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REVIEW PAPER

Clinical use of volumetric capnography in mechanically ventilated patients

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Abstract
Capnography is a first line monitoring system in mechanically ventilated patients. Volumetric capnography supports non-invasive and breath-by-breath information at the bedside using mainstream CO_2 and flow sensors placed at the airways opening. This volume-based capnography provides information of important body functions related to the kinetics of carbon dioxide. Volumetric capnography goes one step forward standard respiratory mechanics and provides a new dimension for monitoring of mechanical ventilation. The article discusses the role of volumetric capnography for the clinical monitoring of mechanical ventilation.

Keywords Volumetric capnography · Carbon dioxide · PEEP · Dead space · Pulmonary blood flow · Gas exchange

1 Introduction

One of the major requirements of the human being is the continuous elimination of carbon dioxide (CO_2) because any disturb in the kinetics of this volatile acid alters cells function through changes in intra/extracellular pH and local perfusion. The CO_2 follows an inverse body kinetics compared than oxygen (O_2) that starts with its metabolic generation (Fig. 1) [1]. There is a close and continuous balance between CO_2 *production* in tissues, *transport* by blood, *diffusion* into alveoli and *elimination* by ventilation [2–5]. Any misbalance on these important steps breaks the homeostasis and led to hypercapnia—a common finding in mechanically ventilated patients [6].

A relevant aspect of the kinetics of CO_2 is the context-sensitive nature, which means that it proper interpretation depends on the clear understanding of the particular patient's clinical situation [7]. The *context* is a clinical event that affects any step of the CO_2 kinetics at time keeping the other steps unchanged; a *sine qua non* feature necessary to know why the elimination of CO_2 has changed. A clinical example is an anesthetized patient that presents a sudden decrement in expiratory CO_2 at constant metabolism and ventilation. In such particular clinical context the diagnosis of a hemodynamic problem based on capnography is quick, simple and feasible. Thus, unsteady states that affect the homeostasis of CO_2 must be clinically interpreted taking in mind this context-sensitive rule.

Capnography—the graphical representation of the expired CO_2—gives information about the CO_2 kinetics of mechanically ventilated patients in a non-invasive and real-time way [7, 8]. The aim of this article is to highlight the role of capnography, especially volumetric capnography (VCap), for the clinical monitoring of mechanical ventilation.

2 Basic concepts about capnography

Capnography refers to the measurement of CO_2 in breathing gases during the respiratory cycle. The concentration or partial pressure of CO_2 is calculated by the absorption of infrared light according to the Beer–Lambert's Law [9]. Capnography is commonly classified according to their graphical presentation. *Time-based* or *standard capnography* is the most popular kind of capnogram where the concentration/partial pressure of CO_2 is plotted as a temporal series (Fig. 2a) [9–12]. *Volume-based* or *volumetric capnography*

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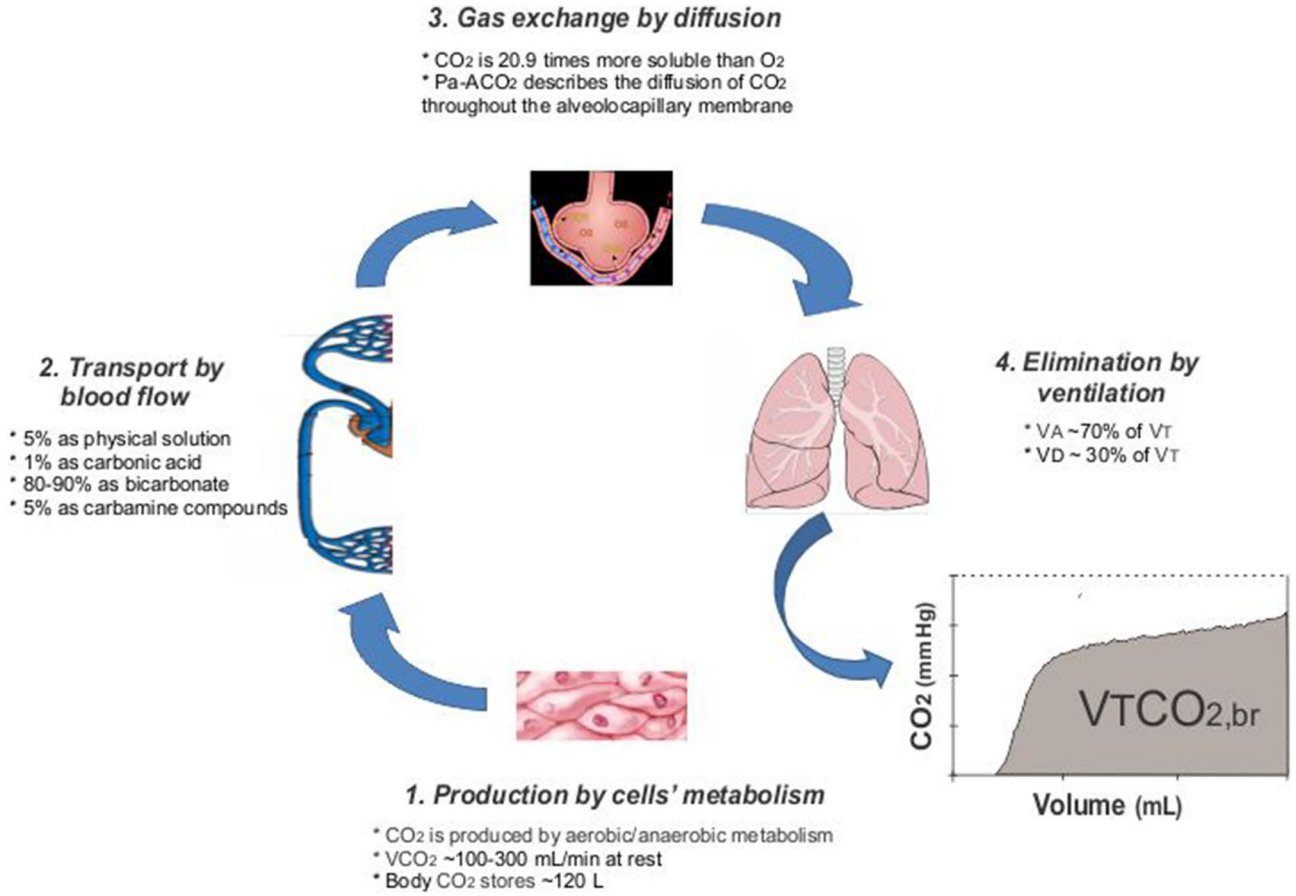

Fig. 1 The kinetics of carbon dioxide in the body. The kinetics of CO_2 in the body starts with its genesis by cellular metabolism (1) followed by its transport by blood flow from tissues to the lungs (2), its diffusion throughout the alveolar-capillary membrane (3) and its elimination by ventilation (4). The amount of CO_2 eliminated in a single breath ($VTCO_{2,br}$—gray area) can be measured noninvasively with volumetric capnography by integration of expired tidal volume and expired CO_2. $VTCO_{2,br}$ is the main capnographic parameter that depends on these four steps. For more details see text

represents the amount of carbon dioxide eliminated in one tidal breath (Fig. 2b, c). Different to standard capnography, VCap has the ability to get *volumetric* parameters of clinical importance like the pulmonary elimination of CO_2 (VCO_2), dead space, and alveolar ventilation [13–15].

VCap like standard capnograms is formed by three known phases (Fig. 2b) [14]. Phase I represents the first part of expiration without CO_2 (approx.10–12% of VT), phase II shows a rapid upswing in CO_2 during expiration (15–18% of VT), and phase III is the portion of VT formed by pure alveolar gas (70–75% of VT). VCap presents two slopes. One is the slope of phase II (S_{II}—normal value 0.36–0.40 mmHg/mL) that represents lung units with different emptied rates of CO_2 into the main airways. The other is the slope of phase III (S_{III}—normal value 0.007–0.017 mmHg/mL) that depends mainly on the non-uniform distribution of ventilation and perfusion within lungs [16, 17].

The area under the curve is the main VCap parameter that represents the amount of CO_2 eliminated in a breath ($VTCO_{2,br}$), which normal values depend on patient's and VT's size (approx. 10–30 mL in adults) [15, 16]. Partial pressure values of CO_2 are important for the calculation of clinical variables like dead space (Fig. 2c). $PETCO_2$ is the partial pressure of CO_2 at the end a normal expiration with values around 33–37 mmHg, considering a normal $PaCO_2$ of 40 mmHg. $PACO_2$ is the mean alveolar partial pressure of CO_2, which is commonly lower than $PETCO_2$ due to the positive sloping of phase III (values 30–35 mmHg). $P\bar{E}CO_2$ is the mixed expired partial pressure of CO_2 that derives from the dilution effect creates by the physiological dead space (values 18–24 mmHg).

The mathematical inflection point (i.e. the point where the sign of the capnogram curvature changes) represents the mean value of stationary interfaces between convective and diffusive transport of CO_2 within lungs, which is placed close to the respiratory bronchioles at end inspiration [17]. Such *mean airway-alveolar interface* determines

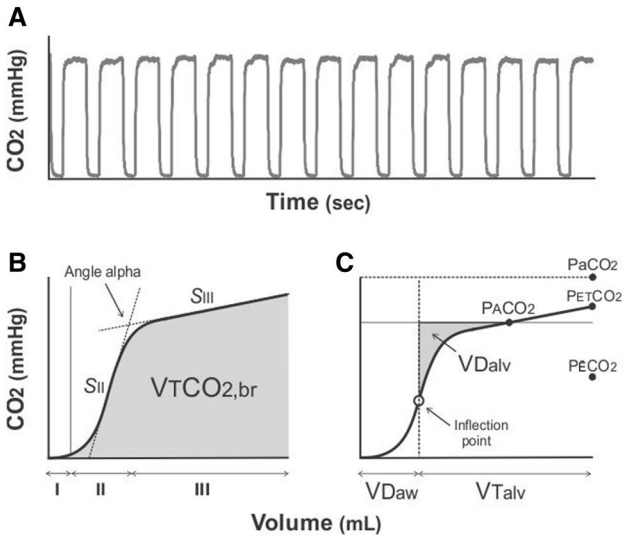

Fig. 2 Capnography based on time or volume. **a** In time-based capnography expired CO_2 is expressed as a temporal series. **b** Volumetric capnography is formed by three phases: phase I and II represents gas in the conducted airways while phase III represents pure alveolar gas. Phases II and III have corresponding slopes (*S*) which intersection constituted the alpha angle. The area under the curve ($VTCO_{2,br}$) is the amount of CO_2 eliminated in one breath. **c** Clinically important partial pressures of CO_2 expressed on the volumetric capnogram. $PETCO_2$ is the end-tidal partial pressure of CO_2, $PACO_2$ is the mean alveolar partial pressure of CO_2, and $P\bar{E}CO_2$ is the mixed expired partial pressure of CO_2. $PaCO_2$ is the partial pressure of CO_2 in arterial blood analyzed by a blood sample and depicted as a dotted line at the top of the capnogram. The capnogram's mathematical inflection point—the called *airways-alveolar interface*—is the limit between airways dead space (VD_{aw}) and alveolar tidal volume (VT_{alv}). The gray area represents the alveolar dead space (VD_{alv})

the limit between airways and alveolar compartments according to the principle described by Fowler [18].

Time-based and volume-based capnography gives non-invasive, breath-by-breath and bedside information of body functions that participate in the CO_2 kinetics [7, 8, 10–12]. They show complementary information and must be used simultaneously. The temporal series allows the continuous monitoring of common events while the volumetric capnograms enable special calculations such as dead space and the elimination of CO_2.

2.1 Metabolic monitoring

Body tissues are fueled by oxygen and nutrients that are metabolized to energy (adenosine triphosphate—ATP) and wasted products (CO_2 and water) [2]. The normal CO_2 production at rest ranged from 100 to 300 mL/min and it is reduced by 15–20% in mechanically ventilated patients under heavy sedation or general anesthesia. CO_2 produced by cells is stored in body tissues as gas, physical solution and chemical reactions [3, 10]. CO_2 molecules diffuse into the circulation depending on the partial pressure of CO_2 gradient between cells and capillary blood. There are many body compartments with different CO_2 kinetics related to the rate of both, local production and local blood flow. Fast changes in ventilation and perfusion affect the CO_2 placed in the highly perfused tissues while slow changes are observed in the low perfused ones [3, 10].

VCap measures the elimination of CO_2 by integrating the partial pressure of CO_2 (PCO_2) over the airway flow in a single breath [14–16]. This value is commonly expressed as occurring in 1 min (VCO_2) multiplying $VTCO_{2,br}$ by the amount of breaths per minute and thus the respiratory rate. According to Breen et al. the CO_2 from instrumental dead space being rebreathed during inspiration [$VTCO_{2,br}$(I)] should be subtracted from the expired value [$VTCO_{2,br}$(E)] to obtain the correct value [15]. Thus, the formula can be written as:

$$VCO_2 = (VTCO_{2,br}\ [E] - [I]) * \text{respiratory rate}$$

The context-sensitive nature of CO_2 kinetics allows VCap to be a surrogate of metabolism under particular conditions in ventilated patients [7]. It can be assumed that the elimination of CO_2 equal to its production only during *steady states* when alveolar ventilation and hemodynamics keep constant [19]. The steady-state is reached once VO_2 and VCO_2 remains unchanged ($\leq 10\%$) for several minutes in normothermic patients. Some authors believe that such steady-state is found in 5 to 10 min of stability [19, 20] while others described that it is needed at least 20 min to reach such condition in mechanically ventilated patients [21]. Many factors alter this steady-state condition either increasing VCO_2 (hyperthermia, shivering, stress, pain, awakening during anesthesia or excess of carbohydrates in the parenteral/enteral nutrition [22–25]) or decreasing it (hypothermia, premedication and hypno-sedative drugs [26–28]).

Assessment of body metabolism by VCap during *unsteady states* is tricky because the changes in metabolism is closely related and goes hand in hand with hemodynamics. For example, a painful stimulus in a ventilated patient increases not only the production of CO_2 but also hemodynamics parameters by sympathetic stimulation that moves more CO_2 molecules from body stores to the lungs. In this context is difficult to determine the pure role of metabolism or hemodynamics on the resultant change in VCO_2.

2.2 Hemodynamic monitoring

The convective traffic of CO_2 molecules in blood, like the delivery of O_2 to tissues, will depend on its content in blood and cardiac output. CO_2 molecules reached alveoli through the pulmonary perfusion or right heart cardiac output [5]. There is a close dependency between the elimination of CO_2 and pulmonary blood flow that was clearly demonstrated in

humans [29, 30]. This link between lung perfusion and CO_2 elimination explains the role of standard capnography for the diagnosis of hemodynamics events and for monitoring the quality of CPR maneuvers [31–34]. Time-based capnography gives *qualitative* information about lung perfusion while VCap can directly *quantify* pulmonary perfusion because VCO_2, a parameter only measured by volume-based capnography, has the dimension of flow (volume/time).

The particular CO_2 kinetics allows the measurement of cardiac output (CO) by VCap using the Fick's principle [35]:

$$CO = VCO_2 / \left(CvCO_2 - CaCO_2\right)$$

where $CvCO_2$ and $CaCO_2$ are the content of CO_2 in mixed venous and arterial blood, respectively. This method does not measure cardiac output but rather the portion of the global CO that crosses the lungs and participates in gas exchange, the called effective pulmonary blood flow (CO_{EPBF}) [7]. This is because the CO_2 sensor placed at the airways opening only recovers information from ventilated and perfused areas of the lungs. In other words, the CO_2 sensor is blind to areas of right-to-left shunt, which constitutes the ineffective part of CO (CO_{SHUNT}). Thus, global CO is formed by the sum of these effective and ineffective parts [7].

The partial rebreathing CO_2 technique was described to get CO_{EPBF} using the Fick's principle but without taking venous and arterial blood samples [36, 37]. The NICO device (Philips, Respironics, Wallingford, USA) applies such technique allowing the rebreathing of CO_2 through an instrumental dead space controlled by a mechanical valve [38]. The patient rebreathes its own CO_2 during 45 s and, later on, the valve bypasses the additional dead space. Patient breathes normally and without rebreathing for another 2 min until the expired CO_2 returns to previous baseline values. All the process takes 3 min to get one CO_{EPBF} value.

The partial CO_2 rebreathing technique then uses the differential Fick's equation:

$$CO_{EPBF} = \left(VCO_2 - VCO_{2r}\right) / \left[\left(CvCO_2 - CvCO_{2r}\right) - \left(CaCO_2 - CaCO_{2r}\right)\right]$$

where "*r*" is the measurement performed during CO_2 rebreathing.

During partial CO_2 rebreathing, it is assumed that the increased alveolar CO_2 content ($CACO_2$) equilibrates with the highest content of CO_2 found in the venous side of the pulmonary capillary. This external load of CO_2 is short-lived. Therefore, the calculation is performed before a complete recirculation of CO_2 has occurred. During the rebreathing period it is assumed that $CvCO_2$ and $CACO_2$ are equal and canceled each other in the above equation, to read:

$$CO_{EPBF} = \Delta VCO_2 / \Delta CaCO_2$$

Δ means the CO_2 changes before and at the end of rebreathing. Δ content of CO_2 in arterial blood ($\Delta CaCO_2$) of the previous equation is substituted by SCO_2, the solubility constant of CO_2 times arterial PCO_2 [39, 40]. As the change in $PaCO_2$ is proportional to the change in $PETCO_2$ during the rebreathing, the NICO assumes that this last change is a surrogate of arterial CO_2. Then, a formula is applied to transform the partial pressure of CO_2 in the "arterial content" of CO_2:

$$CO_{EPBF} = \Delta VCO_2 / SCO_2 \times \Delta PCO_2$$

Nowadays, the differential Fick's principle can be applied without rebreathing. Any brief, cyclic and controlled change in the ventilation, like a change in tidal volume or inspiratory-expiratory pauses for a few breaths, permits the measurement of the CO_{EPBF}—the called *capnodynamic* method [40–43]. Peyton et al. described such a method to obtain CO_{EPBF} based on a brief modification of tidal volume [43–45]. A complete 12 breaths sequence—constitutes by six low VT followed by six high VT—makes a change in alveolar ventilation and the corresponding CO_2 balance from which CO_{EPBF} is derived. A calibration, capacitance and continuous equations are applied to get the final CO_{EPBF} value [43]. The global CO is calculated adding to CO_{EPBF} the CO_{SHUNT} value estimated by the shunt equation, considering pulse pressure oximetry (SpO_2) and assuming a mixed venous saturation of 70%.

Albu et al. described another solution of the capnodynamic equation to get CO_{EPBF} and the effective lung volume (ELV) using a mole balance equation for the carbon dioxide content in the lung [46]. The equation can be applied in a ventilatory algorithm changing the alveolar ventilation with inspiratory or expiratory holds but maintaining VT stable. This pattern alters the alveolar fraction ($FACO_2$) and the amount of expired (VCO_2) carbon dioxide, including three unknown values in the formula—ELV, EPBF and $CvCO_2$:

$$ELV \times \left(FACO_2^n - FACO_2^{n-1}\right) = EPBF \times \Delta t^n \times \left(CvCO_2 - CaCO_2\right) - VTCO_2$$

where n is the current breath, n−1 is the previous breath and Δt^n is the current breath cycle time. The left hand side of the equation represents the difference in CO_2 content in the lungs between two breaths while the right hand side expresses the circulatory supply of CO_2 into the lung. The equation compares the content and elimination of CO_2 during pause-induced fluctuations in alveolar ventilation but without altering airways pressure and lung volumes.

The capnodynamic method showed good accuracy and agreement with the standard CO techniques in experimental models and in real patients [42, 46–48]. Main advantages of the capnodynamic method are the noninvasive and breath-by-breath calculation of CO_{EPBF}, its potential implementation in standard ventilators and without interfering the selected protective ventilatory pattern. The main

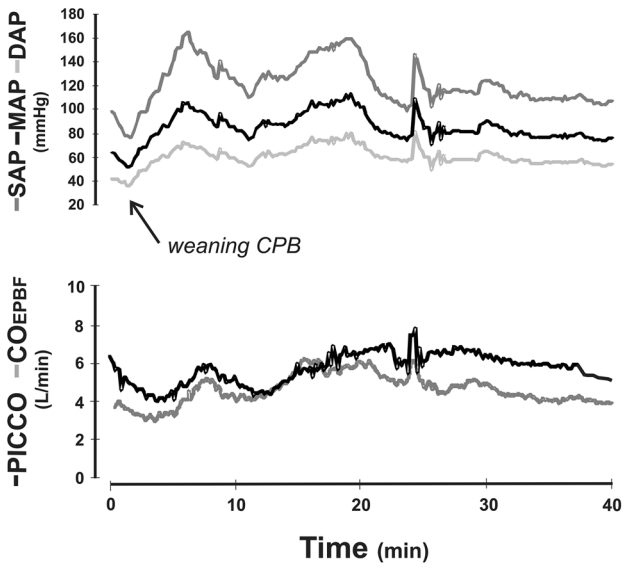

Fig. 3 Effective pulmonary perfusion measured by CO_2. Data were obtained in an anesthetized cardiac surgery patient immediately after weaning from cardiopulmonary bypass (CPB). In the upper figure the systolic (SAP), mean (MAP) and diastolic (DAP) arterial blood pressure are recorded. The lower figure depicts the pulse contour-based cardiac output measured by the PICCO device and the effective pulmonary blood flow measured by the capnodynamic method. During this particular moment of cardiac surgery hemodynamic instability is rather common. Note that both measurements are closely related and changed in accordance with the arterial blood pressure (unpublished personal data)

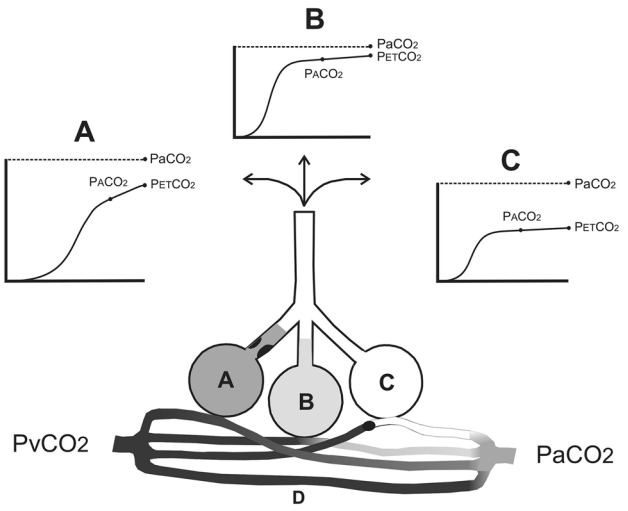

Fig. 4 Ventilation/perfusion ratios and the dead space concept. The Riley's model of the lungs depicts three units: a shunt unit (**a**), a normal unit (**b**) and a dead space one (**c**). **d** constitutes the anatomical shunt pathway. The ventilated C unit does not receive perfusion and constitutes the alveolar dead space (VD_{alv}). The conducted airways does not participate in gas exchange and thus is called airways dead space (VD_{aw}). The sum of both kind of dead space determines the physiological dead space (VD_{phys}). In the top, three theoretical volumetric capnograms derived from lungs with a predominance of shunt units (capnogram A), normal units (capnogram B) or dead space units (capnogram C). The shape of capnograms A and C as well as their Pa-ACO_2 differences are clearly deviated from the normal lung (capnogram B)

disadvantage, common to all CO_2-based method of CO calculation, is the need of controlled ventilation throughout an endotracheal tube.

Figure 3 shows a clinical example of CO_{EPBF} measured by the capnodynamic method and compared to the pulse contour cardiac output calculation after cardiopulmonay by-pass weaning. This period of the cardiac surgery is characterized by hemodynamic instability as shown in this patient. CO_{EPBF} has a good time-resolution and trending ability and goes hand in hand with changes in pulse contour analysis-based cardiac output and arterial blood pressure.

2.3 Gas exchange monitoring

The primary goal of the respiratory system is gas exchange, which depends on pulmonary capillary perfusion, diffusion and ventilation. These three processes interact in a simultaneous and coordinated way explained by the concept of the ventilation/perfusion (V/Q) relationship (Fig. 4). A reference V/Q ratio of "1" means that both, perfusion and ventilation are matched one each other and, therefore, diffusion allows optimum oxygenation and adequate CO_2 removal of capillary blood. Any mismatch in the V/Q ratio can potentially change the PaO_2 and $PaCO_2$, leading to hypoxemia by the *shunt effect* ($V/Q < 1$ to 0) or hypercapnia through the *dead space effect* ($V/Q > 1$ to ∞) [49]. Shunt is caused by diseases that decrease alveolar ventilation but maintaining lung perfusion like atelectasis, pneumonia or ARDS among others. Diseases causing dead space are those that reduce lung perfusion (pulmonary embolism, arterial hypotension, hypovolemia) but keeping normal or increased alveolar ventilation [50].

The arterial blood gas (ABG) analysis is the reference method to evaluate gas exchange [50]. This technique neseds an arterial puncture that is only representative of the moment when the blood sample is taken. As mechanical ventilation is a continuous treatment, it is primordial to develop monitoring tools for the breath-by-breath and non-invasive assessment of gas exchange. Thus, pulse oximetry and capnography provide information of biological gases in real-time fashion, improving the care of mechanically ventilated patients and reducing the need of ABG analysis.

Capnography provides non-invasive information about CO_2 diffusion via its partial pressure values [16]. $PETCO_2$ is the most popular capnographic parameter that represents lung units placed in the lung periphery and/or with low time-constant, which emptied belatedly into the main airways. Contrarily, $PACO_2$ is the mean value of

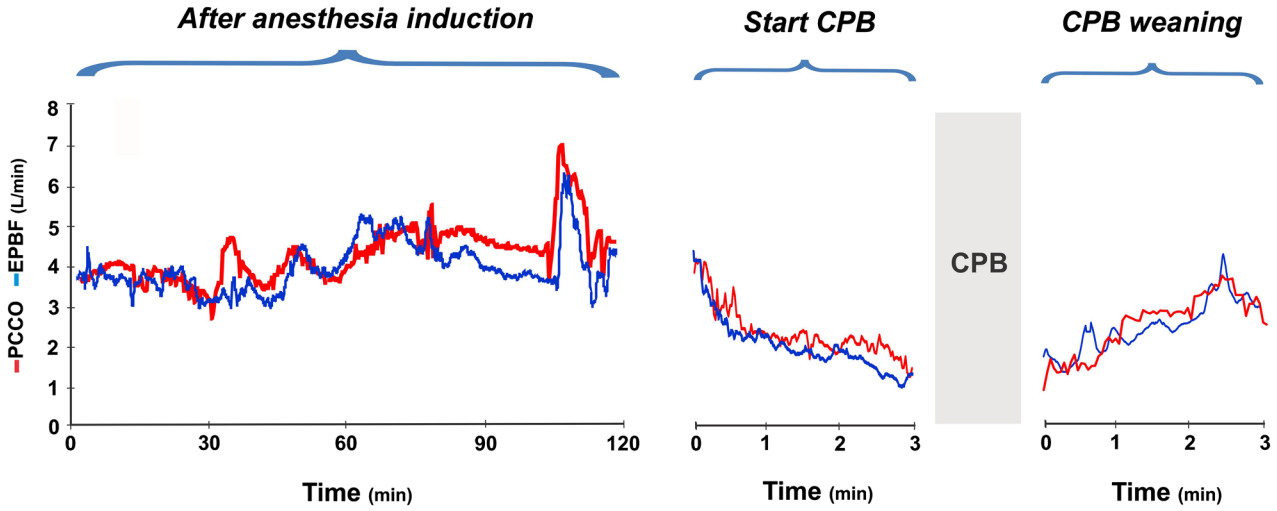

Fig. 5 Volumetric capnography derived-parameters during a lung recruitment maneuver and positive-end expiratory pressure titration (PEEP). Eight pigs subjected to repeated lung-lavages to obtain a model of ARDS were treated with a lung recruitment maneuver (RM) followed by a PEEP titration trial using constant ventilation and stable hemodynamics. Arterial partial pressure of oxygen (PaO_2), alveolar-to-arterial ($PA\text{-}aO_2$) and arterial-to-alveolar ($Pa\text{-}ACO_2$) partial pressure differences are depicted as mean values at each PEEP step. Data is presented as mean ± SD. The arrows indicate the open-lung condition (OLC) according to the lowest PEEP that keeps PaO_2/FiO_2 value ≥ 450 mmHg during the PEEP trial. This OLC was related to low $PA\text{-}aO_2$ and $Pa\text{-}ACO_2$ reflecting an increased area of gas exchange (unpublished personal data)

all lung units with different time-constant [16, 51]. For many years, it was considered that this value cannot be measured at the bedside [52–55]. However, it was recently demonstrated that $PACO_2$ can be accurately determined at the midpoint of the slope of phase III (Figs. 2c and 4) [56]. The rationale is that such point must represent the *averaged* value of CO_2 in all alveoli because phase III is formed by pure alveolar gas. This $PACO_2$ measurement was validated using the alveolar gas equation with data derived from the multiple gas inert technique. This discovery allows the calculus of alveolar ventilation and dead space in real-time and non-invasive fashion [56].

Physicians must be aware that the $PaCO_2$ value cannot replace $PETCO_2$ or $PACO_2$ because the shunt and dead space effects make $PaCO_2$ higher than the other values [7, 8, 12, 14, 49]. This is true even for young people with healthy lungs due to the presence of normal *anatomical* shunt and dead space [16, 49–51]. Therefore, despite capnography can decrease the number of blood samples, ABG analysis should be done anytime physicians suspect an important change in the CO_2 kinetics.

A clinical technique to reduce the number of ABG analysis with capnography is to calculate the arterial-to-alveolar gradient as the $Pa\text{-}ETCO_2$ or $Pa\text{-}ACO_2$ differences [10, 12, 16, 49, 57–59]. Capnography can approximate the $PaCO_2$ value by adding such calculated difference to the noninvasive $PETCO_2$ or $PACO_2$ values. The normal $Pa\text{-}ETCO_2$ value is ≤ 5 mmHg and the normal $Pa\text{-}ACO_2$ is 5–8 mmHg, where any increment from these reference values is related to a V/Q mismatch (Fig. 4) [16, 49, 57–59]. The $Pa\text{-}ACO_2$ must be the right index because it is the averaged value in the alveolar compartment as $PaCO_2$ is at the vascular side [51]. $Pa\text{-}ACO_2$ is similar than the oxygen-derived index $PA\text{-}aO_2$ to analyze diffusion at the alveolar-capillary membrane.

Figure 5 shows how capnography analyzes gas exchange in an experimental model of ARDS. The animals were subjected to a lung recruitment maneuver followed by a PEEP titration trial performed at constant ventilation and stable hemodynamics. The open lung condition (OLC); i.e. a lung without collapse and pathological shunt was defined as a PaO_2/FiO_2 ration ≥ 450 mmHg [60]. Note that $PA\text{-}aO_2$ and $Pa\text{-}ACO_2$ showed very low values during OLC but increased as lungs progressively collapse at low PEEP.

2.4 Monitoring of ventilation

Pulmonary elimination of CO_2 is done during the respiratory cycle. The opposite body kinetics and high solubility of CO_2—compared than O_2—explain why this gas is highly dependent on ventilation for its elimination. CO_2 is then a good tracer of alveolar ventilation (VA) and, therefore, any disturb in the capnogram is used as a continuous ventilatory monitoring. Examples are disconnections, apneas, hypoventilation-hyperventilation, esophageal intubation, bronchospasm, asynchronies, mucus plug, etc.

The first step when mechanical ventilation is established in a patient is to adjust the minute volume ventilation (VE). VE is the product between the tidal volume and the respiratory rate. This initial setting is adapted according to the patient's theoretical body weight and the precepts of protective ventilation. The next step is to determine the *ventilatory efficiency* of the selected VE using the concept of dead space and alveolar ventilation, based in the following formula [51, 61, 62]:

$$VE = VA + VD$$

where VE is formed by the *ineffective* part that does not participate in gas exchange (dead space = VD) and by the *effective* portion, which is the gas in contact with pulmonary capillaries that participates in gas exchange (alveolar ventilation = VA) [51]. VA is surely the interested portion and this is the one physicians want to know anytime mechanical ventilation is applied, which is calculated subtracting VD from VE. The monitoring of VA and VD is the key to determine if one particular ventilatory setting is in agreement with the patient's metabolic rate. This way a diminution in VA (or increment in VD that is the same thing) retains $PaCO_2$ and lead to hypercapnia. Oppositely, an increase in VA (or decrease in VD) will cause hypocapnia. Again, as the CO_2 kinetics is context-sensitive, a quite stable metabolism and hemodynamics is needed to use the CO_2 as marker of VA.

Figure 6 showed an example of the importance of VA eliminating CO_2 in a hemodynamically stable anesthetized patient. Modifications in respiratory rate and VT induced changes in VA that affect partial pressures of CO_2 and VCO_2 in an opposite way. At higher VA, more elimination of CO_2 decreased its partial pressures at both side of the alveolar-capillary membrane leading to hypocapnia. Contrarily, lower VA decreased VCO_2 causing hypercapnia.

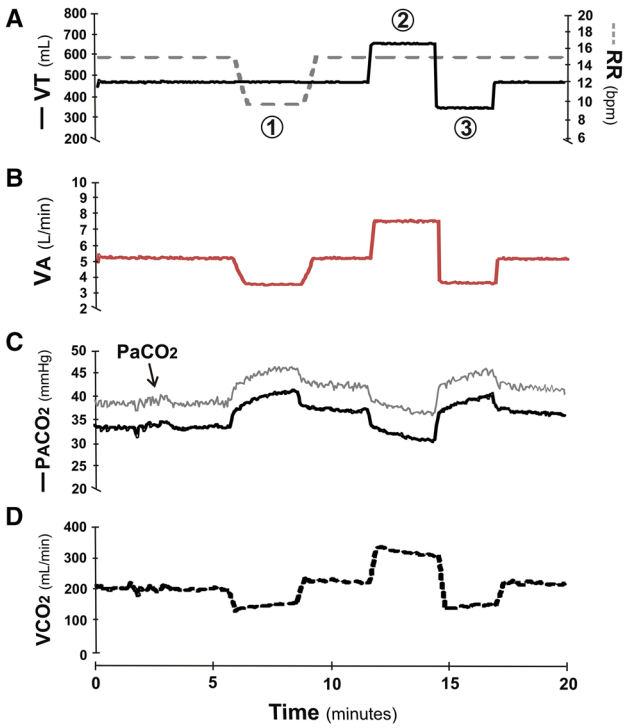

Fig. 6 Data was obtained in a mechanically ventilated anesthetized patient. **a** Tidal volume (VT) and respiratory rate (RR). **b** Alveolar ventilation (VA). **c** The alveolar ($PACO_2$) and arterial ($PaCO_2$) partial pressures of CO_2. **d** Elimination of carbon dioxide (VCO_2). Change in VA was performed by reducing RR from 15 to 10 breaths per minute (1A) or by increasing (2A) or decreasing (3A) VT during mandatory ventilation in a hemodynamically stable patient. Note that VCO_2 and $PACO_2$ change in an opposite fashion. $PaCO_2$ is depicted above $PACO_2$ (gray line in C) (unpublished personal data)

3 The problem of dead space

There is a portion of VT that does not reach the alveolar compartment and remains in the conducted airways called *airways dead space* (VD_{aw}) (Fig. 2c) [13–18]. In mechanically ventilated patients it is common to observe an additional *instrument dead space* (VD_{inst}) caused by connectors, elbows or HME placed between the "Y" piece and the endotracheal tube [18, 63]. At the alveolar compartment, unperfused alveoli that receive ventilation (V/Q = ∞) will not participate in gas exchange and constitutes the known *alveolar dead space* (VD_{alv}). This VD_{alv} is represented by the lung unit C in Fig. 4 [49–51, 64]. VD_{aw} together with VD_{alv} determine the global dead space called *physiological dead space* (VD_{phys}).

VD is calculated by the volumetric capnography using the *Fowler's concept* together the *Bohr's formula* [18, 65].

Fowler's concept postulates that the mean airways-alveolar interface or the inflection point of the capnogram constitutes the limit between the gas transported by convection in convective airways and by diffusion in the alveolar compartment (Fig. 2c). Thus, this concept measures airways dead space non-invasively in each breath.

The Bohr's formula is a mass balance equation that calculates the portion of VT without CO_2 or VD_{phys}:

$$VD_{phys}/VT \text{ or } VD/VT = (PACO_2 - PECO_2)/(PACO_2 - PICO_2)$$

where $PICO_2$ is the inspired partial pressure of CO_2 that is assumed to be zero because fresh gas flow does not contain CO_2. However, this value must be taken into account for a proper dead space calculation when some re-inhalation of CO_2 comes from the "Y" piece and additional VD_{inst}. Finally, the alveolar dead space is calculated subtracting VD_{aw} to VD_{phys}.

Dead space can be expressed as part of minute ventilation (VD in L/min), as absolute values in one breath (i.e. VD_{phys} in mL) or as a ratio with the tidal volume (VD/VT). The last option is the best because dead space is highly influenced

by tidal volume size. Dead space *ratios* normalized by the expired volume allow comparison between individuals of different body mass ventilated with different VT [49].

It is important to know the normal dead space values for proper clinical applications. In healthy and young people breathing spontaneously the VD_{phys}/VT represents the 20–25% of the VT, formed by 15–20% of VD_{aw}/VT and 5–9% of VD_{alv}/VT [16, 66]. Mechanical ventilation in patients with healthy lungs increases VD_{phys}/VT to 30–40% while in critical ill patients increase above 40% [16, 67]. Patients with lung diseases had Bohr's physiological dead spaces higher to 50%, where VD_{aw} and VD_{alv} showed a two or three-fold increments from normal [68–72].

In the past, the Enghoff's modification of the Bohr's formula replaced $PACO_2$ by $PaCO_2$ because the $PACO_2$ was not available at the bedside. This invasive and intermittent calculation overestimates dead space because the $PaCO_2$ value is normally above the $PACO_2$ caused by both, the dead space and shunt effects (Fig. 4). Therefore, the Enghoff's formula calculates an index of gas exchange but not a "dead space" because includes all kind of V/Q mismatches [49]. Nowadays, the Bohr's formula can be entirely applied in a non-invasive way because the measurements of $PACO_2$ and $P\bar{E}CO_2$ by the volumetric capnogram were properly validated [56, 71–74]. The clinical meaning of Bohr dead space and the Enghoff's index is thus different but complementary; and physicians can be use both to get information about V/Q ratio from dead space to shunt [49].

4 Conclusions

Capnography is a first line monitoring system for mechanically ventilated patients. Time-based capnography describes expired CO_2 in a temporal series giving real-time information of the mechanical breaths. Volume-based capnography, on the other hand, provides important clinical "volumetric" data related to the body CO_2 kinetics. Both kind of capnography supports synergic and complementary noninvasive information at the bedside. Nowadays, VCap goes one step forward standard respiratory mechanics and provides a new dimension for monitoring of mechanical ventilation. VCap not only measures the load of CO_2 to be eliminated by ventilation but also describes the efficiency and the hemodynamic repercussion of any selected ventilatory mode and settings.

Conpliance with ethical standards

Conflict of interest Peter Kremeier is employee of Salvia GmbH. Stephan H Böhm performed consulting activities for Salvia GmbH. Gerardo Tusman performed consulting activities for Getinge AB.

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