Volumetric Capnography – The Next Advance in \( \text{CO}_2 \) Monitoring

ABSTRACT
Current trends in monitoring and patient safety are leading to the adoption of capnography as a standard of care in many clinical environments and the recognition of the importance of volumetric capnography. This paper contrasts volumetric capnography with time-based capnography.

INTRODUCTION
Standards – Within the last two decades, the clinical utility of time-based capnography, end-tidal \( \text{CO}_2 \) monitoring, and volumetric capnography have found widespread recognition. Medical societies representing anesthesiology \([12]\), cardiology \([13,14]\), critical care \([15]\), pediatrics \([16]\), respiratory therapy \([17]\), emergency medicine \([18]\) and other organizations have either mandated or strongly recommended the use of capnography for patient monitoring during general anesthesia, conscious sedation, resuscitation, intubation, weaning, transport \([19]\) and a variety of other procedures. Some societies including the American Society of Anesthesiologists have recognized the importance of monitoring carbon dioxide and volume, and while not yet mandating the monitoring of expired volume, have “strongly encouraged” it:

> Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Continual monitoring for the presence of expired carbon dioxide shall be performed unless invalidated by the nature of the patient, procedure or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged. (3.2.1 in [12])

Such requirements in conjunction with Joint Commission on Accreditation of Healthcare Organizations (JCAHO) requirements, indicating the standard of care for sedated patients must be uniform throughout the institution \([20]\), suggest that capnography be performed during sedation on patients throughout the hospital.

Combined monitoring of carbon dioxide and expired volume serves as an important monitoring and diagnostic tool in a number of areas including ventilator management (e.g. PEEP titration), intraoperative assessment, patient transport, cardiopulmonary resuscitation and pulmonary embolism management \([21-23]\). For example, to increase the confidence in safety during conscious sedation it has been recommended that ventilation be monitored in addition to the vital signs and pulse oximetry. While pulse oximetry may detect the onset of hypoxia in sedated patients, it infers the partial pressure of oxygen through a surrogate of \( \text{SaO}_2 \) (i.e., \( \text{SpO}_2 \)). Capnography, on the other hand, provides for earlier detection of ventilatory depression and respiratory failure and as such has become much more widespread in its usage. However, in spite of its broad clinical utility and advantages such as being non-invasive, easy to use, easy to maintain and relatively inexpensive, capnography still remains underutilized \([24]\). This has been attributed to the lack of education and understanding of the wide range of applications of the technology. While easy to use, capnography’s use and interpretation must be performed in a careful and informed manner to avoid clinical errors. Manufacturer specific algorithms must be considered as well as sampling site, sample rate, interfering gases and design specifics. On the other hand, since the transport of volume is central to the function of the lung, volumetric capnography provides a clearer and more comprehensive picture of the patient than a single point measure of the patient such as the end-tidal value.

History – The history of volumetric capnography spans the last century (Figure 1)\([1]\). One of the earliest infrared measurements of \( \text{CO}_2 \) in the expired human breath was reported by John Tyndall in 1865 in his famous Rede Lecture “On Radiation” at Cambridge University. However, it took another century before these measurements reached the bedside. Similarly, some of the earliest measurements of vital capacity reported in 1846 by John Hutchinson preceded the development of devices which permitted convenient measurement of flow (and hence volume) by over 75 years. The importance of measuring volume with carbon dioxide has long been recognized by physiologists and clinicians. Early methods such as the Haldane method and its various derivatives used chemical absorbents (i.e. sodium or potassium hydroxide for \( \text{CO}_2 \)) and measured the diminution of volume, while the gas was kept at a constant temperature and pressure. This served as the reference method for a volumetric measure of \( \text{CO}_2 \) for many years.
Since the early 1900s, gas exchange was often clinically measured by either the “gold standard” Douglas bag method or with the Tissot spirometer. The Douglas bag required the collection of exhaled air in large, impermeable canvas bags (50 l), and subsequent sampling and analysis of the collected gas to measure the mixed gas fractions and the total expired volume by manually “squeezing” the entire contents of the bag through a spirometer. This method provided neither the flow waveform nor capnogram.

One of the earliest descriptions of the volumetric capnogram and a method to determine “airway” dead-space is that of Aitken and Clark-Kennedy (1928) [2]. Fowler (1948) [3] in describing the single breath test for nitrogen (SBT-N2) curve sought to use uniform terminology to clarify the “meaning of dead-space”, and, thus, divided this curve into four phases: I, II, III, and IV. Different methods to sample “alveolar” CO$_2$ gas were developed, including single and multiple breath methods.

Elam (1955) working on the problem of CO$_2$ elimination from closed circuit anesthesia systems under U.S. Army support published early pioneering work in the field. Using newly developed CO$_2$ gas monitors, they were the first to publish capnographic profiles of human respiration in the anesthesiology literature [4]. Their work on CO$_2$ homeostasis, published in a series of four papers, included both normal and abnormal characteristics of the capnographic profile and measurements of dead-space and alveolar ventilation. While single breath curves for CO$_2$ appeared as early as 1961 in the literature, it was not until Fletcher (1980) [5] presented the concepts of dead-space and CO$_2$ elimination in a unified framework known as the single breath CO$_2$ curve that this approach began to gain clinical recognition. In 1976, the Model 930 CO$_2$ analyzer (for use with the 900 Servoventilators) offered the first commercial volumetric capnograph, featuring mainstream CO$_2$ and ventilator derived flow.

In the early 1990’s, the first efforts to integrate CO$_2$ and flow from the airway manifested with the introduction of the on-airway D-lite sensor (Instrumentarium, Helsinki, Finland) combining, in a single adapter piece, a flow-restrictor element for flow and a port to allow sidestream gas sampling. The sidestream approach requires sophisticated computer algorithms to align and compensate the flow and CO$_2$ signals [6].

The mid-1990’s saw the introduction of the first “all-mainstream” devices for on-airway volumetric capnography (Novametrix, Wallingford, CT) [7]. These devices evolved from separate flow and CO$_2$ sensors connected to separate devices (e.g., Ventrac 1550/Capnogard) and became integrated CO$_2$/flow-airway adapters interfaced to the same host system (e.g., CO$_2$SMO+, NICO). The Ventrac Model 1550 system allowed a capnometer (e.g., CO$_2$SMO or Capnogard) to be interfaced via a serial port to the 1550 module so that volumetric capnographic variables such as $\bar{V}CO_2$ and dead space could be computed. The CO$_2$SMO Plus! monitor was the first monitor to integrate on-airway flow measurements with capnography (and pulse oximetry) in a single small package to enable continuous bedside monitoring of mechanically ventilated patients. The NICOC$_2$ monitor introduced to the market in 1998, was the first widely available clinical device to non-invasively measure pulmonary capillary blood flow (and cardiac output) using the indirect Fick partial rebreathing technique. With the use of a NICO sensor (i.e. combined CO$_2$/flow sensor with valve and adjustable loop of tubing) and the use of a rebreathing maneuver controlled by an in-line valve, cardiac output and pulmonary capillary blood flow (PCBF) could be estimated every 3 minutes.

The development of these products and a new family of flow/CO$_2$ adapters (neonatal, pediatric and adult) required a number of key technological developments such as a novel thick-film IR source, a robust, fixed-orifice flow sensor, and extremely sensitive low-cost differential pressure sensors [8]. The combination adult sensor design included the sample cell and fixed-orifice portion side-by-side, with the sample cell proximal to the patient, whereas the combination neonatal sensor used a split orifice design that merged the sample cell and fixed-orifice portions tightly together. These designs allow for relative immunity to unpredictable flow velocity profiles, without the need to add excessive length to the flow sensor adapter (i.e. minimizing dead space). (For more details on the development of these products please refer to the whitepaper “From Novametrix to Philips – A History of Innovation, 1978-2010” OEM1106A).
Figure 1 - Timeline - History of Volumetric Capnography (From Jaffe, MB, “Volumetric Capnography – A Brief History”, Abstracts of the 2011 Annual Meeting of the American Society of Anesthesiologists, Chicago, Illinois).
TIME-BASED CAPNOGRAPHY OVERVIEW
The concentration of carbon dioxide is expressed either as a gas fraction \( \text{FCO}_2 \) or partial pressure \( \text{PCO}_2 \). It can be displayed graphically in both time and volume-based formats. Capnography when used without qualification refers to time-based capnography. In addition to capnometry\(^1\), capnography includes a plot of the instantaneous \( \text{CO}_2 \) concentration over the course of a respiratory cycle [25]. From this plot the cyclic changes from inspiration and expiration can be visualized. The “textbook” capnogram (Figure 2) comprises two segments, an expiratory and inspiratory segment, which while suggestive in name is actually somewhat misleading [26]. The expiratory segments consist of a varying upslope that will level to a constant or slight upslope whereas the inspiratory segment consists of a sharp downslope that settles to a plateau of negligible inspired \( \text{CO}_2 \). Waveform patterns distinctly different from the typical pattern can often be used to qualitatively assess adequacy of ventilation and/or anesthesia, and faults in the breathing circuit. Various journal articles and even textbooks [22,23,27,28] have been written outlining these patterns. However, other than the end-tidal partial pressure of \( \text{CO}_2 \) only breathing frequency and a measure of inspiratory \( \text{CO}_2 \) levels are clinically reported. This is the case because, while the transition between the expiratory and inspiratory segments appear to be delineated in the capnogram, only in the absence of rebreathing does this transition correspond to the time of the actual beginning of inspiration, as can be reliably identified by the flow waveform. The transition between inspiration and expiration cannot be reliably discerned from the capnogram because of the presence of anatomic dead space that fills with inspiratory gas at end-expiration. This uncertainty further complicates the clinical decision making process. For example, is the alveolar ventilation adequate?\(^2\)

While time-based capnographic measurements of height, frequency, rhythm, baseline, and shape have been used in the research literature, the terminology used to characterize features of time-based capnography has exhibited little uniformity and provided conflicting usage of the same terminology [26]. A terminology that has been adopted and is analogous in some respects to volumetric capnography allows comparisons to be drawn more easily between time-based and volumetric approaches (Tables 1,2). Both approaches designate phases I, II and III and the mechanisms underlying each phase for both approaches are similar. However, to allow these phases of the time-based capnogram to be better defined, they are delineated using the start and end of inspiration (i.e., zero crossing points) from simultaneously recorded flow. As such, with the addition of the flow waveform to the \( \text{CO}_2 \) waveform, time-based capnography would no longer be just the capnogram, although volumetric capnography can present the data in a more useful form. Regardless, this “creepage” of time-based capnography strengthens the actual and perceived value of volumetric capnography, and over time should lead to a greater adoption of volumetric capnography for a wider range of clinical uses.

\(^1\) Capnometry - the measurement of carbon dioxide in a volume of gas; Capnography - the measurement of inhaled and exhaled carbon dioxide concentrations, as recorded on a capnogram. (From Dorland’s Medical Dictionary, 2007)

![Image 334x432 to 560x560](image)

Figure 2 - Time-based Capnogram. Inspiratory segment (Phase 0) and expiratory segment (divided into Phases I, II, III) \( \alpha \) angle = angle between Phase II and Phase III, \( \beta \) angle = angle between Phase III and descending limb of Phase 0 (inspiration) (Adapted from Kodali BS, Philips J. Anesth Analg. 2000; 91 (4): 973-7.)

VOLUME CAPNOGRAPHY OVERVIEW
The integration of flow or volume signals with the \( \text{CO}_2 \) signal and the measurement of indices characterizing this curve is widely referred to as volumetric capnography. It has also been referred to as the single breath test for \( \text{CO}_2 \) [29] and \( \text{CO}_2 \) spirography [30]. It provides information based in physiology using an established and uniform terminology. This terminology was originally used by Fowler to describe the SBT-\( \text{N}_2 \) (single breath test for nitrogen) curve where instantaneous nitrogen concentration is plotted against expired volume [31]. This curve was used to study uneven ventilation in lungs and is divided into four phases labeled phases I through IV. If instantaneous \( \text{CO}_2 \) fractional concentration is plotted against the expired volume, the resulting curve resembles the SBT-\( \text{N}_2 \) curve in shape and has been referred to as an SBT-\( \text{CO}_2 \) curve [29] or volumetric capnogram [32]. The graphical presentation shown in Figure 4 provides a unified framework for such physiological measures as \( \text{CO}_2 \) elimination, alveolar deadspace and rates of emptying. This plot of \( \text{CO}_2 \) vs. volume has been divided into three phases I through III [29], (Table 2) (Figure 3).
Figure 3 - The three phases of a volumetric capnogram. Phase I is the CO$_2$-free ineffective tidal volume. Phase II represents the transition between airway and alveolar gas. Phases II and III together are the CO$_2$ containing part of the breath, the effective tidal volume, $V_{t\text{eff}}$.

Phase I comprises the CO$_2$ free volume while phase II comprises the transitional region characterized by a rapidly increasing CO$_2$ concentration resulting from progressive emptying of the alveoli. Phase III, the alveolar plateau, typically, has a positive slope indicating a rising PCO$_2$. Using these three recognizable components of the volumetric capnogram, physiologically relevant measures such as the volumes of each phase, the slopes of phase II and III, carbon dioxide elimination as well as deadspace tidal volume and ratios of anatomic and physiologic deadspace can be determined.

Carbon dioxide elimination ($\dot{V}CO_2$), the net volume of CO$_2$ eliminated can be viewed as the area between the expiratory and inspiratory curves (Figure 5). With no rebreathing, the volume of CO$_2$ eliminated during expiration is the area under the volumetric capnogram. However, the presence of inspiratory CO$_2$ must be accounted for when reporting and interpreting $\dot{V}CO_2$ [33].

During steady-state conditions the lung will excrete CO$_2$ at the same rate as the total body production rate, and there will be no net change in body CO$_2$ stores. In this case $\dot{V}CO_2$ is representative of total body production. However, changes in $\dot{V}CO_2$ can provide an instantaneous indication of the change in alveolar ventilation [34].
The respiratory dead space also known as “wasted” ventilation is considered to be that volume of each breath that is inhaled but does not participate in gas exchange. Airway deadspace, a functional surrogate of anatomic deadspace, is calculated from the CO$_2$-volume curve by Fowler’s method [31], which requires that the slope of phase III be estimated. Physiologic dead space, the sum of the airway dead space and alveolar dead space, can also be calculated but requires an estimate of the alveolar PCO$_2$. Arterial PCO$_2$ often serves as an estimate of alveolar PCO$_2$ given the normally close relationship [35]. The portion of the physiologic dead space that does not take part in gas exchange but is within the alveolar space is considered the alveolar dead space. It is considered to be that volume of each breath that is inhaled but does not reach functional terminal respiratory units. The term functional has important implication, because alveolar ventilation depends upon the output of CO$_2$. A respiratory unit that is ventilated but not eliminating CO$_2$ (i.e., deprived of its blood flow) is included in the alveolar dead space volume. An increase in the alveolar dead space also occurs when regions of the lung are ventilated, but under-perfused. Alveolar dead space is affected by any condition that results in a V/Q mismatch. This includes (a) hypovolemia, (b) pulmonary hypotension, (c) pulmonary embolus, (d) ventilation of non-vascular air space, (e) obstruction of pre-capillary pulmonary vessels, (f) obstruction of the pulmonary circulation by external forces, and (g) over extension of the alveoli [36].

Additionally, other potentially useful parameters have been calculated from the combination of CO$_2$ and volume including new surrogates and better estimates of alveolar CO$_2$, estimates of ventilatory efficiency, measures of the non-synchronous emptying of the alveoli with unequal ventilation/perfusion ratios [37] and additional normalized measures of CO$_2$ elimination using a concept known as the mean distribution time [39]. Efficiency, as defined, requires an arterial blood gas and provides a single value that summarizes the emptying of the lung relative to an ideal lung (Table 2). Alveolar ejection volume has been suggested by Romero [37] to serve as a measure of the non-synchronous emptying of the alveoli with unequal ventilation/perfusion ratios [37] but characterized as a misnomer by Fletcher [38]. This measure of emptying can be contrasted with physiologic deadspace, which can be viewed as reflecting the emptying characteristics of different alveoli [37]. The better understanding of respiratory physiology and related disease processes that volumetric capnography can help provide is only now beginning to be realized.

**Figure 5** - Plot of PCO$_2$ vs. volume illustrating both the expiratory and inspiratory portions. While often the inspiratory portion is negligible, the net CO$_2$ volume per breath is the difference between the area under the expired and inspired portions of the curve or similarly the area within the loop.
Volumetric Gas Measurements - Measurement Site Considerations (OEM 1109A).

The ventilation-perfusion relationships of the lung are accurately reflected in the slope of phase III by a volumetric capnogram rather than in that of a time-based capnogram in which the gradient of the phase III slope is usually less obvious and can be misleading. This may be because a smaller volume of expired gases (approximately the final 15%) often occupies half the time available for expiration, so that a similar change in the CO$_2$ concentration is distributed over a greater length of time in the time-based capnogram than in the volumetric capnogram. This phenomenon is illustrated in Figure 6. Figure 6a illustrates a neonatal subject with a long expiratory pause period during which very minor inspiratory efforts are made resulting in a capnogram that is difficult to interpret. In Figure 6b the plot of the expired volume vs. the partial pressure of CO$_2$ during expiration clearly shows the plateau from which an end-tidal value may be determined as well as all of the parameters associated with volumetric capnography, including the physiologic dead space and carbon dioxide elimination, which cannot be determined from a time-based capnogram. However, VCO$_2$ may only accurately reflect the underlying physiology when there are no leaks in the collecting system and where conditions permit the measurement of all the gas that is considered part of the alveolar ventilation (i.e., absence of pneumothorax with leak or endotracheal tube cuff leaking on exhalation).

Table 1 - Time-Based and Volumetric Capnography Measurements

<table>
<thead>
<tr>
<th>Basic Measurements</th>
<th>Units</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TIME-BASED CAPNOGRAPHY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO$_2$</td>
<td>Partial pressure (torr)</td>
<td>End-tidal CO$_2$ and respiratory rate</td>
</tr>
<tr>
<td><strong>VOLUMETRIC CAPNOGRAPHY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO$_2$</td>
<td>Gas fraction mHg/%/kPa)</td>
<td>Time-based measurements plus VCO$_2$, dead space(s) and other measurements</td>
</tr>
<tr>
<td>Flow (volume)</td>
<td>L/min (ml)</td>
<td></td>
</tr>
<tr>
<td>Airway pressure*</td>
<td>cm H$_2$O</td>
<td></td>
</tr>
</tbody>
</table>

*flow and airway pressure provides respiratory mechanics

Figure 6 - Time-based and volumetric capnogram for a neonatal subject with a long expiratory pause. Note: CO$_2$ units for time capnogram are in mmHg whereas units for the volumetric capnogram are often shown in %.
### Volumetric Capnography

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Volumetric Capnography</th>
<th>Time-based Capnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-tidal CO₂</td>
<td>Time based average</td>
<td>Time based average</td>
</tr>
<tr>
<td>Inspired CO₂</td>
<td>Various measures may be computed including inspired CO₂ volume</td>
<td>Minimum value during inspiratory segment often calculated</td>
</tr>
<tr>
<td>Breathing frequency</td>
<td>May be computed using flow waveform and/or capnogram</td>
<td>Inverse of time between the transition from expiratory to inspiratory segments of successive breaths</td>
</tr>
<tr>
<td>Inspiratory/Expiratory Time</td>
<td>Timing from start of inspiration and expiration determined from flow waveform.</td>
<td>Approximate values may be calculated if deadspace and rebreathing not significant</td>
</tr>
<tr>
<td>Mixed Expired CO₂ (PeCO₂ or FeCO₂)</td>
<td>Volume weighted average of CO₂. Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>CO₂ Elimination (VCO₂)</td>
<td>Net volume of CO₂ measured at the mouth or airway, and calculated as the difference between expired and inspired CO₂</td>
<td>Not available</td>
</tr>
</tbody>
</table>

### PHASES

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description</th>
<th>Volumetric Capnography</th>
<th>Time-based Capnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>CO₂ free gas from the airways</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>Time from start of expiration to increase in PCO₂</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>Volume from start of expiration to increase in PCO₂</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>Rapid S-shaped upswing on the tracing caused by the mixing of dead space gas with alveolar gas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>Time from end of phase I to intersection of predictive slopes of phase II and III</td>
<td>Approximate measure available</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>Volume during phase II</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>Curve fit of central portion of phase II volume</td>
<td>Curve fit of central portion of time-based phase II</td>
<td></td>
</tr>
<tr>
<td>Phase III</td>
<td>Alveolar plateau representing CO₂ rich gas from the alveoli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>Time from end of phase II to end of expiration</td>
<td>Approximate measure available</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>Volume during phase III</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>Curve fit of central portion of phase III volume</td>
<td>Curve fit of central portion of time-based phase III</td>
<td>Angle between phase II &amp; III (usually ranges between 100 &amp; 110 degrees)</td>
</tr>
<tr>
<td>Alpha Angle</td>
<td>Angle between phase II and III</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### DEAD SPACE(S)

<table>
<thead>
<tr>
<th>Dead Space</th>
<th>Description</th>
<th>Volumetric Capnography</th>
<th>Time-based Capnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway</td>
<td>Volume of the conducting airways at the 'midpoint' of the transition from dead space to alveolar gas</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Physiologic</td>
<td>Total dead space as calculated includes alveolar, airway and apparatus deadspaces</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Alveolar***</td>
<td>Dead space that is not airway dead space volume and is calculated by subtracting the airway dead space volume from the 'physiologic' dead space</td>
<td>Not available</td>
<td></td>
</tr>
</tbody>
</table>

### DEAD SPACE RATIOS

<table>
<thead>
<tr>
<th>Dead Space</th>
<th>Description</th>
<th>Volumetric Capnography</th>
<th>Time-based Capnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airway</td>
<td>Functional anatomic deadspace calculated via Fowler's method divided by expired tidal volume</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Physiologic</td>
<td>Total deadspace calculated graphically, with Enghoff -modified Bohr equation or alternate methods</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>Alveolar</td>
<td>Alveolar volume divided by expired tidal volume</td>
<td>Not available</td>
<td></td>
</tr>
</tbody>
</table>

### OTHER

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Volumetric Capnography</th>
<th>Time-based Capnography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficiency</td>
<td>Ratio of volume of CO₂ contained in the breath and the volume of CO₂ that would have been eliminated by an ideal lung at the same effective volume and end-tidal fractional CO₂</td>
<td>Not available</td>
<td></td>
</tr>
<tr>
<td>ftlate</td>
<td>Late dead-space fraction (arterial-end-tidal PCO₂ difference at 15% predicted total lung capacity/ arterial PCO₂)</td>
<td>Not available</td>
<td></td>
</tr>
</tbody>
</table>

**Definitions derived from Fletcher [5], Arnold [29], Eriksson [80] and other sources; Figures 3-5 illustrates a number of these definitions. ***Requires PaCO₂**
CLINICAL UTILITY OF TIME-BASED AND VOLUMETRIC CAPNOGRAPHY

The measured concentration of carbon dioxide is the result of ventilation, perfusion and metabolism, and their interactions, and is affected by changes of any of these components (Table 3). Knowledge of the absolute values of and changes in the time-based and volumetric capnograms can assist in the diagnosis of a variety of physiological and pathological phenomena and serve as a valuable tool during a wide variety of clinical situations (Table 4). The clinical utility of time-based and volumetric capnography for many of the indications listed in Table 4 are contrasted in Table 5. Selected references for time and volumetric capnography are provided supporting the respective indication. Note some applications are more established and this has been noted.

Table 3 - Factors that determine PCO₂ Levels
(adapted from Foley [41])

<table>
<thead>
<tr>
<th>Increased PCO₂</th>
<th>Decreased PCO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Cardiac arrest</td>
</tr>
<tr>
<td>Malignant hyperthermia</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>Hyperventilation</td>
</tr>
<tr>
<td>Bicarbonate bolus</td>
<td>Hypometabolic states</td>
</tr>
<tr>
<td>Venous carbon dioxide embolism</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Increased cardiac output</td>
<td>Decreased cardiac output</td>
</tr>
<tr>
<td>Restoration of pulse with cardiopulmonary resuscitation</td>
<td>Esophageal intubation</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>Disconnection from ventilator</td>
</tr>
<tr>
<td></td>
<td>Extubation</td>
</tr>
</tbody>
</table>

In some of these clinical situations, accurate knowledge of the end-tidal value may be clinically sufficient while in other situations the time-based capnogram is required for proper clinical interpretation. In many clinical scenarios, the time-based capnogram is inadequate as a reliable diagnostic tool or indicator. However, volumetric capnography can serve as a more reliable clinical tool and indicator for a number of clinical situations including intubation and pulmonary embolism screening, although the added clinical value of these monitoring modalities often remain unrecognized.

The recognition of the value of a physiologic-based approach such as volumetric capnography continues to grow and new clinical applications continue to be uncovered. While not all research to date on this subject has proved fruitful, the clinical value of volumetric capnography is rapidly expanding allowing insight into complex physiological phenomena.

Table 4 - Current and potential indications for capnography
(adapted from Genuit [42])

<table>
<thead>
<tr>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute clinical situations</td>
</tr>
<tr>
<td>Endotracheal Intubation</td>
</tr>
<tr>
<td>Feeding tube placement</td>
</tr>
<tr>
<td>Acute Airway obstruction/ assessment of broncho-spasm</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Routine Monitoring</td>
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<tr>
<td>Intraoperative monitoring (including intubation)</td>
</tr>
<tr>
<td>Postoperative ventilator weaning</td>
</tr>
<tr>
<td>Transport of ventilated patients</td>
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<tr>
<td>Monitoring of mechanical ventilation</td>
</tr>
<tr>
<td>Assessment of pulmonary perfusion</td>
</tr>
<tr>
<td>Ventilator weaning</td>
</tr>
<tr>
<td>Titration of PEEP with V̇CO₂ and V̇d_phys</td>
</tr>
<tr>
<td>Assist pulmonary artery and central venous pressure during insertion</td>
</tr>
<tr>
<td>Monitoring during conscious sedation</td>
</tr>
</tbody>
</table>

CONCLUSION

Only recently has time-based capnography become widely adopted as a standard of care for a number of applications and is considered an essential tool for the clinician. Its use during general anesthesia is nearly universal in the developed world, and it has been recommended that the use of continuous capnography in other clinical environments (e.g. ICU) be universally adopted as well [43]. Additionally, clinicians are just now beginning to appreciate the application and importance of volumetric capnography. The wealth of relevant physiological information afforded by volumetric capnography is beginning to be tapped, allowing for a better understanding of cardiopulmonary physiology. Volumetric capnography has significant applications for patients with lung disease such as acute respiratory distress syndrome, chronic obstructive pulmonary disease, and asthma as well as adult and pediatric patients with cardiovascular disease. The use of this important technique will allow for an even better understanding of cardiorespiratory interactions.

The costs, medical and legal, associated with adverse outcomes related to respiratory events have been significant [44]. Clinical tools made possible through the use of volumetric capnography which offer so much more than capnography alone have potential for improved patient monitoring and management and the associated reduction the cost of patient care.
### Clinical Use | Time-based Capnography | Selected Refs/Status | Volumetric Capnography | Selected Refs/Status
---|---|---|---|---
#### ACUTE CLINICAL SITUATIONS

**Avoiding esophageal intubation during ETT placement**
- Fast detection of exhaled CO₂, verifies placement, Can give false positives
- Presence of CO₂ and flow strongly indicative of tracheal intubation
  - [45-51], Accepted
  - [52] [22 P 49-50], Speculative

**Avoiding tracheal intubation during NG tube placement**
- Fast detection of exhaled CO₂ to verify incorrect placement.
- Lack of CO₂ and flow strongly indicative of not in trachea
  - [53], Developing
  - [57], Speculative

**Avoiding endobronchial intubation during ETT placement**
- Variable, Not-sensitive, Significant changes in end-tidal levels may be observed
- Combination of CO₂, flow, airway pressure and derived measures can assist detection
  - [54-56], Developing
  - [22 P 41], [57], Speculative

**Prognosis and adequacy of cardiopulmonary resuscitation**
- PETCO₂ can guide efforts and indicate patients response; predictive of survival
- In addition – provides a direct assessment of ventilation
  - [58-63], Accepted
  - [64], Speculative

**Assessment of airway obstruction**
- Variable
- Slope of phase III
  - [65-70], Accepted
  - [71-72], [73-74]**, Speculative

**Screening for suspect pulmonary embolism**
- Poor, Useful only in extreme cases
- Alveolar deadspace or fidate combined with D-dimer
  - [75-76], Developing
  - [77-87], Speculative

#### ROUTINE MONITORING

**Preoperative assessment of disease**
- Potential quick screening tool, as part of OSA screening
- See airway obstruction - above
  - [88], Developing
  - —, Speculative

**Detection of circuit leaks and/or rebreathing**
- Good but may miss some leaks, rebreathing assessment only qualitative
- Allows for quantitative assessment of leaks and rebreathing
  - [90], Accepted
  - [89,91], [89,97-100], Developing

**Detection of disconnection**
- Monitoring of PETCO₂ and waveform in intubated patients helps identify tube displacement
- Monitoring of the capnogram and flow can alert clinician to even partial disconnects
  - [92-93], [22 pp 49-50], Accepted
  - [22-23,89], Developing

**Weaning, Outcome predictor**
- Limited Use by itself
- Allows for wide range of relevant measures used in protocols to be computed (i.e., VCO₂, RSBI)
  - [94-96], Developing
  - [89,97-100], Developing

**PEEP Titration**
- Arterial end-tidal difference
- VCO₂, Slope of Phase III
  - [101], Developing
  - [102-103], Developing

**PETCO₂ as a Surrogate of PaCO₂**
- Normal and constant ET-a gradients→improved PaCO₂ estimate and less blood gas samples
- PETCO₂ predictive of PaCO₂, if physiological deadspace not too large
  - [104-108], Developing
  - [109-110], Developing

**Pulmonary Capillary Blood Flow/Cardiac Output Estimation**
- PETCO₂ variable
- VCO₂ surrogate with stable VE; partial rebreathing Fick method for PCBF
  - [111-112], Developing
  - [113-116], Developing

**Monitoring during transport**
- Identifies tube displacement, verifies continuous ventilation helps to optimize ventilation
- Proximal CO₂, flow and airway pressure (and derived variables) allows for continuous assessment of cardiorespiratory status
  - [117-120], [23 Ch 8, Ch9], Accepted
  - [23 Ch 8 Ch 9], Speculative

**Intraoperative Assessment**
- Good as front line monitor (see breathing circuit leaks and detection of disconnection)
- Proximal CO₂, flow and airway pressure (and derived variables) allows for continuous assessment of cardiorespiratory status
  - [12], [23 Ch 6], Accepted
  - [12], [23 Ch 6], Developing

**Assessment/safety of sedation/paralytic therapy**
- Improved patient safety
- CO₂ with flow allows for better identification of hypoventilation
  - [121-130], [23 Ch 12], Accepted
  - [23], Speculative

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**Key:** Accepted - Widely accepted as standard practice, Developing - Developing application, OSA - Obstructive sleep apnea, fidate - see Table 4, RSBI - Rapid shallow breathing index, ** COPD references
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Additional References for Table 5

Intubation

Airway obstruction
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Pre-operative screening

Mechanical Ventilation

Leaks, rebreathing

Disconnection

Weaning

PEEP Titration

PetCO₂ as PaCO₂ surrogate

Cardiac Output

Transport


Sedation


