END-TIDAL CARBON DIOXIDE AS A MEASURE OF ARTERIAL CARBON DIOXIDE DURING INTERMITTENT MANDATORY VENTILATION

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ABSTRACT. To determine if end-tidal carbon dioxide tension ($PETCO_2$) is a clinically reliable indicator of arterial carbon dioxide tension ($PaCO_2$) under conditions of heterogeneous tidal volumes and ventilation-perfusion inequality, we examined the expiratory gases of 25 postcardiotomy patients being weaned from ventilator support with intermittent mandatory ventilation. Using a computerized system that automatically sampled airway flow, pressure, and expired carbon dioxide tension, we were able to distinguish spontaneous ventilatory efforts from mechanical ventilatory efforts. The $PETCO_2$ values varied widely from breath to breath, and the arterial to end-tidal carbon dioxide tension gradient was appreciably altered during the course of several hours. About two-thirds of the time, the $PETCO_2$ of spontaneous breaths was greater than that of ventilator breaths during the same 70-second sample period. The most accurate indicator of $PaCO_2$ was the maximal $PETCO_2$ value in each sample period, the correlation coefficient being 0.768 ($P < 0.001$) and the arterial to end-tidal gradient being 4.24 ± 4.42 mm Hg ($P < 0.01$ compared with all other measures). When all values from an 8-minute period were averaged, stability was significantly improved without sacrificing accuracy. We conclude that monitoring the maximal $PETCO_2$, independent of breathing pattern, provides a clinically useful indicator of $PaCO_2$ in postcardiotomy patients receiving intermittent mandatory ventilation.

KEY WORDS: Carbon dioxide: tension. Ventilation: artificial; intermittent mandatory ventilation. Surgery: cardiac.

Monitoring end-tidal carbon dioxide tension ($PETCO_2$) has become an important component of respiratory care in the critical care setting. Although many investigators have demonstrated reasonably good agreement between values for $PETCO_2$ and those for arterial carbon dioxide tension ($PaCO_2$) in a variety of patient populations [1–5], such agreement has not occurred under conditions of heterogeneous tidal volumes and significant ventilation-perfusion inequality. A common example of this situation is the use of intermittent mandatory ventilation (IMV) to wean patients from ventilatory support after cardiac surgery, because there can be marked variability in spontaneous and mechanical respiratory rates and tidal volumes and a significant degree of postcardiotomy ventilation-perfusion mismatch. Therefore, we compared arterial blood gas results with concurrently obtained samples of expired CO_2 to determine whether monitoring of $PETCO_2$ is clinically useful in this patient population.

MATERIALS AND METHODS

After receiving the approval of the Human Subjects Committee at our institution, we studied 25 unselected

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Table 1. Clinical Characteristics of Patients Studied

Characteristic	No. of Patients	
	CABG	Valve Replacement
PREOPERATIVE HISTORY		
Myocardial infarction	17	0
Smoking (>50 pack-yr)	7	0
Atrial fibrillation	0	4
Congestive heart failure	3	3
Cerebrovascular disease	2	0
Subacute bacterial endocarditis	0	2
Peripheral vascular disease	2	0
Medically treated pulmonary disease	1	0
NYHA CLASSIFICATION		
II (moderate symptoms)	5	2
III (significant symptoms)	14	1
IV (incapacitating symptoms)	2	1
ASA CLASSIFICATION		
III (significant systemic disease)	21	3
IV (life-threatening disease)	0	1
IVE (life-threatening emergency)	2	0
POSTOPERATIVE COMPLICATIONS		
Perioperative myocardial infarction	3	0
Reoperation for persistent bleeding	1	1
Perioperative stroke	2	0
Intraoperative gastric aspiration	1	0
Intraoperative transfusion reaction	1	0
Total	21	4

CABG = coronary artery bypass graft; NYHA = New York Heart Association; ASA = American Society of Anesthesiologists.

adult cardiac surgical patients. There were 21 men and 4 women, and their mean age was 60 ± 9 years. All but three of the coronary artery bypass graft or intracardiac valve replacement procedures were elective. Table 1 presents some of the clinical characteristics of our study population. Fifteen patients had some history of smoking (mean ± SD, 49 ± 26 pack-years). The 8 patients who underwent preoperative pulmonary function testing generally exhibited mild to moderate obstructive disease (mean forced expiratory volume in one second = 76% ± 17% of the predicted value; forced ventilatory capacity = 80 ± 18; maximum midexpiratory flow rate between 50 and 75% of the vital capacity = 84 ± 33). Three patients were thought to have significant preoperative pulmonary disease, but in none was it considered severe enough to anticipate the need for prolonged postoperative ventilatory support.

After being premedicated with morphine and diazepam, patients were anesthetized with intermittent bolus doses of fentanyl (68 ± 25 μg/kg) and diazepam (0.34 ± 0.12 μg/kg), as well as nitrous oxide. Two patients received morphine rather than fentanyl in an equieffective dosage. Radial artery catheters were generally inserted, using a standard technique, by the anesthesiologist immediately before induction of anesthesia. The surgical procedures lasted an average of 298 ± 78 minutes, and extracorporeal circulation lasted 116 ± 24 minutes.

Postoperatively, all patients were mechanically ventilated using a Bennett MA-1 respirator modified for IMV with continuous-flow capability. Weaning from the ventilator was not instituted until the patients were hemodynamically stable and were receiving minimal vasoactive agents (e.g., low-dose dopamine), usually 10 to 12 hours postoperatively. Ventilator settings were adjusted based on routine clinical measurements, and not on the results of our monitoring. In patients who were smoothly weaned, the IMV rate was generally decreased by two breaths every two hours. Thus, most successfully weaned patients were extubated by the end of their first postoperative day.

No patient received parenteral hyperalimentation, and none had clinical evidence of pulmonary embolism in the postoperative period, both of which are known to alter the arterial to end-tidal CO_2 gradient [$\Delta P(a - ET)CO_2$]. No instances of clinically significant postoperative hypotension occurred, although one patient had hypertension during weaning that required vasodilator therapy. During the course of weaning, the mean level of positive end-expiratory pressure was 6.7 ± 2.6 cm H_2O. The mean inspired oxygen concentration was 37 ± 7% (range, 21 to 75%), whereas the calculated shunt was 10.6 ± 3.5%.

Respiratory flows and pressures were monitored continuously by a variable-orifice pneumotachograph (Accutach, American Pharmaseal) and a differential pressure manometer connected between the endotracheal tube and the Y-connector. Expired CO_2 concentration was measured with a Perkin-Elmer MGA-110 mass spectrometer (accuracy, ±3%) in the first 11 patients. To compare two common methods of monitoring expired gas, we used the Hewlett-Packard continuous infrared capnometer (reported accuracy, 2 to 8%, depending on the $P_{ET}CO_2$ range [6]) for the last 14 patients.

A previously described computer program [7], which was run on a Hewlett-Packard patient data management system, sampled the data at a rate of 25 Hz and automatically distinguished between spontaneous breaths and ventilator breaths on the basis of flow and pressure criteria. The computer then calculated spontaneous rates, ventilator rates, and tidal volumes, as well as mean and maximal $P_{ET}CO_2$ at successive 70-second intervals. The

$P_{ET}CO_2$ value for each breath was taken as the peak measurement during the respiratory cycle. Respiratory efforts were excluded from analysis if tidal volume was less than 10 ml.

For each 70-second sample period, the computer determined the mean spontaneous (SET), maximal spontaneous (SMAX), mean ventilator (VET), and maximal ventilator (VMAX) values of $P_{ET}CO_2$. In addition, it calculated three measures of $P_{ET}CO_2$ that were independent of breath type: a mean value for all breaths during the sample period (ET); a maximal value (TMAX); and a value in which each breath, whether spontaneous or mechanical, was weighted by its tidal volume (VWT) [7]. An eight-minute average of sequential TMAX values was also determined.

To compare $P_{ET}CO_2$ and $PaCO_2$, we selected the 70-second interval of respiratory data at the time of each arterial sample. Blood gas samples were drawn by the intensive care unit (ICU) nursing staff based on an established clinical protocol. Thus, arterial blood gas determinations were made for each patient 20 minutes after any adjustment in ventilatory settings, upon any unexpected change in clinical status, and at least every 2 to 3 hours during active weaning. To minimize the effects of short-term variations in $PaCO_2$, 3 ml of arterial blood was collected during a 30-second period through a radial artery cannula. The value of $PaCO_2$, corrected for patient temperature (measured either in the right atrium or the rectum), was determined with a Corning 175 blood gas analyzer.

The data were analyzed with the Statistical Package for the Social Sciences by standard techniques of *t* test and linear regression analysis [8]. The statistical significance of the correlation coefficients was evaluated by the method described by Snedecor and Cochran [9].

RESULTS

There were no statistically significant differences between our results from the mass spectrometer and those from the infrared capnometer.

We found large breath-to-breath variations in $P_{ET}CO_2$ values. $P_{ET}CO_2$ generally varied more in spontaneous breaths than in ventilator breaths. In the 86 sampling periods that included both spontaneous and ventilator breaths, the spontaneous $P_{ET}CO_2$ was greater than the ventilator $P_{ET}CO_2$ two-thirds of the time (58 cases). This was particularly true at higher mean carbon dioxide values.

For all samples, the average maximal $P_{ET}CO_2$ was 38.5 ± 7.3 mm Hg, whereas the average $PaCO_2$ was 42.2 ± 5.1 mm Hg, thereby yielding a mean $\Delta P(a - ET)CO_2$ of 3.7 ± 4.7 mm Hg. Neither the $\Delta P(a - ET)CO_2$ nor any other measure of $P_{ET}CO_2$ or $PaCO_2$ correlated with the positive end-expiratory pressure, the degree of shunt, or the preoperative clinical status of the patient population.

Because of the breath-to-breath variation, we evaluated eight measures of $P_{ET}CO_2$ to determine which one most consistently and accurately predicted $PaCO_2$ (Table 2). For all patient samples (n = 159), we found that the TMAX during each sampling period had the best correlation with $PaCO_2$ (Fig 1). The standard error of the estimate (S_{xy}) for TMAX versus $PaCO_2$ was the smallest of the eight measures. In addition, $\Delta P(a - ET)CO_2$ for TMAX was significantly smaller than that of any of the other measures of $P_{ET}CO_2$ (range, −11.1 to 12.9 mm Hg; $P < 0.01$). Averaging the maximal breath-type-independent $P_{ET}CO_2$ values during an 8-minute period yielded an even better measure of $PaCO_2$. The 8-minute $\Delta P(a - ET)CO_2$ was significantly

Table 2. Correlation between Various Measures of $P_{ET}CO_2$ and $PaCO_2$

	Measures of $P_{ET}CO_2$[a]							
	SET	VET	SMAX	VMAX	ET	VWT	TMAX	8-Minute Average TMAX
Correlation coefficient	0.739	0.683	0.722	0.685	0.746	0.720	0.768	0.818[b]
SEE (S_{xy})	3.46	3.80	3.38	3.63	3.41	3.55	3.13	2.83
$\Delta P(a - ET)CO_2$[c]	7.37 ± 6.66	6.42 ± 5.11	6.22 ± 6.77	5.92 ± 4.61	6.30 ± 4.65	6.30 ± 4.65	4.24 ± 4.42[d]	4.74 ± 4.11[e]

[a] The measures are the mean and maximal spontaneous $P_{ET}CO_2$ (SET and SMAX, respectively) and mean and maximal ventilator $P_{ET}CO_2$ (VET and VMAX, respectively) during each 70-second sampling interval. There are three breath-type-independent measures of $P_{ET}CO_2$: a mean value for all breaths during each sampling period (ET), a maximal value (TMAX), and a value in which each breath is weighted by its tidal volume (VWT). Finally, an 8-minute average of sequential TMAX values is included.
[b] Significantly different compared with VET ($P < 0.01$), VMAX ($P < 0.05$), and VWT ($P < 0.05$).
[c] Values (mean ± SD) are given in mm Hg.
[d] Significantly different compared with all other gradients using 70-second $P_{ET}CO_2$ values ($P < 0.01$).
[e] Significantly different compared with all other gradients ($P < 0.01$) except the 70-second TMAX.

$P_{ET}CO_2$ = end-tidal carbon dioxide tension; $PaCO_2$ = arterial carbon dioxide tension; SEE = standard error of the estimate.

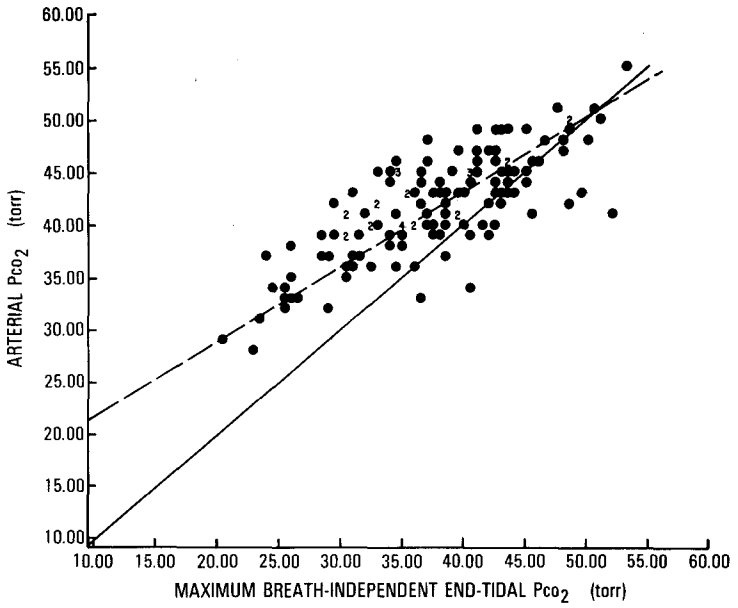

Fig 1. Among measurements averaged over a 70-second interval, the maximal breath-type-independent $P_{ET}CO_2$ (end-tidal carbon dioxide tension) is the most accurate and stable predictor of $PaCO_2$ (arterial carbon dioxide tension) in postcardiotomy patients being weaned from ventilatory support with intermittent mandatory ventilation. (R = *0.768;* $P_{ET}CO_2 = 0.545 \times PaCO_2 + 21.34$; *and the* $PaCO_2$ *to* $P_{ET}CO_2$ *gradient = 4.24 ± 4.42 mm Hg.*) P_{CO_2} = *carbon dioxide tension.*

different ($P > 0.01$) from all others except for the 70-second measure of TMAX. Compared with TMAX, the 8-minute $P_{ET}CO_2$ value exhibited a much smaller degree of scatter about the line of best fit and a smaller range of gradient values (−7.4 to 12.1 mm Hg).

The $\Delta P(a - ET)CO_2$ sometimes fluctuated significantly, but not always consistently with other indexes of the patient's pulmonary status. In an attempt to analyze the stability of the $\Delta P(a - ET)CO_2$, we determined the correlation between successive values of the gradient in all patients with multiple samples (Fig 2). Because of the design of our study, successive samples were usually taken one to two hours apart. Although there was a statistically significant correlation ($R = 0.622$, $P < 0.01$) in this clinical situation, the successive gradient values could only be predicted to within approximately 6 mm Hg in either direction.

DISCUSSION

Respiratory failure is the cause of death in up to 30% of patients in critical care units. Weaning from mechanical ventilation is an empirical process based largely on clinical criteria that, if managed improperly, may contribute to the significant incidence of postcardiotomy pulmonary morbidity [10]. Arterial blood gas analysis is the cornerstone of respiratory monitoring in the ICU. Yet its periodic nature is unsatisfactory for closely monitoring the pulmonary status of severely ill patients. Because the $PaCO_2$ value is obtained intermittently, a trend of respiratory compromise could go undetected for clinically significant periods of time.

Monitoring of $P_{ET}CO_2$ is a simple and noninvasive technique that appears to accurately indicate $PaCO_2$ in a variety of clinical situations [1,11,12]. Its use in patients being weaned from ventilator support with IMV has thus been advocated for many years mainly on the basis of anecdotal reports of its benefits [13,14]. However, its reliability under conditions of significant ventilation-perfusion inequality or heterogeneous tidal volumes has been questioned [15]. For instance, the degree of enlargement of the $\Delta P(a - ET)CO_2$ value can indicate the severity of pulmonary embolism [2]. We found that, although the postcardiotomy patient receiving IMV is not the optimal candidate for the monitoring of $P_{ET}CO_2$, clinically useful data can be obtained.

The $P_{ET}CO_2$ varied appreciably from breath to breath. In many cases, spontaneous breaths of variable tidal volumes far outnumbered ventilator breaths but still contributed relatively little to alveolar minute ventilation. A number of investigators have suggested that larger tidal volumes are necessary to measure $P_{ET}CO_2$ accurately because small (e.g., spontaneous) breaths may fail to "wash out" the anatomic dead space [11,13,16,17]. In contrast, we found that most spontaneous breaths (including, in 1 patient, breaths as small

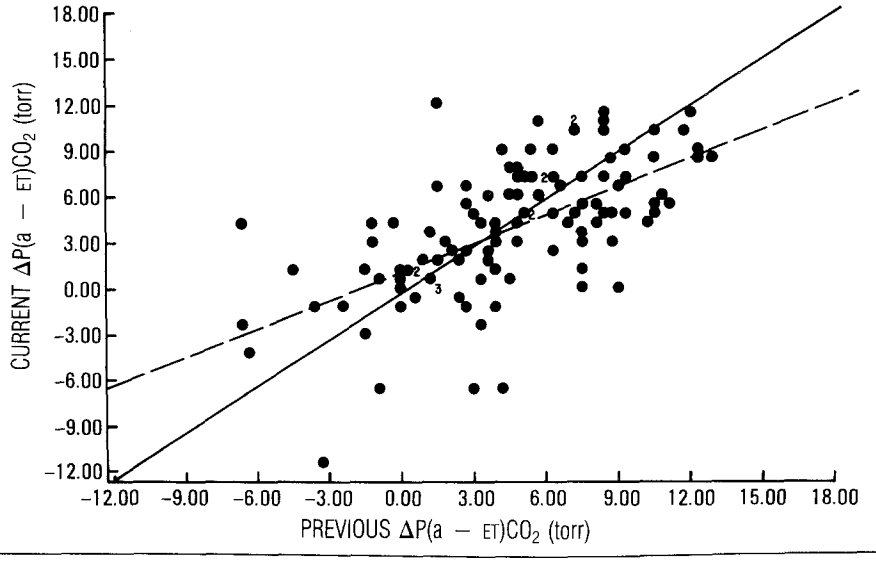

Fig 2. The stability of the arterial to maximal end-tidal carbon dioxide tension gradient [$\Delta P(a - ET)CO_2$] *is assessed by plotting all values of* $\Delta P(a - ET)CO_2$ *in patients with multiple samples against the preceding value of the gradient in the same patient. Although there is a statistically significant correlation between successive values of* $\Delta P(a - ET)CO_2$ *with this type of analysis* (R = *0.622), its clinical utility is not clear.*

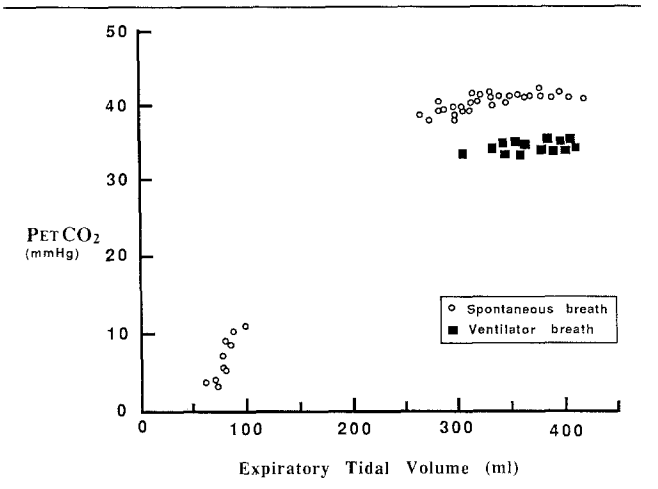

Fig 3. The end-tidal carbon dioxide tension ($PETCO_2$) *versus expiratory tidal volume is presented for 1 representative subject. The graph demonstrates the two classes of spontaneous breaths, as well as the fact that the* $PETCO_2$ *for spontaneous breaths with moderate tidal volumes is generally greater than that for ventilator breaths.*

as 100 ml) produce reliable $PETCO_2$ values. Thus, although they still contain some dead space air, smaller tidal volume breaths can result in alveolar ventilation [18] sufficient to allow end-expiratory air to represent alveolar carbon dioxide content. Figure 3 presents an example from a single patient during a short time span. One can identify three types of breaths: small tidal volume spontaneous breaths with very low $PETCO_2$ values; large tidal volume ventilator breaths with intermediate levels of $PETCO_2$; and moderate to large tidal volume spontaneous breaths with high $PETCO_2$ values.

The most important reason why the $PETCO_2$ values from spontaneous breaths are generally larger than those from ventilator breaths is the dilutional effect of the large inspired tidal volumes of ventilator breaths [7,17,19,20]. The equilibration between the inspired air and the existing alveolar air, which results in the transfer of arterial carbon dioxide to the expired airstream, is a time-dependent and volume-dependent process. Thus, the $PETCO_2$ of smaller breaths attains the level of alveolar carbon dioxide tension more rapidly.

Our use of an IMV circuit with a continuous fresh gas flow (rather than a demand valve) may have decreased the $PETCO_2$ values we obtained. Ventilator breaths may have been affected slightly more than spontaneous breaths simply because of their longer duration. If this effect was significant, then the use of a demand valve rather than continuous flow to provide IMV capability would produce $PETCO_2$ values that are in even greater agreement with $PaCO_2$ values. Our results support the notion that $PETCO_2$ values can vary markedly (even by 10 mm Hg or more) during periods as short as several minutes. Figure 4 presents an example of the effects of short-term disconnections from mechanical ventilation (presumably for suctioning) on $PETCO_2$, particularly during periods of relative hypoventilation, shortly after a decrease in the IMV rate during weaning. A marked increase in $PETCO_2$ has been reported during acute cardiovascular compromise [1,21], but is probably also

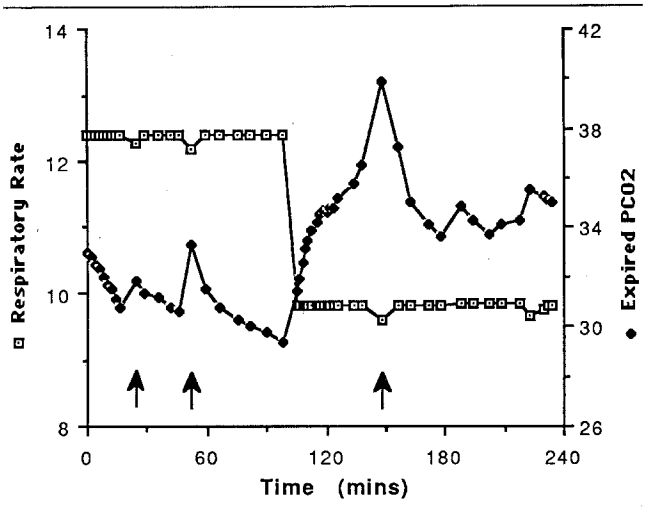

Fig 4. The effects of short-term disconnections from mechanical ventilation (arrows) *on end-tidal carbon dioxide tension ($P_{ET}CO_2$) are shown in 1 patient during weaning. These acute decreases in minute ventilation (presumably during suctioning) cause significant increases in the $P_{ET}CO_2$, particularly during the period of apparent relative hypoventilation shortly after a decrease in the intermittent mandatory ventilation rate from 12 to 10 (arrow on right).* P_{CO_2} = *carbon dioxide tension.*

common after suctioning, sedation, adjustments in ventilator settings, or simply allowing the patient to sleep. Additionally, recent studies have demonstrated short-term variations in $PaCO_2$, even during single breathing cycles [22]. We drew each arterial sample during the course of several breaths to minimize these cyclic variations.

Because of the marked variability of $P_{ET}CO_2$, we averaged TMAX over an 8-minute period and found this measure to correlate better with $PaCO_2$ than did the 70-second measures. The mean $\Delta P(a - ET)CO_2$, although not significantly smaller when averaged over an 8-minute period, appeared to yield less fluctuation in $P_{ET}CO_2$ over time.

Although successive values of $\Delta P(a - ET)CO_2$ correlated significantly, the great degree of variance (scatter about the line of unity on the graph) limits their predictive value in the clinical setting. The data suggest that, in our patient population, one could only predict with some certainty that a subsequent value for $\Delta P(a - ET)CO_2$ would be within about 6 mm Hg in either direction of the current value. In many clinical situations this degree of certainty would be insufficient. We were able to decrease the variance in our data somewhat by averaging the $P_{ET}CO_2$ values over an 8-minute period. In addition, a few of the severe outlying values found in Figure 2 could be excluded in clinical practice because they occurred during situations of obvious instability of gas exchange (for example, immediately after suctioning or other iatrogenic interventions).

Raemer et al [23] also found a wide range in values for $\Delta P(a - ET)CO_2$ over time. However, they measured the mean peak expired carbon dioxide tension over a period of only 15 seconds. Under the conditions of our study, averaging maximal $P_{ET}CO_2$ values over a longer time span improved the stability and reliability of the $\Delta P(a - ET)CO_2$. This may permit less frequent measurement of $PaCO_2$.

Because TMAX values are independent of respiratory flow volumes and pressures, $P_{ET}CO_2$ can be monitored with a simple infrared capnometer that may obviate the need for more complex and expensive systems in some clinical settings. We conclude that the continuous measurement of $P_{ET}CO_2$ can be a reliable and clinically useful indicator of the adequacy of alveolar ventilation in postcardiotomy patients receiving IMV.

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