Review

Carbon dioxide kinetics and capnography during critical care

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Abstract

Greater understanding of the pathophysiology of carbon dioxide kinetics during steady and nonsteady state should improve, we believe, clinical care during intensive care treatment. Capnography and the measurement of end-tidal partial pressure of carbon dioxide (P_{ETCO_2}) will gradually be augmented by relatively new measurement methodology, including the volume of carbon dioxide exhaled per breath ($V_{CO_{2,br}}$) and average alveolar expired P_{CO_2} ($P_{\bar{A}\bar{E}CO_2}$). Future directions include the study of oxygen kinetics.

Keywords: airway, capnography, carbon dioxide, carbon dioxide kinetics, expirogram, nonsteady state, ventilation

Introduction

Carbon dioxide is produced in the tissues by aerobic plus/minus anaerobic metabolism (Fig. 1a), transported in blood to the lung by venous return (essentially equal to cardiac output [$\dot{Q}_T$]), and eliminated from the lung by minute ventilation ($\dot{V}_E$) [1]. In this model the lung is a simple mixing chamber and the alveolar fractional carbon dioxide (F_{ACO_2}) is given by

$$F_{ACO_2} = \dot{V}_{CO_{2,ti}}/\dot{V}_A + F_{ICO_2} \quad (1)$$

where $\dot{V}_{CO_{2,ti}}$ is the tissue carbon dioxide production, $\dot{V}_A$ is alveolar ventilation, and F_{ICO_2} is the inspired F_{CO_2}. If one assumes no diffusion defect for carbon dioxide, then the partial carbon dioxide tension (P_{CO_2}) of arterial blood (Pa_{CO_2}) leaving the lung is the perfusion-weighted average alveolar P_{CO_2} (P_{ACO_2}). Note that pulmonary shunt will add mixed venous blood with high P_{CO_2} ($P_{\bar{v}CO_2}$) to arterial blood and slightly increase Pa_{CO_2} [2]. $\dot{V}_A$ is the product of respiratory frequency and expired tidal volume (V_T). Expired V_T is composed of alveolar V_T and total physiologic dead space ($V_{D_{phy}}$). The fraction $V_{D_{phy}}/V_T$ is given by

$$V_{D_{phy}}/V_T = (Pa_{CO_2} - P\bar{E}CO_2)/Pa_{CO_2} \quad (2)$$

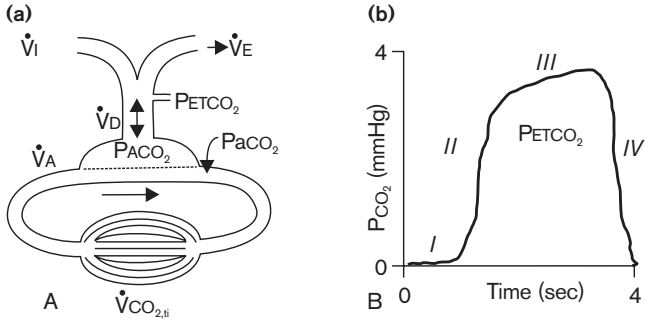
where $P\bar{E}CO_2$ is the mixed expired P_{CO_2} [2]. In turn, $V_{D_{phy}}$ is partitioned into anatomic dead space ($V_{D_{ana}}$; conducting airways that do not participate in gas exchange) and alveolar dead space ($V_{D_{alv}}$; ventilated alveolar units that are devoid of perfusion; Fig. 2). $V_{D_{alv}}/V_{T_{alv}}$ is given by

$$V_{D_{alv}}/V_{T_{alv}} = (Pa_{CO_2} - P_{ACO_2})/Pa_{CO_2} \quad (3)$$

where P_{ACO_2} is the alveolar P_{CO_2}, estimated either from P_{ETCO_2} or $P_{\bar{A}\bar{E}CO_2}$ [2] (see below). The Pa_{CO_2}–P_{ETCO_2}

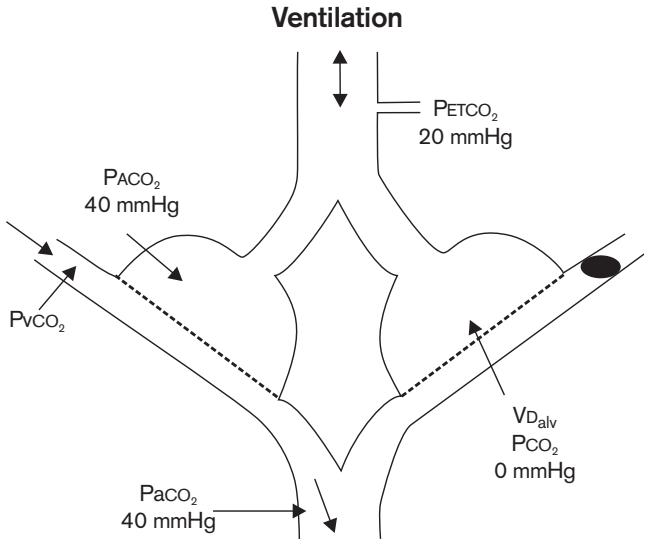
CPR = cardiopulmonary resuscitation; ETT = endotracheal tube; F_{CO_2} = fractional carbon dioxide; FRC = functional residual capacity; P_{CO_2} = partial carbon dioxide tension; PEEP = positive end-expiratory pressure; $\dot{Q}$ = blood flow; RPA = right pulmonary artery; V = volume; $\dot{V}$ = ventilation.

Figure 1



(a) Scheme of carbon dioxide stores and transport. P_{aCO_2}, arterial P_{CO_2}; P_{ACO_2}, alveolar P_{CO_2}; P_{ETCO_2}, end-tidal P_{CO_2}; $\dot{V}_A$, alveolar ventilation; $\dot{V}_{CO_{2,ti}}$, tissue carbon dioxide production; $\dot{V}_D$, dead space ventilation; $\dot{V}_E$, expired ventilation; $\dot{V}_I$, inspired ventilation. **(b)** Normal capnogram (tidal P_{CO_2} versus time). Phase I, inspiratory baseline; Phase II, expiratory upstroke; Phase III, alveolar plateau; and Phase IV, inspiratory downstroke. Adapted from Breen [61].

Figure 2



Effect of alveolar dead space ($V_{D_{alv}}$). The right lung compartment receives no perfusion and contains no carbon dioxide (ignoring interlung unit ventilation). By mass balance for carbon dioxide, $V_{D_{alv}}/V_{T_{alv}} = (P_{aCO_2} - P_{ETCO_2})/P_{aCO_2}$. For the sample condition shown, $V_{D_{alv}}/V_{T_{alv}} = (40-20)/40 = 50\%$. P_{aCO_2}, arterial P_{CO_2}; P_{ACO_2}, alveolar P_{CO_2}; P_{ETCO_2}, end-tidal P_{CO_2}; $P_{\bar{v}CO_2}$, mixed venous P_{CO_2}; $V_{T_{alv}}$, alveolar tidal volume. Adapted from Breen [61].

gradient results from the presence of $V_{D_{alv}}$ or high alveolar ventilation-to-blood flow ($\dot{V}_A/\dot{Q}$) lung regions (see also Capnography during weaning from mechanical ventilation, below).

The normal capnogram is the measurement of P_{CO_2} at the airway opening during the ventilatory cycle (Fig. 1b) [1]. Phase I (inspiratory baseline) reflects inspired gas, which is normally devoid of carbon dioxide. Phase II (expiratory upstroke) is the transition between $V_{D_{ana}}$, which does not participate in gas exchange, and alveolar gas from the respiratory bronchioles and alveoli. Phase III is the alveolar plateau. Traditionally, P_{CO_2} of the last alveolar gas sampled at the airway opening is called the P_{ETCO_2}. Finally, phase IV is the inspiratory downstroke, the beginning of the next inspiration.

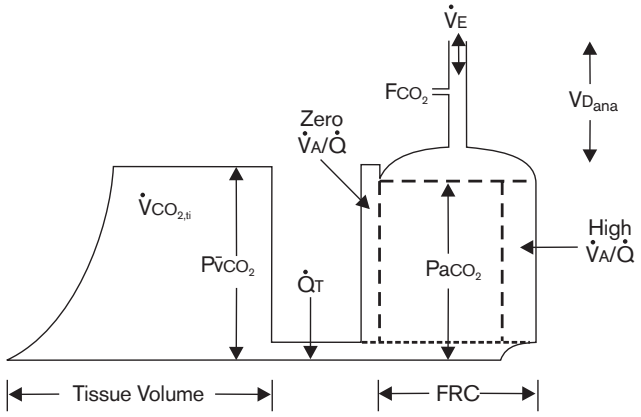
However, the capnogram contains no volume information. Accordingly, the $P_{\bar{A}ECO_2}$ [2,3], which is the volume-averaged alveolar P_{CO_2}, is a better index of P_{ACO_2} than is P_{ETCO_2}, which is just a single measurement of P_{CO_2} at the end of exhalation [2]. A more informative determination of pulmonary carbon dioxide elimination is $V_{CO_{2,br}}$, which is starting to garner clinical acceptance. $V_{CO_{2,br}}$ is the multiplication and integration of airway flow and P_{CO_2} over an entire respiratory cycle [4–6]. See the section on Future directions of carbon dioxide kinetics monitoring, below, for an interpretation and contrast of the measurements of $V_{CO_{2,br}}$ and P_{ETCO_2}.

The disposition of carbon dioxide can also be represented in a hydraulic model (Fig. 3) [3,7]. The large peripheral tissue compartment drains through a conduit ($\dot{Q}_T$) into the small central pulmonary compartment. The central compartment can be further divided into pulmonary shunt ($\dot{V}_A/\dot{Q} = 0$), normal lung ($\dot{V}_A/\dot{Q}$ near unity), and high $\dot{V}_A/\dot{Q}$ lung units, including $V_{D_{alv}}$. The tissues produce carbon dioxide ($\dot{V}_{CO_{2,ti}}$), which empties into the peripheral tissue compartment. Then, carbon dioxide flows by gravity ($\dot{Q}_T$) from the higher level peripheral tissue compartment to the lower level pulmonary compartment. $\dot{V}_A$, which equals $\dot{V}_E$ minus $V_{D_{ana}}$ and the effects of high $\dot{V}_A/\dot{Q}$ units, eliminates carbon dioxide from the lung. In this model, $\dot{Q}_T$ affects the distribution and total amount of carbon dioxide in the body. For example, at low $\dot{Q}_T$, retention of carbon dioxide occurs in the peripheral tissue compartment, and higher $P_{\bar{v}CO_2}$ is required to restore carbon dioxide delivery to the lungs. This hydraulic model can help to understand the meaning of P_{ETCO_2} during successful cardiopulmonary resuscitation (CPR), and to compare P_{ETCO_2} with P_{aCO_2} in the assessment of ventilator parameters. See the section, Effect of positive end-expiratory pressure on carbon dioxide kinetics, below, which highlights the utility of the hydraulic model.

Capnometry: current technologies

Capnometry is the measurement of F_{CO_2} in tidal gas at the airway opening [1,8]. Capnography is the graphic display of measured F_{CO_2} versus time. Capnometry most commonly utilizes infrared light absorption or mass spectrometry [9]. Both methods are reliable and relatively accurate. Capnometers that are used in clinical practice use two different sampling techniques: sidestream or mainstream

Figure 3



Hydraulic model of carbon dioxide kinetics in the body. Large peripheral tissue carbon dioxide compartment (left) drains through cardiac output ($\dot{Q}_T$) into the smaller central pulmonary carbon dioxide compartment (right). F_{CO_2}, fractional carbon dioxide; FRC, functional residual capacity; Pa_{CO_2} arterial P_{CO_2}; $P\bar{v}_{CO_2}$, mixed venous P_{CO_2}; $\dot{V}_A/\dot{Q}$, ventilation : perfusion ratio; $\dot{V}_{CO_{2,ti}}$, tissue carbon dioxide production; $V_{D_{ana}}$, anatomical dead space; $\dot{V}_E$, exhaled ventilation (see text). Adapted from Breen and Mazumdar [3].

sampling. A mainstream capnometer has an airway adaptor cuvette attached in-line and close to the endotracheal tube (ETT). The cuvette incorporates an infrared light source and sensor that senses carbon dioxide absorption to measure P_{CO_2}. A sidestream capnometer uses a sampling line that attaches to a T-piece adapter at the airway opening, through which the instrument continually aspirates tidal airway gas for analysis of carbon dioxide.

Mainstream capnometry

The main advantage of the mainstream analyzer is its rapid response, because the measurement chamber is part of the breathing circuit. The sample cuvette lumen, through which inspired and expired gases pass, is large in order to minimize the work of breathing, and pulmonary secretions generally do not interfere with carbon dioxide analysis. Compared with sidestream sampling, the airway cuvette is relatively bulky and can add dead space. However, within the past few years lighter and smaller airway cuvettes have been developed to allow its use in neonates [10,11]. The analyzer is warmed to prevent condensation on the sample chamber window, and caution must be taken to prevent burns. The monitoring of P_{ETCO_2} in nonintubated patients is more difficult with mainstream sampling.

Sidestream capnometry

The sidestream P_{CO_2} analyzer adds only a light T-adapter to the breathing circuit, and can be easily adapted to nonintubation forms of airway control. Because the sampling tubing is small-bore, it can be blocked by secretions. During sidestream capnography, the dynamic response, the steepness of the expiratory upstroke and inspiratory downslope, tends to be blunted because of the dispersive mixing of gases through the sampling line [4,12,13], where gas of high P_{CO_2} mixes with gas of low P_{CO_2}. In addition, a washout time is required for the incoming sampled gas to flush out the volume of the measuring chamber. The overall effect is an averaging of the capnogram, resulting in a lowering of the alveolar plateau and an elevation of the inspiratory baseline. Thus, P_{ETCO_2} may be underestimated and rebreathing can be simulated [12,14]. These problems are exacerbated by high ventilatory rates and by the use of long sampling catheters. In addition, the capnogram is delayed in time by transport delay, the time required to aspirate gas from the airway opening adapter through the sampling tubing to the sampling chamber [4,12]. In conditions of low fresh gas flow (eg closed circle circuit anesthesia), the amount of gas sampled and removed from the breathing circuit needs to be considered.

Portable capnometers

Although portable capnometers exist, their use in the field can be hindered by cost and requirement for calibration [15]. The portable infrared analyzer will not operate in temperatures that are subzero or greater than 40°C. Another device that is used for measurement of P_{CO_2} is the chemical colorimetric airway detector [16], which uses a pH-sensitive indicator to detect breath-by-breath exhaled carbon dioxide [15]. The colorimetric airway detector is interposed between the ETT and the ventilation device. They have an unopened shelf-life of 15 months. Both adult and pediatric adaptors exist, but they cannot be used in infants who weigh less than 1 kg. Because of excessive flow resistance, they are not suited for patients who are able to breath spontaneously, and excessive humidity will render them inoperative in 15–20 min. The devices can be damaged by mucous, edematous or gastric contents, and by administration of intratracheal epinephrine. Despite these drawbacks, colorimetric sensors have been found to be useful in guiding prehospital CPR both in intubated patients and those with a laryngeal mask airway [15,17].

Traditional use of capnography: airway patency and assessment of ventilation

Because the lung is the only body compartment in which carbon dioxide normally and continuously accumulates, the presence of cyclic exhaled carbon dioxide can be used to confirm airway patency and pulmonary ventilation. Although initially adopted for anesthesia monitoring in the operating room, the use of capnography to confirm airway patency and lung ventilation has expanded over the past 8 years to include critical care, emergency medicine, field resuscitation, and conscious sedation settings [1,8,15,18–22].

However, there are pitfalls in the use of capnography to confirm endotracheal intubation. Potential problems with

technology are described above. In addition, several scenarios have been described that impact on the ability of capnography to assess the airway and ventilation.

First, during circulatory arrest, pulmonary ventilation will result in low and decreasing values of exhaled carbon dioxide because $\dot{Q}_T$ and carbon dioxide transport from the tissues to the lung are decreased or absent in the presence of continuing $\dot{V}_A$ [23–25]. In the clinical setting, however, Vukmir *et al* [19] demonstrated that infrared capnography was 100% specific and sensitive in the detection of endotracheal versus esophageal intubation in 100 critical care cases of airway management, 17 of which were cardiac arrests.

Second, positive-pressure ventilation by face mask can force pharyngeal gas, containing exhaled carbon dioxide from the previous breath, into the esophagus and stomach [1]. Likewise, ingestion of carbonated beverages can also generate carbon dioxide in the stomach [26]. Subsequent esophageal intubation and gastric ventilation can result in initial cyclic 'exhaled' carbon dioxide. However, esophageal intubation usually causes an initial 'P_{ETCO_2}' that is less than 10 mmHg and that decreases with each 'exhaled breath' as inspiration dilutes carbon dioxide in the stomach [27]. In the case of suspected esophageal intubation, consider interpreting the value of exhaled carbon dioxide after the sixth breath [15].

Third, in a case report in a neonate weighing under 700 g [28], although the ETT tube was correctly positioned in the trachea, displacement of the ETT against the lateral wall of the trachea resulted in a flat capnogram and an erroneous diagnosis of esophageal intubation.

Fourth, pathology that causes absence of ventilation, including severe bronchospasm, patient apnea, or plugged ETT will result in absence of expired carbon dioxide and a falsely negative diagnosis that the ETT is not in the trachea.

Finally, it is prudent to remember that a normal capnogram confirms ventilation of the lungs through a patent airway, but not necessarily a secure airway. In a case report [29], a normal capnogram resulted during ventilation through an ETT positioned at the glottic opening, but not securely placed in the trachea.

Despite these potential drawbacks, capnography remains the most reliable monitor of airway patency in a variety of experimental and clinical settings. Mickelson *et al* [30] demonstrated that exhaled carbon dioxide was the most reliable indicator of esophageal intubation in canine model. Likewise, Knapp *et al* [31] studied current methods of verifying tracheal tube placement in the critical care setting, and found that capnography was superior to auscultation or other devices such as the lighted stylet. Capnography can also recognize esophageal intubation in neonates [32]. In the field, compared with other devices carbon dioxide monitoring best detects esophageal intubation by limiting the number of false negatives and false positives [15].

In addition to confirmation of ETT placement in the trachea, capnography may aid in cases of difficult intubation. During awake, blind, nasotracheal intubation, the end of a sidestream capnometer sampling probe can be placed through and positioned at the distal end of the ETT [33]. Then, increasing values of cyclic exhaled P_{CO_2} can help guide the ETT to the glottic opening. During a difficult intubation, effective ventilation can be maintained through a tube at the tip of the pharynx (guided by the expiratory carbon dioxide waveform), until other adjuncts to intubation are available [34].

Sidestream capnography adapts well to the nonintubated, sedated patient. Croswell *et al* [35] compared monitoring by capnography, pulse oximetry and clinical observation in sedated, pediatric, dental patients. Capnography provided a minimum 15 s warning of potential arterial desaturation, and was the most sensitive method for detecting airway compromise, especially during deeper levels of sedation. With oral/nasal capnometry in pediatric patients after active seizures, Abrams *et al* [36] demonstrated that P_{ETCO_2} is a useful predictor of hypercapnia and is more sensitive than pulse oximetry in predicting impending respiratory failure. Other studies [8,37] have supported the assertion that capnography provides the earliest warning of airway obstruction and respiratory compromise.

Finally, capnography is a useful monitor during transport of intubated, critically ill patients [38,39]. Beside the obvious advantage of early warning against ETT dislodgment and/or compromise of ventilation, monitoring of P_{ETCO_2} (as an estimate of Pa_{CO_2}) may aid the management of patients in whom hypercapnia is detrimental, such as patients with head injury with raised intracranial pressure and pediatric patients with pulmonary hypertension [38].

Capnography during weaning from mechanical ventilation

Capnography has been considered a potentially useful noninvasive monitor to assess the weaning of patients from mechanical ventilation in critical care settings [40]. However, studies have shown variable results in the ability of P_{ETCO_2} to predict Pa_{CO_2}. Whether the use of P_{ETCO_2} can limit the need for invasive arterial blood gas monitoring has yet to be established.

In a 1985–1991 literature review of the efficacy of noninvasive blood gas monitoring in the adult critical care unit [41], the Technology Subcommittee of the Working

Group on Critical Care (Ontario Ministry of Health) concluded that changes in P_{ETCO_2} need to be interpreted with extreme caution. Healey *et al* [42] compared the correlation of P_{ETCO_2} with P_{aCO_2} before and after withdrawal of assist control mechanical ventilation. P_{ETCO_2} paralleled changes in P_{aCO_2} ($r = 0.82$). Saura *et al* [43], in a prospective study to evaluate the relationship between P_{aCO_2} and P_{ETCO_2} before and during weaning with continuous positive airway pressure ventilation, also found that P_{ETCO_2} could detect clinically relevant hypercapnic episodes. However, there was a high incidence of false positives that led to arterial blood gas sampling. Withington *et al* [44] found that, after a gradient between P_{aCO_2} and P_{ETCO_2} was established, P_{ETCO_2} was a useful parameter in the weaning of postcardiac surgery patients.

The assessment of P_{ETCO_2} may be misleading if not considered in the context of changing hemodynamics and ventilatory pattern. Although there can be significant correlation of P_{ETCO_2} with P_{aCO_2}, clinically acceptable sensitivity and specificity may only occur in the absence of significant changes in $\dot{Q}_T$ or $\dot{V}_A/\dot{Q}$ relationships. In evaluating the use of capnography as a noninvasive monitor of P_{aCO_2} in critical care patients, Morley *et al* [45] observed that P_{ETCO_2} was useful as a predictor only in patients without significant parenchymal lung disease. Prause [46] found that P_{ETCO_2} was useful for the adjustment of ventilatory parameters in prehospital emergency care patients only if they had no major cardiopulmonary damage. As depicted in Fig. 2, the gradient between P_{ETCO_2} and P_{aCO_2} depends on $V_{D_{alv}}$ (ie the amount of lung regions with high or infinite $\dot{V}_A/\dot{Q}$ ratios) [2,25]. Lung regions with high $\dot{V}_A/\dot{Q}$ ratios can result from high alveolar pressures (eg large V_T, positive end-expiratory pressure [PEEP]), low pulmonary perfusion pressures (eg low $\dot{Q}_T$, upright position), and obstruction of pulmonary blood flow (eg thrombus, gas, or fat embolism). Thus, in the critically ill patient, $V_{D_{alv}}$ often changes and affects the ability of P_{ETCO_2} to predict P_{aCO_2} and be a substitute for arterial blood gas sampling.

Capnography during nonsteady-state conditions

Capnography during cardiopulmonary resuscitation

An important and relatively successful application of capnography in the nonsteady-state clinical setting has been during CPR [1,3,25]. During cardiac arrest, the abrupt decrease in $\dot{Q}_T$ results in reduction in carbon dioxide transport from the tissues to lung and, hence, decreased carbon dioxide elimination from the lung. With subsequent successful CPR, the increase in $\dot{Q}_T$ restores pulmonary blood flow and carbon dioxide transport, and increases pulmonary elimination of carbon dioxide. Contrast this nonsteady-state effect of $\dot{Q}_T$ upon carbon dioxide kinetics with the steady-state equation (Eqn 1) for carbon dioxide kinetics. $\dot{Q}_T$ does not even appear in Equation 1, although it is the conduit for $\dot{V}_{CO_{2,ti}}$.

The measurement of exhaled carbon dioxide is the best signal of return of spontaneous circulation during CPR [23,24]. Capnography is also a useful noninvasive index of the adequacy of pulmonary perfusion during closed-chest cardiac compression [47,48]. In fact, capnography may be used to compare the efficacy of different modes of chest compression [49].

Moreover, the quantitative measurement of P_{ETCO_2} may have predictive value during CPR. This was recognized as early as 1939, when Eisenmenger wrote "If during a resuscitation attempt the analysis of the expired air, performed about twice per hour, still shows plenty of carbon dioxide, then continuation of artificial respiration (and circulation) would be indicated" [50]. Asplin and White [20] measured the 1-min value, the 2-min value, and the maximum value of P_{ETCO_2} during CPR in 27 patients. The initial P_{ETCO_2} values were prognostic for return of spontaneous circulation. Finally, the predictive value of P_{ETCO_2} has been studied in hospital settings. Domsky *et al* [51], in a retrospective chart review of 100 critically ill surgery patients, found that a persistent P_{ETCO_2} of 28 mmHg or less was associated with a mortality rate of 55%, versus a mortality of 17% in patients with higher P_{ETCO_2}. Mortality rate was also increased in patients with a persistent P_{aCO_2}–P_{ETCO_2} difference of 8 mmHg or more. Quantitative capnography during resuscitation will continue to evolve.

Future directions of carbon dioxide kinetics monitoring

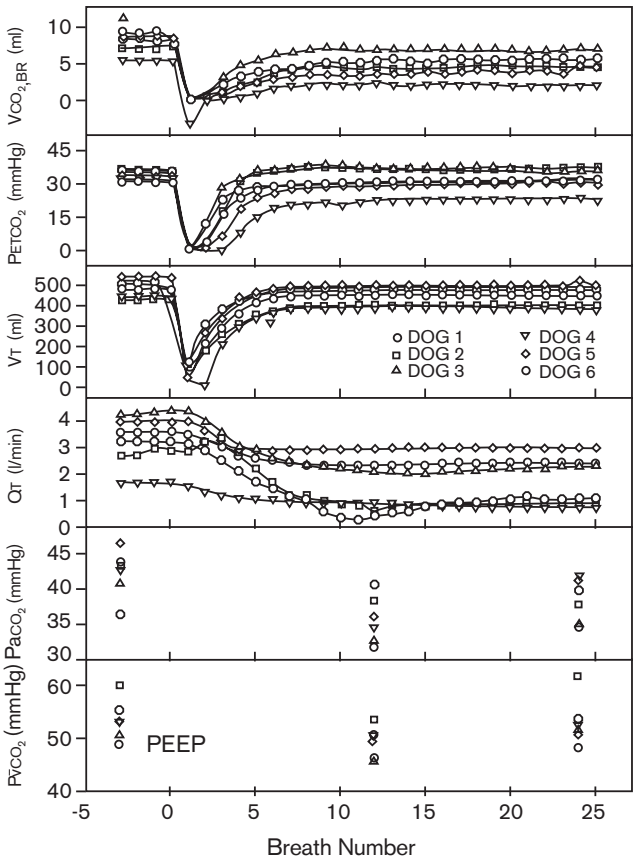
The following three sections examine how clinically relevant perturbations (application of PEEP, onset of pulmonary embolism, and recovery from pulmonary embolism) affect nonsteady-state carbon dioxide kinetics. The use of relatively new measurements ($V_{CO_{2,br}}$, $P\bar{A}_{CO_2}$) will help define pathophysiology and will improve, we believe, clinical diagnosis and treatment.

Effect of positive end-expiratory pressure on carbon dioxide kinetics

The addition of PEEP to mechanical ventilation should acutely decrease $V_{CO_{2,br}}$, due to decreased $\dot{V}_A$ (increased $V_{D_{phy}}$) and decreased carbon dioxide transfer to the lung (decreased $\dot{Q}_T$ and venous return) [1,3]. Then, gradual recovery of $V_{CO_{2,br}}$ would occur if peripheral tissue carbon dioxide retention caused sufficient increase in $P\bar{v}_{CO_2}$ (especially at sustained low $\dot{Q}_T$) to restore carbon dioxide delivery to the lung (Fig. 3).

The initial effects during the first 25 breaths after adding 11 cmH_2O PEEP to mechanical ventilation of anesthetized dogs are shown in Fig. 4 [3]. The summation of the decreases in V_T, compared with the baseline value, permitted calculation of increased functional residual capacity (FRC) at 1152 ml. P_{ETCO_2} paralleled the decrease in V_T, but recovered to baseline by breath 10. $V_{CO_{2,br}}$ decreased from baseline (7.6 ml) to zero in the first couple of exhala-

Figure 4



Initial breath-by-breath effects of adding 11 cmH_2O PEEP in mechanically ventilated anesthetized dogs on carbon dioxide volume exhaled per breath ($V_{CO_{2,br}}$), end-tidal P_{CO_2} (P_{ETCO_2}), exhaled tidal volume (V_T), and cardiac output ($\dot{Q}_T$, aorta flow probe). P_{aCO_2}, arterial P_{CO_2}; $P_{\bar{v}CO_2}$, mixed venous P_{CO_2}. Adapted from Breen and Mazumdar [3].

tions. However, $V_{CO_{2,br}}$ had only increased to 4.9 ml by breath 25. From a baseline value (3.3 l/min), $\dot{Q}_T$ (ascending aorta flow probe) decreased to 1.6 l/min by breath 10, which was sustained through breath 25. During measurements extended to 25 min, depressed $\dot{Q}_T$ was sustained and $V_{CO_{2,br}}$ was still 17% less than baseline. PEEP caused an immediate and sustained increase in $V_{D_{phy}}$ from 312 to 366 ml, resulting entirely from the increase in $V_{D_{ana}}$. P_{ETCO_2} continued to increase to the 25 min value (43 ± 6 mmHg), which was significantly greater than baseline. There were parallel changes in P_{aCO_2} and $P_{\bar{v}CO_2}$.

A study of the hydraulic model of carbon dioxide kinetics (Fig. 3) will help to summarize [1,3]. PEEP immediately decreased $V_{CO_{2,br}}$ by the following mechanisms: decreased $\dot{V}_A$, itself caused by the increase in $V_{D_{ana}}$ and by appearance of new high $\dot{V}_A/\dot{Q}$ lung units; and decreased P_{aCO_2} caused by decreased $\dot{Q}_T$ and, hence, reduced carbon dioxide transfer from the tissues to the lung. Dilution of P_{aCO_2} with fresh gas as FRC increased at onset of PEEP was offset by decreased $V_{CO_{2,br}}$ (including the effect of initial decreased exhaled V_T). Sustained decrease in $V_{CO_{2,br}}$ at 25 min occurred because $\dot{V}_A$ remained depressed from continued increased $V_{D_{phy}}$. Then, $V_{CO_{2,br}}$ could only recover to the baseline value if P_{aCO_2} significantly increased. However, at persistently decreased $\dot{Q}_T$, the increase in tissue carbon dioxide retention and $P_{\bar{v}CO_2}$ were not enough to restore carbon dioxide delivery to the lung and sufficiently increase P_{aCO_2}. P_{ETCO_2}, because it does not measure exhaled volume, failed to correctly estimate $V_{CO_{2,br}}$. Steady state was not reached by 25 min of PEEP. A parallel study of the effects of PEEP on carbon dioxide kinetics in anesthetized patients [52] demonstrated less marked changes, presumably because the intact thorax in patients blunted the increase in FRC and $V_{D_{ana}}$ and the intact pleural pressure gradient limited the generation of high $\dot{V}_A/\dot{Q}$ lung units. Other studies, in patients with acute respiratory failure [53,54], have demonstrated the limitations of interpreting changes in the P_{aCO_2}–P_{ETCO_2} gradient during PEEP.

Effect of pulmonary embolism on carbon dioxide kinetics

Pulmonary embolism should cause a different $\dot{V}_A/\dot{Q}$ abnormality, the generation of pure $V_{D_{alv}}$. The embolus will block perfusion to lung units, converting them into $V_{D_{alv}}$ [1,25]. The increase in $V_{D_{alv}}$ will increase $V_{D_{phy}}$ and result in decreased $\dot{V}_A$ and, hence, $V_{CO_{2,br}}$. Eventually, tissue carbon dioxide retention and increased $P_{\bar{v}CO_2}$ would restore carbon dioxide delivery from the tissue to the lung and $V_{CO_{2,br}}$. Presumably, persistent $V_{D_{alv}}$ during pulmonary embolus would preclude the accuracy of P_{ETCO_2} as an estimate of either P_{aCO_2} or $V_{CO_{2,br}}$.

To examine these hypotheses, an animal model similar to the PEEP study (above) was invoked, except that the perturbation was abrupt tightening of a snare around the right pulmonary artery (RPA) [1,55]. Compared with baseline (9.3 ml), average $V_{CO_{2,br}}$ decreased to 7.0 ml by 1 min after RPA occlusion (Fig. 5). At the same time, P_{ETCO_2} decreased from 29 to 22 mmHg. During the following 70 min of RPA occlusion, $V_{CO_{2,br}}$ steadily increased to approach the baseline value. In contrast, at 70 min of RPA occlusion, P_{ETCO_2} was still 13% less than baseline. P_{aCO_2} and $P_{\bar{v}CO_2}$ progressively converged on their maxima (high values) by 70 min. $\dot{Q}_T$, despite an initial tendency to decrease, did not change significantly.

In summary, large experimental pulmonary embolus immediately decreased $V_{CO_{2,br}}$ by 25%, almost entirely due to an increase in $V_{D_{alv}}$ (Fig. 2). $V_{CO_{2,br}}$ increased and recovered to baseline as carbon dioxide was retained in the body, signaled by the progressive increases in P_{aCO_2} and $P_{\bar{v}CO_2}$. P_{ETCO_2} remained significantly less than baseline due to persistent increased $V_{D_{alv}}$, and detected neither the

increase and recovery of $V\dot{C}O_{2,br}$ nor the increase in $PaCO_2$. Because $\dot{Q}T$ did not significantly decrease, $P\bar{v}CO_2$ could increase sufficiently to restore carbon dioxide delivery to the lung.

Resolution of pulmonary embolism

Patients with large pulmonary embolism can suffer progressive hypercapnia and may require emergent embolectomy, either by the transvenous or open thoracic approach. Conceivably, the functional recovery of carbon dioxide exchange could signal reperfusion of the affected pulmonary circulation and help guide the course of surgical therapy.

Accordingly, using the experimental model of pulmonary embolism (above), the RPA was occluded for 70 min to approach steady state. Then, the RPA snare was abruptly released and measurements were repeated during 70 min of RPA reperfusion [1,56]. At onset of RPA reperfusion, $V\dot{C}O_{2,br}$ abruptly increased from 9 to 12 ml. By 70 min of RPA reperfusion, $V\dot{C}O_{2,br}$ returned to the baseline value. Immediately after RPA reperfusion, $PETCO_2$ increased from 25 to 33 mmHg because VD_{alv}/VT_{alv} decreased by 41%. At 70 min, $PETCO_2$ was still greater than baseline. $PaCO_2$ and $P\bar{v}CO_2$ steadily decreased during 70 min of RPA reperfusion, modeling the release of carbon dioxide retention in the central pulmonary and peripheral tissue carbon dioxide compartments. $\dot{Q}T$ did not change significantly.

In summary, $V\dot{C}O_{2,br}$ detects and follows the resolution of carbon dioxide retention in lung and tissues during reperfusion after experimental pulmonary embolus. In contrast, $PETCO_2$ did not detect the secondary slow decrease in $V\dot{C}O_{2,br}$ back to baseline because $PETCO_2$ measures neither exhaled volume nor the shape of the PCO_2 waveform.

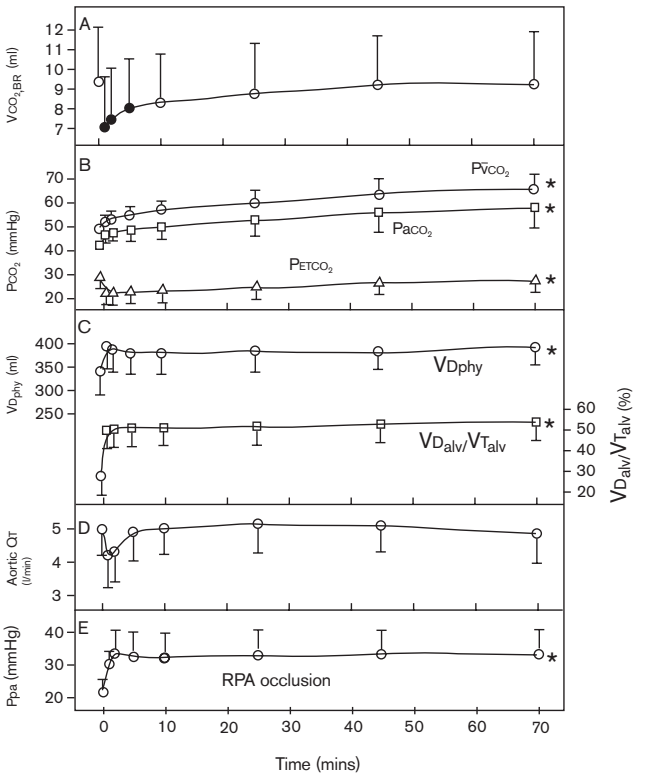
Accordingly, during onset and resolution of pulmonary embolism, this analysis of nonsteady-state carbon dioxide kinetics may aid the clinical assessment of pulmonary embolism [57].

Although beyond the scope of the present review, volumetric capnography (ie the carbon dioxide expirogram, the plot of exhaled PCO_2 versus exhaled volume) can also yield information about lung volume [58], dead space [59], and pulmonary blood flow (carbon dioxide rebreathing technique) [60].

Conclusion

In our opinion, better understanding of pathophysiology of carbon dioxide kinetics during steady and nonsteady state should improve clinical care during intensive care treatment. Capnography and the measurement of $PETCO_2$ will gradually be augmented by relatively new measurement methodology (including $V\dot{C}O_{2,br}$ and $P\bar{A}\bar{E}CO_2$). Future directions include the study of oxygen kinetics [1].

Figure 5



In five mechanically ventilated dogs, effect of 70 min of RPA occlusion on the following: **(a)** carbon dioxide volume exhaled per breath ($V\dot{C}O_{2,br}$); **(b)** PCO_2; **(c)** dead space (VD); **(d)** ascending aortic cardiac output ($\dot{Q}T$); and **(e)** mean pulmonary artery pressure (Ppa). RPA occlusion began after time 0 (baseline). Solid symbol denotes significant difference ($P < 0.05$) from baseline measurement. *All stages during RPA occlusion were significantly different from baseline. $PaCO_2$, arterial PCO_2; $PETCO_2$, end-tidal PCO_2; $P\bar{v}CO_2$, mixed venous PCO_2; VD_{alv}/VT_{alv}, alveolar dead space : tidal volume fraction; VD_{phy}, physiologic dead space. From Breen *et al* [55].

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