ETCO_2}$ high ≤ P$_{ETCO_2}$	No change
Unexplained hyperventilation	f high ≤ f	V$_T$ low ≤ V$_T$	P$_{ETCO_2}$ < 20 mm Hg	No change
Normal ventilation	f low ≤ f < f high	V$_T$ low ≤ V$_T$	P$_{ETCO_2}$ < P$_{ETCO_2}$ high	Decrease (weaning)
Hyperventilation	f < f low	NA	P$_{ETCO_2}$ < P$_{ETCO_2}$ high	Decrease

* This table presents all SmartCare diagnosis or classifications functions of different parameters' values as compared to their threshold. It also presents the consequences on pressure support for each classification. The zone of respiratory comfort corresponds to normal values for the 3 parameters.
V$_T$ = tidal volume (ml)
P$_{ETCO_2}$ = end-tidal partial pressure of CO$_2$
f low = lower limit of spontaneous breathing frequency: 15 breaths/min
f high = upper limit of spontaneous breathing frequency: 30 breaths/min (34 breaths/min with neurological disorders)
f max = maximum limit of spontaneous breathing frequency: 36 breaths/min
V$_T$ low = lower limit of V$_T$: 300 mL (250 ml, for body weight < 55 kg)
P$_{ETCO_2}$ high = upper limit of P$_{ETCO_2}$: 55 mm Hg (65 mm Hg for patients with COPD)
NA = not applicable

non-COPD patients. In the non-COPD patients, however, there was a higher correlation coefficient between P$_{aCO_2}$ and maximum P$_{ETCO_2}$ (r = 0.77 versus r = 0.81), whereas the correlation coefficient was not different (r = 0.8) in the COPD patients. In both the COPD and non-COPD patients the difference between P$_{ETCO_2}$ and P$_{aCO_2}$ was similarly smaller with the maximum P$_{ETCO_2}$.

We did not measure intrinsic PEEP, which can influence the difference between P$_{aCO_2}$ and P$_{ETCO_2}$. Blanch et al[16] addressed this issue in 24 paralyzed and sedated patients on volume-controlled ventilation. They partitioned their population into 2 groups, according to the presence of intrinsic PEEP (13 patients) or not (11 patients). They found a higher P$_{aCO_2}$-P$_{ETCO_2}$ difference in the intrinsic PEEP group and a better correlation of P$_{ETCO_2}$ with P$_{aCO_2}$ in patients without intrinsic PEEP.

SmartCare and P$_{ETCO_2}$

SmartCare uses P$_{ETCO_2}$ as a security threshold to delimit the zone of respiratory comfort (Table 3) and in the algorithm by which it classifies the patient's ventilatory status.[17-19] High P$_{ETCO_2}$ (> 65 mm Hg for COPD, > 55 mm Hg for non-COPD), respiratory rate, and V$_T$ cause SmartCare to classify the ventilation period into a diagnosis such as central hypoventilation, hyperventilation, or insufficient ventilation. Low P$_{ETCO_2}$ (< 20 mm Hg) is also used to classify unexplained hyperventilation, defined by a high

respiratory rate and normal V$_T$ unresponsive to changes in pressure level.[19] In SmartCare the use of maximum P$_{ETCO_2}$ would better classify the patient's ventilatory status in a very small but potentially important number of cases. Indeed, SmartCare uses different safety thresholds (depending on the presence of chronic CO$_2$ retention, as indicated by the user) to detect central hypoventilation, defined as a low respiratory rate and a high P$_{ETCO_2}$, or insufficient ventilation, as a low V$_T$ and a high P$_{ETCO_2}$. These are rare situations but need to be recognized. If P$_{ETCO_2}$ markedly underestimates P$_{aCO_2}$, the diagnosis will occur late (ie, with a very high P$_{aCO_2}$ value). If at least one P$_{ETCO_2}$ value during a 2-min or 5-min period is above a P$_{ETCO_2}$ threshold, it would change SmartCare's ventilatory status classification. Using the maximum P$_{ETCO_2}$ would make SmartCare more sensitive to higher CO$_2$ values, which might result in better classification. It could also offer more stability in situations where there is alternation between pathological and non-pathological classifications, because abnormal ventilation would be diagnosed earlier. The use of maximum P$_{ETCO_2}$ would increase the classifications of hypoventilation and insufficient ventilation, leading SmartCare to increase pressure support or to alarm. The use of maximum P$_{ETCO_2}$ would have changed 1.6% of the classifications in our patients. There were 28 changes from normal ventilation to insufficient ventilation, which represents 57% of the overall changes in classification. In this study, however, the classification changes were retrospective and did not affect our care decisions.

Conclusions

Currently, P$_{ETCO_2}$ measurement via infrared sensor usually underestimates P$_{aCO_2}$. Maximum P$_{ETCO_2}$ seems to be closer to alveolar CO$_2$ than averaged P$_{ETCO_2}$. Use of maximum P$_{ETCO_2}$ could improve the accuracy and efficiency of SmartCare without being harmful to the patient.

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