SEMARAK ILMU PUBLISHING

Semarak Current Biomedical Technology Research Journal

Journal homepage:
*https://semarakilmu.com.my/journals/index.php/scbrj/index*
ISSN: XXX-XXX


# A Narrative Review of Capnography Usage in Clinical Medicine

Bhuwaneswaran Vijayam[1,2*], Sriwathi Angeline Hendricks[3], Ratnadeep Saha[4], Asila Shamirali Jiwa[5], Aneesa Maryam Basheer Ahmad[5], Kafuko Trevor Wamumbe[6]

[1] Department of Clinical Medicine, Newcastle University Medicine Malaysia (NUMed), 79200 Iskandar Puteri, Johor, Malaysia.
[2] Regenerative Medicine Working Group, Newcastle University Medicine Malaysia (NUMed), 79200 Iskandar Puteri, Johor, Malaysia
[3] Independent Researcher, 81300, Skudai, Johor, Malaysia
[4] Department of Pre – Clinicals, Newcastle University Medicine Malaysia (NUMed), 79200 Iskandar Puteri, Johor, Malaysia
[5] NUMed Research Society, Newcastle University Medicine Malaysia (NUMed), 79200 Iskandar Puteri, Johor, Malaysia
[6] Super Protection Limited, Riaba, 240 Malabo, Equatorial Guinea

**ARTICLE INFO**

***Article history:***
Received 29 March 2024
Received in revised form 9 May 2024
Accepted 20 May 2024
Available online 31 May 2024

***Keywords:***
Capnograph; capnometry; capnogram; capno; capnography; end-tidal carbon dioxide; carbon dioxide physiology

**ABSTRACT**

Capnography is the graphical study of carbon dioxide during expiration. Capnography has evolved and is more than merely a biomedical device that is used in the emergency department and intensive care unit (ICU). There are volume based and time-based capnographs. Although end tidal $CO_2$ ($EtCO_2$) is the most used parameter in clinical medicine, there are an abundance of other parameters from the capnometer. The capnographic parameters could originate from specific plot points of the time- or volume-based curves, the area under the curve or other mathematical and computationally transformed data of the $CO_2$. Although research of capnometry since its inception has focused on the respiratory aspects of the $CO_2$ signal with $EtCO_2$, newer parameters could be used to monitor, diagnose and prognose certain circulatory and metabolic disorders. In short, capnography is inevitably one of the important vital signs of modern medicine. As physiologically challenging conditions such as deep-sea diving and the now rampant space travel are becoming more common, there might be a need for familiarization with capnogram usage. In this narrative review, we go through the physiologic, mathematical, physics and clinical aspects of capnography.

## 1. Introduction

The Coronavirus disease 2019 (COVID-19) pandemic made us realize the importance of point-of-care devices and respiratory diagnostic tools for theranostic purposes [1,2]. In addition, parameters such as the pulse oximetry ($SpO_2$) which was widely used during the COVID-19 pandemic showed mixed results skewed towards being less reliable [3,4]. Besides that, the area of telemedicine had a growth spurt as the need for quarantine, isolation and minimal to non-contact diagnosis, supervision and surveillance were needed during the COVID-19 pandemic [5,6].

With all these factors, there were emergence and re-emergence of biomedical devices that served all these purposes. One of these was the capnometer. The capnometer measures the carbon dioxide pressure signal in millimeter mercury (mmHg). When this is represented as a graph, the term

* *Corresponding author.*
*E-mail address: bhuwaneswaran.vijayam@newcastle.edu.my*

capnography is used instead. In this narrative review, we go through the physiologic, mathematical, physics and clinical aspects of capnography. For brevity, capnography may be interchangeably referred to as 'capno' in this manuscript.

## 2. Carbon Dioxide Physiology in the Body

### *2.1 Breathing: A Physiological Process*

Breathing is an indispensable physiological process which involves the exchange of gases between the lungs and the pulmonary capillary blood, which is also one of the most vital parameters of life. This process permits the body to remove $CO_2$ from the blood whereas the intake of oxygen ($O_2$) complements the need to support cellular respiration. Cessation of breathing often indicates an impending death and is one of the medico-legal criterions of death [7]. Breathing could be divided into two phases, namely the inspiratory and the expiratory phases. While breathing, the air needs to traverse a series of zones such as the upper conducting zone (nose, mouth, pharynx and larynx) followed by the lower conducting zone (trachea, bronchi and terminal bronchioles) and lastly to the respiratory zone (respiratory bronchioles, alveolar ducts and alveoli). During inspiration, air is sampled from the atmosphere to the terminal units of the lungs where $O_2$ is normally received into the bloodstream while $CO_2$ as biproduct of cellular metabolism of the body is deserted from the tissues to the blood and expelled into the atmosphere by expiration. It is also worth mentioning that the air residing in the respiratory tract does not partake in true gaseous exchange processes and is termed as anatomical dead space. This amounts to approximately 150 ml in healthy adults or nearly one third of the total tidal volume [8]. Physiological dead space refers to anatomical dead space and any other amount of dead space that fails to participate in gaseous exchange processes within the lungs despite being within the respiratory zone. Unutilized air residing within the respiratory zone usually represents negligible amount in healthy lungs and thus physiological dead space almost equals to anatomical dead space. This however is subjected to increase in various pathological instances when the diffusion capacity of the lungs (interstitial fibrosis) or the ventilation-perfusion ratio is compromised (pulmonary embolism and emphysema) [9–12].

### *2.2 Physiological Control to $CO_2$ Expiration*

The lungs' role in regulating $CO_2$ level in the blood is enormous. When we breathe in, inhaled oxygen is transported *via* the bloodstream to the tissues which is then utilized to yield energy and subsequently produce $CO_2$ as a waste product. This is carried through the blood back to lungs and removed through exhalation. Generally, the ventilatory control is sensed and exerted by a variety of receptors. Thoracic neural receptors residing in upper airways, trachea, lungs, chest wall and pulmonary vessels respond to lung volumes and various chemicals (histamines and prostaglandins) including irritant components (exogenous noxious agents) and chiefly responsible to the local chemical environment [13]. Activation signals to the respiratory center elicit alterations in breathing patterns primarily by increasing the respiratory rate and/or stimulating cough, bronchoconstriction and mucus production. Those with asthma, interstitial lung disease, pulmonary oedema, pneumonia and pulmonary embolism tend to show hyperventilation when these types of receptors are activated. Peripheral chemoreceptors while being in the carotid and aortic bodies are responsible to react if there is a change in arterial oxygen ($PaO_2$). However, they also equally enhance signaling to the brain in the event of hypercapnia and acidosis. Generally, discharge enhances when the partial pressure of arterial oxygen goes below 75 mmHg, and shows noticeable increase when it goes below 50-55 mmHg [14]. The combined impact of hypoxemia and hypercapnia always produce greater responses

of the body than it does singly. Centrally located most pronounced chemoreceptors are mainly found close to the ventral surface of medulla and retrotrapezoid nucleus and play a significant role to act with urgency and powerfully to correct acid base irregularities by calibrating ventilation in response to a heightened $PCO_2$ situation. Owing to the lipophilic nature of $CO_2$, it crosses the blood brain barrier easily and thus is sensed rapidly by the brain to bring concomitant enhancement in ventilatory pattern and alteration in acidity. Pertinent to say that the influence of activation on centrally located chemoreceptors are much less while the acid base changes are metabolic in origin in contrast to respiratory type. The alveolar sacs are distal anatomical structures that are usually placed at the 20$^{th}$ to 23$^{rd}$ successful bifurcation of an ideal lung tissue [15]. Figure 1 shows the trends of $O_2$ and $CO_2$ values in mmHg in the atmospheric (1), inspired (2), alveolar (3), artery (4), vein (5) and expired air (7). Red arrows indicate the movement of respired air while blue arrows indicate expired air. The "METABOLISM" arrow shows the steady state of cellular respiration in which oxygenated RBCs are converted to deoxygenated RBCs.

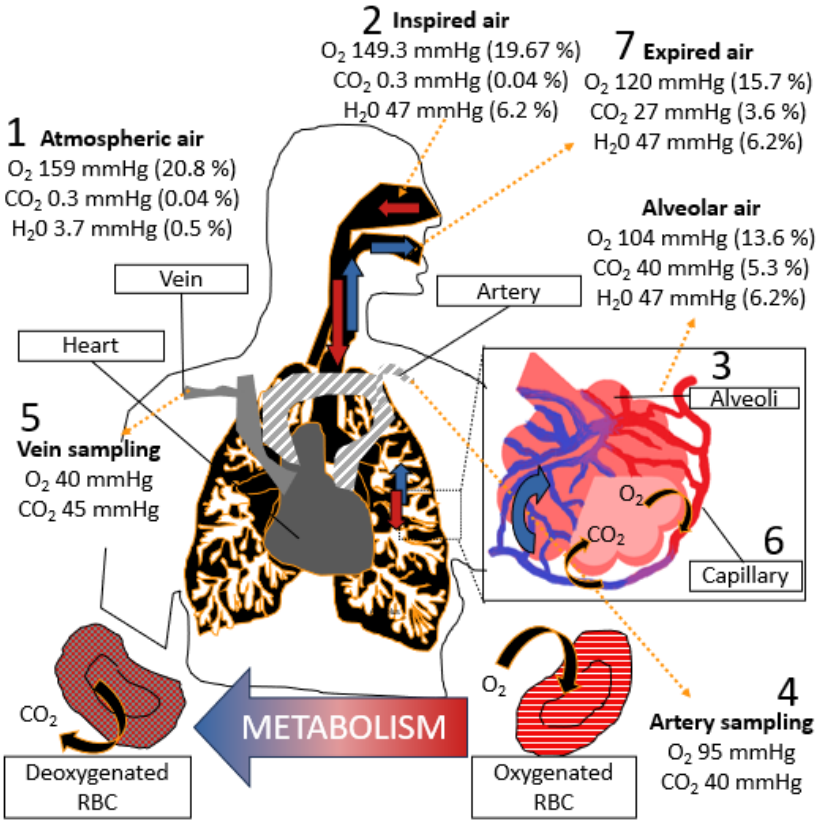


**Fig. 1.** Oxygen and carbon dioxide metabolism in the body

## 3. The Science of Capnography

### *3.1 Carbon Dioxide Fate: From One Red to Another*

The content of carbon dioxide in the atmosphere is approximately 0.3 mmHg which makes up 0.04 % of the total gaseous content. Upon exhalation, the carbon dioxide increases to 27 mmHg. The content of carbon dioxide is higher in the alveolar region at 40 mmHg. The humidity of the inspired air is higher than the atmospheric air but remains unchanged in the expired and alveolar air [16,17]. The gaseous exchange in the alveoli could also be evaluated in the circulatory system *via* blood sampling of both the arteries and veins. Typically, the arterial blood would show a higher yield of oxygen and a lower carbon dioxide of 75 - 100 mmHg and 40 mmHg, respectively. The venous sample

on the other hand has a lower oxygen and higher carbon dioxide concentration at 40 and 45 mmHg, respectively [18]. The arterial blood gas sampling remains the gold standard theranostic tool for cellular respiration in the clinical setting [19].

The gaseous exchange of carbon dioxide happens *via* diffusion through the deoxygenated red blood cells (RBCs) or better known as carbaminohemoglobin from the capillaries into the alveoli. $CO_2$ is transported from cells in the circulation towards the lungs in three forms which are the carbaminohemoglobin, bicarbonates ($HCO_3^-$) and the gaseous $CO_2$ form. Only 23 % of the $CO_2$ is transported *via* haemoglobin binding in contrast to $HCO_3^-$ which owes to 70 % [20]. The $CO_2$ is 20 times more soluble than $O_2$ in the serum [20]. The carbaminoahemoglobin utilizes the reverse effect of Bohr or better known as the Heldane's effect for the transport of $CO_2$ into the alveoli [21,22]. In the capillaries of the alveoli, as the oxygen binds to the haemoglobin, the affinity of the haemoglobin towards the $CO_2$ is weakened owing to its diffusion from the capillaries to the alveoli. Other than that, the acidity of the haemoglobin is altered at this state to be more acidic thus converting the $HCO_3^-$ to carbonic acid which readily cleaves into $CO_2$ and water. The $CO_2$ continuously diffuses through the alveoli [22]. Of note, other forms of metabolites such as carbon monoxide (CO) also undergo similar diffusion into the haemoglobin of the RBCs to form carboxyhaemoglobin.

As of late, non-dispersive infrared (NDIR) sensors are commonly used in medical devices. NDIR does not "disperse" or become scattered by substances between the light source and a detector [23]. NDIR sensors detect the $CO_2$ in a gaseous environment by its characteristic absorption and the vital components are an infrared (IR) source, a light tube, an interference filter (wavelength) and an infrared detector [24]. The exhaled $CO_2$ could be measured non-invasively through the manipulation of Lambert-Beer's Law (LBL) [25,26]. The equation of LBL is calculated from Eq. (1).

$$I = I_0 e^{-acl} \tag{1}$$

Where, *I* represents the intensity of light striking the photodetector. $I_0$ represents the intensity of light of an empty sample chamber. *a* is absorption coefficient of $CO_2$. *c* is the concentration of $CO_2$ in $mol/cm^3$. $l$ is the path length between the light source and the light detector. By using the LBL, the concentration of gas is typically calculated in IR spectroscopy [27]. From the same equation, radiation at wavelength 4.26 µm is associated with $CO_2$ concentration. Voltage corresponding to the amount of light which is absorbed by $CO_2$ contained in the respiratory gas is detected by a light-receiving element, thus detecting the $CO_2$.

Usually most small gaseous molecules exhibit a vibrational mode that also lies in the mid-infrared (MIR) range of 2.5 - 25 µm, and is also related with stretching, twisting, or bending their bonds. $CO_2$ gas has three vibrational modes: A symmetric stretch mode, a bending mode and an anti-symmetric stretch mode. The anti-symmetric stretch mode corresponds with the previously mentioned wavelength 4.26 µm in MIR and this is the most useful wavelength for measuring $CO_2$ because there are only few molecules which have a very little amount of significance of absorption at 4.26 µm range [23]. These concepts have also opened the manipulation of radiolabeled carbon dioxide presence, ratio, and recovery over time [28]. IR sensors are usually prioritized compared to other sensors such as chemical sensors which have a very low lifetime and need to be calibrated to maintain long term stability [29]. In summary, the $CO_2$ needs to be translocated from the 'red' blood cell to the infra-'red' sensor to display capnographic signals.

### *3.2 The Many Names of Capno*

In 1860 John Tyndall inaugurally measured expired $CO^2$ by utilizing spectrum absorption with infrared technology [24-30]. This revolutionized the study of expiratory $CO_2$. "Capnometry' is the expirometric study of the $CO_2$ gas. It has been used for centuries and there are literatures as early as 1962 of its usage [31,32]. As it is conventionally known, the study of capnometry focuses mainly on usage of end-tidal carbon dioxide ($EtCO_2$). Although it is used interchangeably with "capnography", "capnometry" means only the measurement of $CO_2$ in respiratory gas without a continuous written record or waveform [33]. In an earlier paper in 1990, the author suggested that the measurement of $EtCO_2$ in numerical form is called a capnometry and when such occurrence is done in a continuous fashion whilst involving the analysis of the waveform, "capnography" is a better term [34]. The device which measures both capnometry and capnography is called a "capnometer". Meanwhile, colorimetric capnometry is often a victim of the misnomer capnography. The colorimetric approach does not yield any waves [35]. "Capnodynamic" is the combination of capno signals with positive end-expiratory pressure (PEEP)[36]. It could be used to detect cardiac output [37,38]. Figure 2 shows the summary of the differences between the discussed terms. Of note, although somewhat related, capnodynamic and quantification of radiolabeled carbon dioxide displacement would not be discussed as it is beyond the scope of this manuscript. These have been narrated extensively elsewhere [28,36,38].

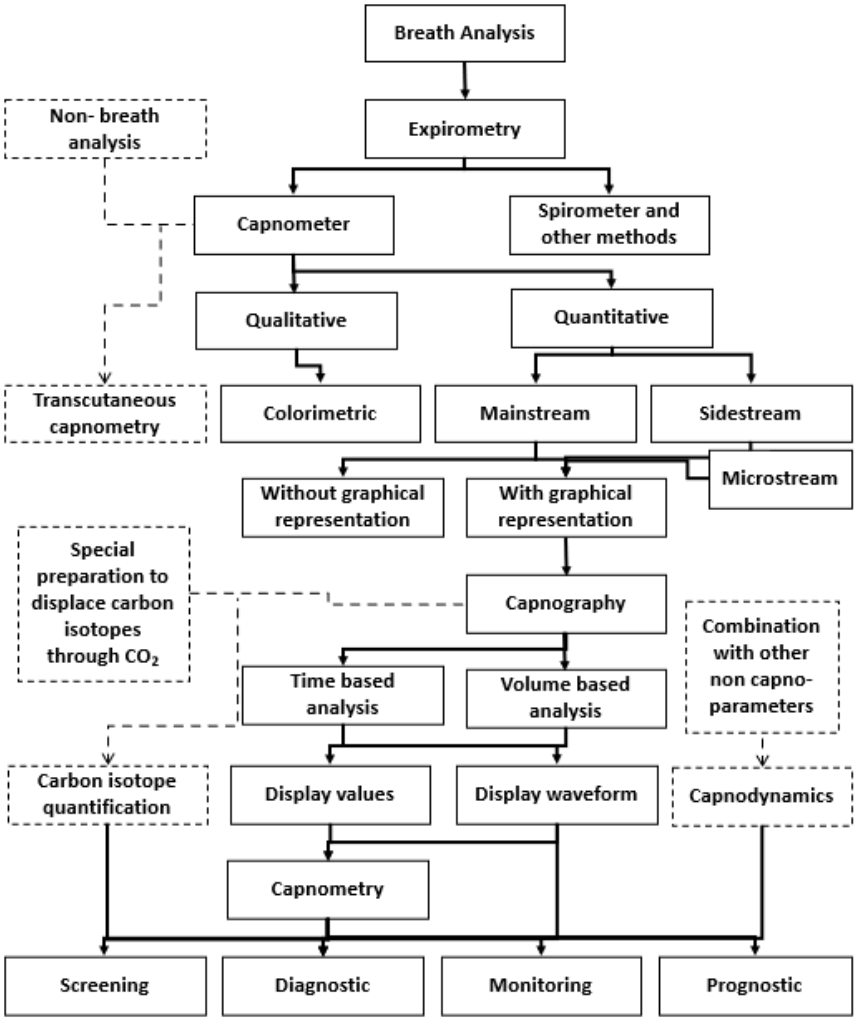


**Fig. 2**. The many names of capno: Grams, graph, meter, metry and others

### *3.3 The Physics Behind Capnometry Stream, Waveform Signal, Flow, Volume and Time*

Mainstream capnometers sensors are placed in between the proximal ET tube and the ventilatory circuit [39]. The mainstream capnometer could withstand flow range of the ventilator. Side stream capnometers use tubing connected to an airway adaptor and sampling line between the ETT and the breathing circuit to aspirate airway samples [39]. With side stream techniques, an IR sensor in a monitor could be placed which could be further away from the patient [39]. The flow rate for side stream varies between 150-200ml/L [40]. The side stream could be utilized in both intubated and non-intubated patients [41]. The low flow side stream or sometimes known as micro stream technology uses a flow rate of 50 ml/min [40,42]. Of note, there is a non-breath capnometer called the transcutaneous capnometer as depicted in Figure 2. This is discussed elsewhere as it is beyond the scope of this manuscript [43].

The time based capnograph is represented by $CO_2$ concentration on the y-axis and time on the x -axis as opposed to volume in the x-axis for volume based capnograph. The time based and volume based capno are sometimes abbreviated to TCap and VCap, respectively [44]. The TCap shows four phases which are phase 0, I, II and III. In contrast, the VCap does not have phase 0 as this represents inspiration [45]. Phase I represents free $CO_2$ in the anatomical and apparatus dead space [46]. Phase II represents mixing of dead space and alveolar $CO_2$ depicting the S-shape [46]. Phase III represents the alveolar plateau and the maximum point which represents the $EtCO_2$ [46,47]. Additionally, in some articles, phase 0 is used interchangeably with phase IV [48]. Furthermore, SI, SII, SIII and SI are sometimes represented numerically as S1, S2, S3 and S4. Figures 3 and 4 show the TCap and VCap with the location of the phases. Phase I (depicted as magenta): Represents the $CO_2$-free gas from the airways (anatomical and apparatus dead space). Phase II (depicted as dark blue): Consists of a rapid S-shaped upswing on the tracing (due to mixing of dead space gas with alveolar gas). Phase III (depicted as orange): The alveolar plateau represents $CO_2$-rich gas from the alveoli. It almost always has a positive slope, indicating a rising $PCO_2$. Phase IV or 0 (depicted as cyan) represents the drop of $CO_2$ signal upon inspiration.

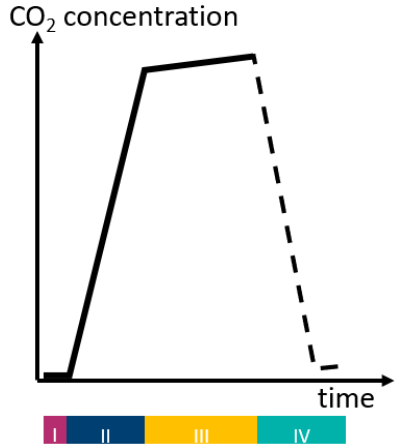


**Fig. 3.** Time-based capnography (TCap)

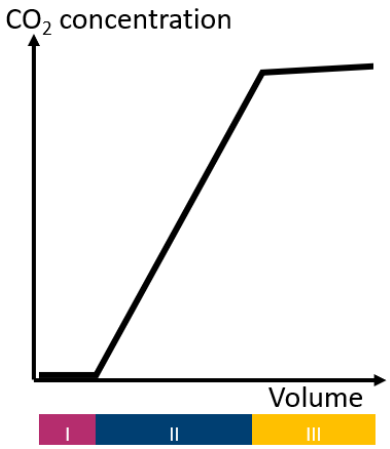


**Fig. 4.** Volume-based capnography (VCap)

Other major differences between the TCap and VCap includes the lack of dead space and dead space ratio calculation in TCap. On the other hand, the VCap lacks duration and temporal based capnometrics [49]. Both TCap and VCap could be manipulated to exert capnometric parameters such as frequency, efficiency, slopes, volume dead spaces and dead space ratios [49].

### *3.4 Capnometric Features*

There are numerous of parameters that could be utilized ad manipulated in both TCap and VCap. We have divided these to at least seven proposed features. These includes carbon dioxide concentration points and coordinates, slopes, angles, areas and volumetric studies, transformation of capnometric data, combination of data with other non-capnometric parameter and morphological changes. These has been depicted in Figure 5.

#### *3.4.1 Carbon dioxide concentration and time points and coordinates which signify certain clinical importance*

An example of these phenomena is the $EtCO_2$ which is the peak of carbon dioxide concentration of at the alveolar level. Clinically, this also signifies the end of the expiration. This capnographic feature has the most usage in clinical practice. Other examples of points usage would be the Bohr's partial pressure of carbon dioxide ($PaCO_2$) based on the location of $EtCO_2$ [50]. Other than that, the determination of the beginning and end of a breath cycle which may be used to estimate the ratio and frequency of breathing.

#### *3.4.2 Slopes*

In 1994, You utilized the S1, S2 and its ratio to differentiate bronchospastic and non-bronchospastic patients [51]. This finding was later reiterated by Howe in which increment in both S1 and S2 was found in bronchospastic diseases [52] .Recent papers suggest the usage of slope II and slope III which slightly differs from the S1 and S2 as it uses the percentage of the whole breath duration rather than fixed coordinates in the S1 and S2 [53].

#### *3.4.3 Angles*

Few angles that have been in use are the take-off angle, alpha and beta angle. The alpha angle seems to be increased in bronchospastic diseases as reported by two separate papers by Howe and Nik Hisamuddin [52,54]. Other than that, congestive heart failure has shown different wave morphology when compared to normal cases [55]. Although no research on the morphological feature has been explained, we hypothesize that the beta angle and inspiration time would be increased in congestive heart failure cases.

#### *3.4.4 Areas and volumetric studies*

The volumes can measure at any point of both the inspiration and expiration phase. Other than that, the area under the curve (AUC) via the integration of a concentration wave over time can be used to estimate the tidal volume per breath ($VTCO_2Br$) at the alveoli per breath as done in previous studies by Tusman [56]. Meanwhile, the area above the curves (ABC) has been used by Bohr and Enghoff for dead volume studies as well as for the estimation of the arterial partial pressure of carbon dioxide $PaCO_2$ and mean expired carbon dioxide ($PeCO_2$) [57].

### *3.4.5 Functional transformation of wave data*

A few other studies have optimized the functional transformation of data mathematically which uses the Hjorth parameter by squaring the mean variance of the S2 and S1 ratio [58,59]. Lukic *et al.,* [60] has used Root Mean Square (RMS) of $CO_2$ wave for the entire breath length for a better representation than mean value of the $CO_2$ obtained by standard equation [60]. A Linear Predictive Coding (LPC) was previously described by [58]. The same authors also proposed the usage of Power Spectral Density (PSD) *via* utilization of the frequency domain. The PSD was significant to differentiate bronchospastic conditions [58]. Of note, the VCap is more efficient and robust than the TCap in calculation of volume based capnometrics. Bothe the Bohr's ad Enghosff's spaces could be readily available with a VCap [61,62].

### *3.4.6 Combination of data with other non-capnometric parameter*

Other than that, the transformation of the wave data may utilize the usage of other non-capnographic parameters. Capnodynamic which utilizes bot capnographic signals which combines CO2 signals from capno and PEEP is an example [37,38]. Other clinical significance of these combination of parameters for both time and volume based capno has been covered extensively elsewhere [48].

### *3.4.7 Morphological changes*

Morphological change is the qualitative measure in evaluating capnography. Typically, the capnograph waveforms in TCap are quasiperiodic [63]. Among the common deviation from normal capnographic wave morphology includes absence of waves, changes in amplitude, duration and volume, cardiogenic oscillation, rebreathing patterns and the shark-fin pattern seen in bronchospasm. These are clearly depicted extensively elsewhere [64,65]. Figure 6 shows an example of the 'Crurare Cleft' pattern from our clinical experience in a patient who was not deeply sedated upon intubation. Meanwhile, as return of spontaneous circulation (ROSC) and pneumothorax's signal changes would be discussed in later part of this manuscript, apnea exerts morphological changes and $CO_2$ signal disappearance as reported by [66].

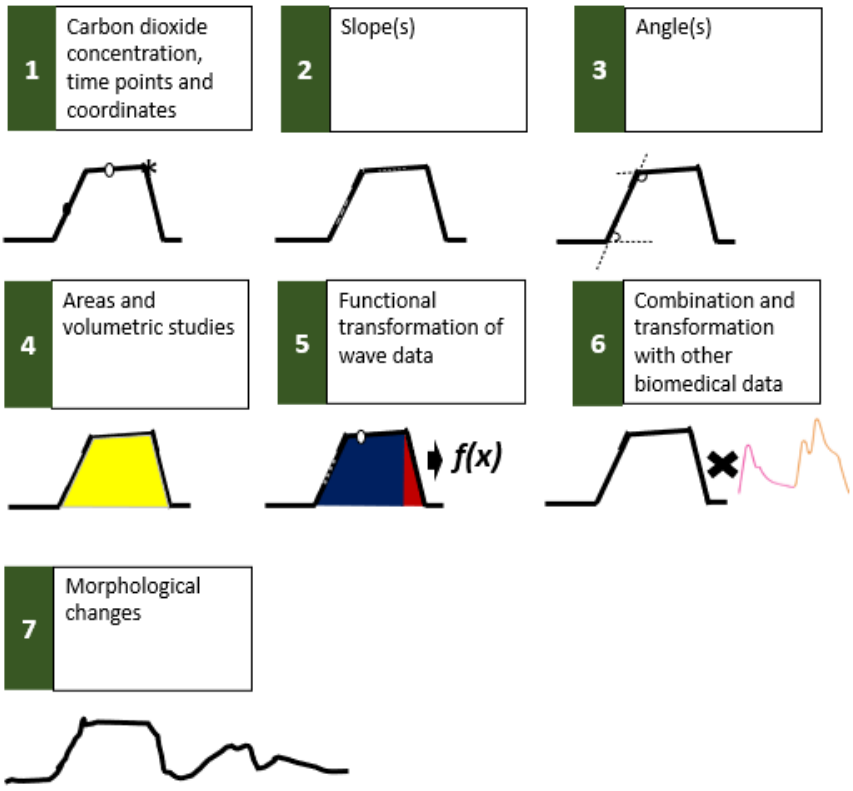


**Fig. 5.** Suggested feature classifications of capnometry

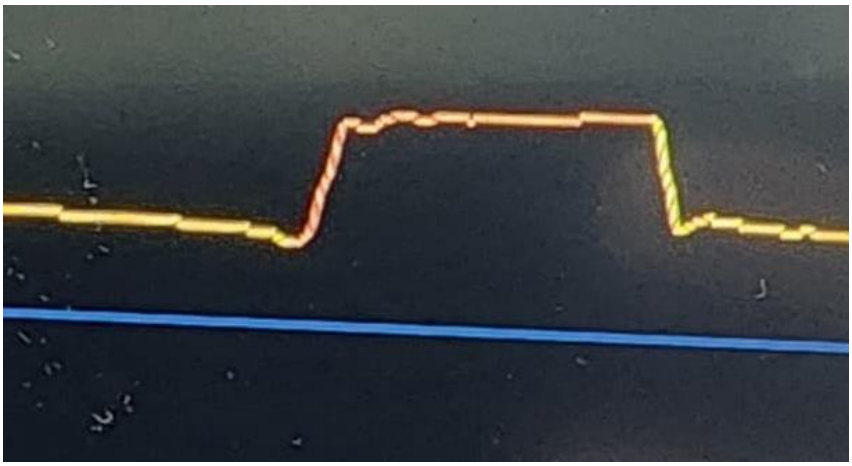

**Fig. 6.** Example of crurare cleft *(image courtesy of Dr Muhammad Aizuddin*)

Other clinical capnometric parameters for both TCap and VCap that has not been mentioned in this manuscript has covered elsewhere [48].

### *3.5 Capnograph Beyond $EtCO_2$*

Most modern capnometers are still sole based on $EtCO_2$. Due to the limitations of current capnometers, the addition of custom signal processing or digitization methods are needed to yield capnometric parameters [67-70]. Figure 7 is an example of a signal derived from a TCap which shows several other non $EtCO_2$ parameters. S1, S2, S1-S2 slope, tidal volume per breath, alpha angle, Bohr's $PACO_2$ (represented as black diamond), $EtCO_2$ (represented as black star), inspiration plus expiration time and ratio. This could be programmed and computed as discussed by [67].

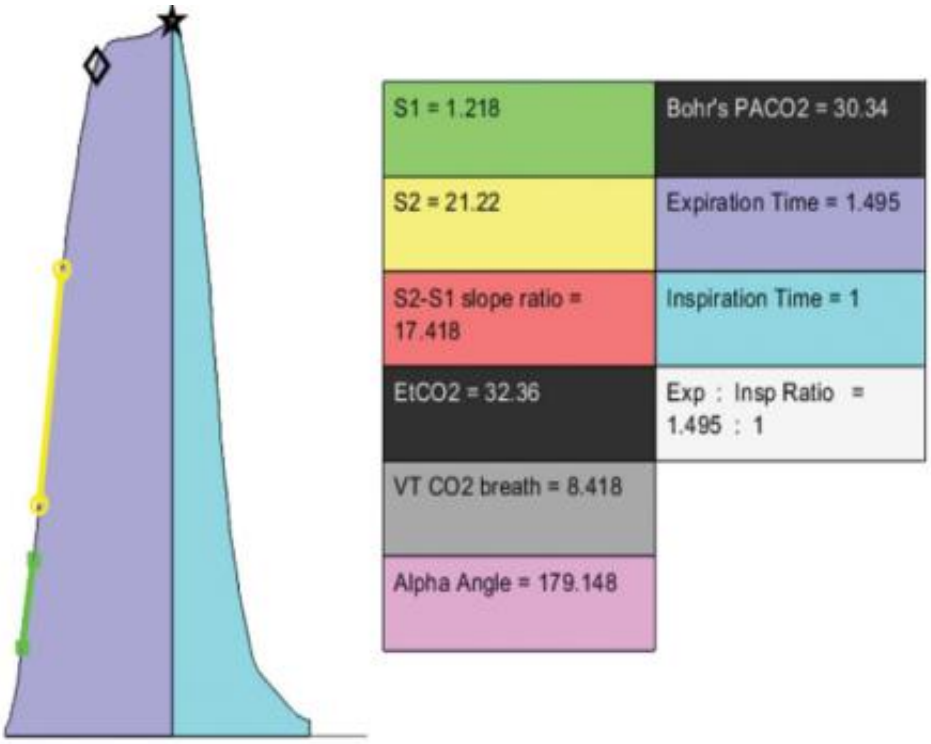


**Fig. 7.** Capnometric parameters in a digitized capnograph. Figure adapted and modified from [67]

### *3.6 Factors Affecting the Capnograph*

Among the factors that may affect the capnograph signal originates from the subject or technical abnormalities. Factors such as rebreathing, depletion of $CO_2$ absorber, faulty valve, kinking, obstruction of the ET tube and extubation of the ET tube may all play a role in affecting the capnograph [43]. Meanwhile, subject conditions that leads to increase or decrease in $CO_2$ production, tachypnea or bradypnea and blood acidity levels are also the contributors for signal abnormalities [43].

## 4. Capnography and Clinical Medidcine

### *4.1 Conventional Usage of the Capnometer / Capnograph*

Capnography has been used by anaesthetic and emergency clinicians to determine the placement of an endotracheal (ET) tube, to monitor the depth of sedation, to monitor respiratory acidosis and as a preventive measure to avoid carbon dioxide narcosis. Over the years, the usage has expanded towards the study of metabolism, circulation, lung perfusion and diffusion, quality of spontaneous respiration and the patency of airways, outside of its typical usage in the anaesthetic and emergency medicine field [71,72]. Additionally, ventilatory and device factors such as patency of the ET tube, state of connecting tubes, activity of $CO_2$ absorber and patient positioning on the operation table could also be monitored [72]. There are more parameters which are now recognized and being used at both bench side and bed beyond the sole usage of $EtCO_2$ in the capnometry alone. In 2017, Jaffe proposed that the capnographic analysis includes indices, slopes and angles, area, $CO_2$ waveform measures and statistics, frequency transformations, Hjorth parameters and areas [73].

Other interesting and selected capnometric parameters are shown in Table 1 and Figure 8. For easy reference, Table 1 has been sorted alphabetically according to the author's name.

**Table 1**
Selected clinical studies with distinct capnometric parameter(s)

| No. | Referance and citation | Capno parameters involved | Clinical Condition | Capnometer / Technology utilized |
|---|---|---|---|---|
| 1 | Abramo *et al.,* [74]. | $EtCO_2$ | Detection of respiratory failure and assess the requirement for intubation in actively seizing and post-ictal patients. | Sidestream capnometer (Pryon, Menomonee Falls, WI) |
| 2 | Alessandro *et al.,* [75]. | $EtCO_2$ | Chronic ketosis | Vmax Encore 29 System (Vmax) (Viasys Healthcare, Inc., Yorba Linda, CA). |
| 3 | Ansarin *et al.,* [76]. | EtCO2 | Mild and overt hypothyroid patients | (Microstream®; Oridion, Needham, MA) |
| 4 | Araujo-Preza *et al.,* [77]. | $EtCO_2$ | Feeding tube placement | The Easy-Cap (end-tidal $CO_2$ detector) |
| 5 | Baudendistel *et al.,* [78]. | $EtCO_2$ | Malignant hyperthermia | $CO_2$ Monitor (Datex) |
| 6 | Baudin *et al.,* [79]. | $EtCO_2$, KPIV , $EtCO_2$ + KPIV, $EtCO_2$ + KPIV + $FiO_2$* | Estimation of arterial $PaCO_2$ in mechanically ventilated children | Capnostat 5 mainstream pediatric; Philips Healthcare, Markham, ON, Canada – volumetric Capnometry |
| 7 | Bradley *et al.,* [80]. | $CO_2$ signal trace | Assist / anticipate difficult intubation with bougie | sidestream capnograph (FilterLine H Set Infant/ Neonate, Koninklijke Philips N.V, Amsterdam, Netherlands) |
| 8 | Brat *et al.,* [81]. | $EtCO_2$, dead space volume to tidal volume ratio (VD/VT), VE/ VCO2 slope and VE/VCO2 ratio | Hyperventilation Syndrome | PowerCube-Ergo system (Ganshorn Medizin Electronic GmbH, Germany) |
| 9 | Brown *et al.,* [82]. | Mean forced expiratory $CO_2$ values (1-6 seconds), slope of forced expiratory $CO_2$ curve | | Capnostat® 5 mainstream CO2 sensor, Philips Respironics, Amsterdam, Netherlands). |
| 10 | Chebl *et al.,* [83]. | $EtCO_2$ | Diabetic Ketoacidosis | Philips intellivue MX700 Philips healthcare, Andover, MA). |
| 11 | Crures *et al.,* [84]. | EtCO2 after a 3 second inspiratory hold (PLATCO2) | Approximation of arterial $CO_2$ pressure in acute respiratory distress syndrome in paediatrics | Sidestream technique via EngströmCarestation™ (GE Datex) and mainstream technique *via* Hamilton G5™ (Hamilton) MV |
| 12 | Diniz *et al.,* [85]. | RR, Vd, VD/VT, $EtCO_2$, $PeCO_2$, $VCO_2Br$, slopes, inspiration and expiration time | Capnometric parameter and CT scan correlation in COPD | CO2SMO Plus (Dixtal/Novametrix Incorporation, Wallingford, CT, USA) |
| 13 | Dony *et al.,* [86]. | $EtCO_2$ | Hypocapnia under general anaesthesia and post | sidestream $CO_2$ sampling (Perseus A500, Dräger, Lübeck, Germany |

| | | | | |
|---|---|---|---|---|
| | | | operative 30 days mortality rate | |
| 14 | Eriksson *et al.*, [87]. | SBT-$CO_2$, fDLate, PaCO2-EtCO2? VDPhys/VT | Diagnosis of pulmonary embolism | $CO_2$ analysis ($CO_2$ / Analyzer 130, Siemens Elema) |
| 15 | Fouzas *et al.,* | SII, SIII, VT, RR | Bronchopulmonary dysplasia | Unspecified $CO_2$ sensor |
| 16 | Howe *et al.,* [88]. | $EtCO_2$, Phase II slope, Phase III slope | Asthma | Novametrix® capnometry |
| 17 | Jarenbäck *et al.,* [89]. | Phase II, phase III, TLC, EFFi | Correlation of a new parameter (EFFi) with GOLD staging in COPD | Exhalyxer D: Mainstream capnograph |
| 18 | Kasuya *et al.,* [90]. | $PaCO_2^*$ – $EtCO_2$ difference | Obese and non-obese subjects with and without sleep apnea | Cap-ONE mainstream capnometer system (Nihon Kohden) and Microcap sidestream capnometer |
| 19 | Kean *et al.,* [91]. | A1, A2, AR slope 1, slope 2, Slope ratio, alpha angle Hjorth Parameters | Asthma diagnosis | Nihon Kohden Bedside Monitor BSM-2301K. |
| 20 | Kerklaan *et al.,* [92]. | $VCO_2$ | Energy expenditure in critically ill ventilated children | Servo-I® ventilator with the Capnostat-III sensor, |
| 21 | Lavillegrand *et al.,* [93]. | Color change | Placement of feeding tube | Colorimetric capnometer |
| 22 | Lin *et al.,* [94]. | $EtCO_2$, VD/VT | Surfactant therapy efficacy in preterm infants with low birth weight | Philips M2501A Mainstream Capnography |
| 23 | Luiz *et al.,* [95]. | Tidal volume (TV), dead space (DS), DS/TV ratio, $VCO_2$, inspiratory and expiratory volume, Slopes | Respiratory function in Duchenne muscular dystrophy patients | $CO_2$SMO® Plus respiratory profile monitor (DX-8100 model, Novametrix Inc., CT, USA; Analysis Plus!® software). |
| 24 | Malarvilli *et al.,* [70]. | A1-A6, S1-S6(All parameters are subsegments of the CO2 TCap signal) | ARDS diagnosis in COVID-19 | Unnamed custom capnometer |
| 25 | Mieloszyk *et al.,* [55]. | exhalation duration; $ETCO_2$; time spent at $ETCO_2$ ; and end-exhalation slope | Capnographic feature classification in COPD and congestive heart failure (CHF) | Capnostream 20( Oridion Medical, Needham, MA) |
| 26 | Moreira *et al.,* [96]. | P(a-et) $CO_2$ gradient, $EtCO_2$, SIII III, fDlate | Pulmonary embolism monitoring / prognosis post thrombolysis | $CO_2$ SMO PLUS 8100 Dixtal/Novametrix™ |
| 27 | Neumann *et al.,* [97]. | KPIV | BPD | Ultrasonic flowmeter (Exhalyzer D, ECO MEDICS AG) which incorporates a mainstream carbon dioxide ($CO_2$) sensor (Philips Respironic) |
| 28 | Nitzan *et al.,* [98]. | $CO_2$ signal detection | Minimally Invasive Surfactant Treatment (MIST) catheter placement in infants with respiratory distress | Commercial CO2 detector (Pedicap, Nellcor Colorado, USA) |

| | | | | |
|---|---|---|---|---|
| 29 | Norweg *et al.,* [99]. | $EtCO_2$ | COPD therapeutic option | Information not provided |
| 30 | Peyton *et al.*, [100]. | $VCO_2$ and $EtCO_2$ | Cardiac output approximation in patient undergoing cardiac or liver surgeries | $CO_2$SMO+ inline infrared capnograph transducer and differential pressure pneumotachograph (Novametrix/Respironics USA) |
| 31 | Poon *et al.,* [101]. | $EtCO_2$ for 3 minutes | ROSC in cardiac arrest patents | NellcorTM Microstream model N85 by Medtronic was |
| 32 | Ribeiro *et al.,* [102]. | RR, inspiratory time (IT), expiratory time (ET), and the phase III slope normalized by expiratory volume (phase III slope/Ve). | Evaluation of airway obstruction in cystic fibrosis | $CO_2$SMO Plus Analyzer® (Respironics, Murrysville, PA, USA) |
| 33 | Shikama *et al.,* [103]. | EtCO2, Slope III | Bronchospasm resolution | Information not provided |
| 34 | Singh *et al.*, [104]. | $EtCO_2$, RR and Hjorth activity | Asthma diagnosis | Unnamed custom capnometer |
| 35 | Szakál *et al.,* [105]. | EtCO2 and gastric artery PaCO2* | Estimation of splanchnic perfusion and a prognostic index also in critically ill neonates | Sidestream Microcap Handheld Capnograph. |
| 36 | Takaki *et al.,* [106]. | EtCO2 | Deep breathing exercise post abdominal surgery | Microstream, AG-400R, (Nihon-Kohden, Tokyo, Japan) |
| 37 | Talker *et al.,* [107]. | α, β, γ, and δ angles; gradients and residuals derived from fitting curves to phases, absolute and short-term variability of pCO2; curvature; ratio of the expiratory to inspiratory phase ; area under the curve (AUC. | Real time diagnosis of COPD using machine learning | TidalSense's N-Tidal™ device |
| 38 | Tsai *et al.,* TBFL | Capno waveform | Pneumothorax | No information provided |
| 39 | Veronez *et al.,* [108]. | RR, $VCO_2$, Phase 3 Slopes normalized for tidal volume (P3Slp/VE) | Lung disease evaluation in Cystic Fibrosis and Noncystic Fibrosis Bronchiectasis | $C0_2$SMOS Plus Analyser (Respironics, Murrisville, PA) |
| 40 | Vijayam *et al.,* [109]. | EtCO2 | Acute ketosis / Nutritional ketosis | Microstream Capnostream-20 capnometer (Covidien, Mansfield, MA), |

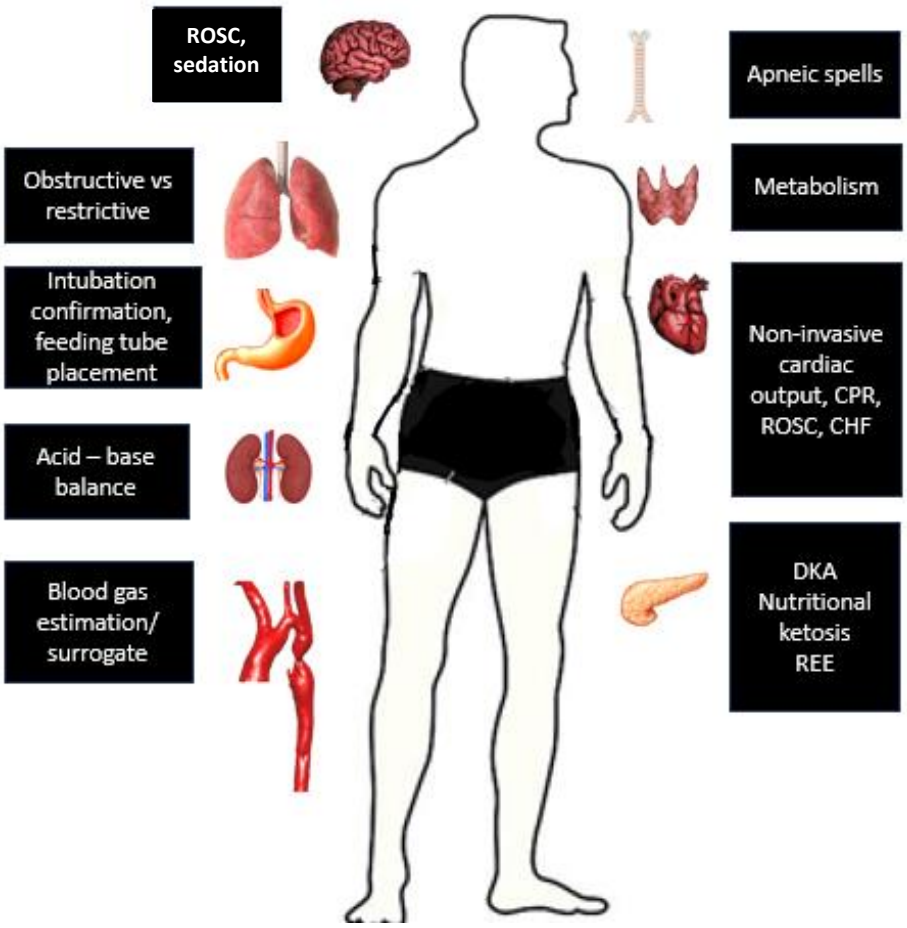


**Fig. 8.** The current possible clinical usages of capno

## 5. Current Limitations and Challenges in Capno Usage

### *5.1 Limitation of Capnography*

There has been a vast capnometric usage of $EtCO_2$ despite the presence of capnograph in modern medicine. To add to this dilemma, the current medical exposure and training of capnometry is still low compared to colorimetric capnometer [110]. Other than that, most capnometers that are time based do not have flow as one other adjunct or complementary parameter. Likewise, the physiologic dead space parameters cannot be calculated when utilizing a time based capnometer. The mainstream and side stream devices serve different issues when it comes to dead space and inaccuracies when low tidal volumes are encountered [111].

From a clinical perspective, signals and waveform patterns of diseases such as pneumothorax and pleural effusion are not represented and have been depicted in any scientific article at the point of writing this manuscript.

### *5.2 Challenges in Capnography*

Older devices show graphical representation with $EtCO_2$ value being the sole capnometric parameters. Additional measures must be taken to analyze other capnometric parameters. Signal processing of digital data or digitization of the capnographic images to analog prints may be applied [67–69].

## 6. Future Prospects of Capnography

### *6.1 Future Prospects*

Among the prospects of capnograpy is the current expansion of usage. More diseases could be tested out as the capnography can be utilized for surveillance, monitoring diagnosis and prognosis. A particular are of interest would be metabolism as REE could be approximated by capnometric parameters [92]. Other than that, more integration and combination of non-capnometric parameters with the capnograph would yield better diagnostic sensitivity and specificity.

As for the device, there is a need for major improvement for the integration of capnographic parameters in newer devices. For older devices, signal processing or digitization of the capnograph could be a strategy to obtain the capnometric parameters as we have discussed earlier. Future devices should also focus on reducing device related errors such as rebreathing artefacts, motion artefacts and $CO_2$ signal leakage. Currently there are works in laser spectroscopy for high resolution capnography [112]. In addition, there are numerous techniques to obtain other capnometric parameters by manipulation both the VCap and TCap [113]. The utilization of artificial intelligence also increases the accuracy of capnometric parameters and may perhaps lead t discovery of newer ones [107].

There is a huge role of capnography is for space travel, monitoring in confined spaces underwater exploration and telemedicine to name a few [114–117]. These endless possibilities are depicted in Figure 9.

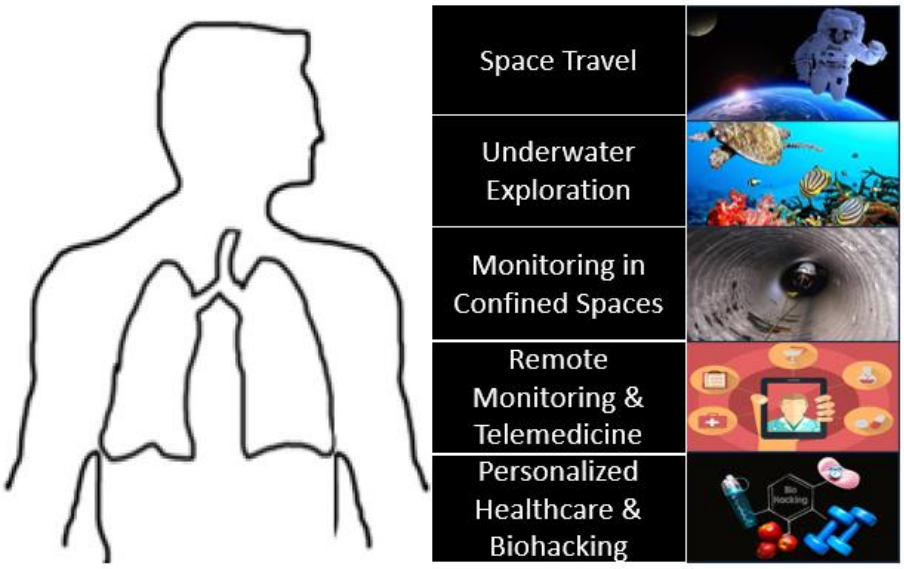


**Fig. 9.** Future possibilities and prospects of capnograph

## 7. Conclusions

The use of capnographs outside of the operating room, intensive care unit and emergency department is becoming more prominent. Capnographic data and interpretation are needed for both lung and non-lung diseases. As the age of telemedicine and remote human voyage and scavenging has already taken place, we believe that we have provided ‘breathtaking’ evidence that the capnography is a deserving candidate for the sixth vital sign in humanity.

## References

[1] A. Korsós, F. Peták, R. Südy, Á. Schranc, G.H. Fodor, B. Babik, Use of capnography to verify emergency ventilator sharing in the COVID-19 era, Respir Physiol Neurobiol 285 (2021) 103611. https://doi.org/10.1016/j.resp.2020.103611

[2] Y. Wang, H. Xu, Z. Dong, Z. Wang, Z. Yang, X. Yu, L. Chang, Micro/nano biomedical devices for point-of-care diagnosis of infectious respiratory diseases, Med Nov Technol Devices 14 (2022) 100116. https://doi.org/10.1016/j.medntd.2022.100116

[3] A. Gürün Kaya, M. Öz, İ. Akdemir Kalkan, E. Gülten, G. Çınar, A. Azap, A. Kaya, Is pulse oximeter a reliable tool for non-critically ill patients with COVID-19?, Int J Clin Pract 75 (2021). https://doi.org/10.1111/ijcp.14983

[4] L.S. Nguyen, M. Helias, L. Raia, E. Nicolas, P. Jaubert, S. Benghanem, Z. Ait Hamou, P. Dupland, J. Charpentier, F. Pène, A. Cariou, J.-P. Mira, J.-D. Chiche, M. Jozwiak, Impact of COVID-19 on the association between pulse oximetry and arterial oxygenation in patients with acute respiratory distress syndrome, Sci Rep 12 (2022) 1462. https://doi.org/10.1038/s41598-021-02634-z

[5] A. Kichloo, M. Albosta, K. Dettloff, F. Wani, Z. El-Amir, J. Singh, M. Aljadah, R.C. Chakinala, A.K. Kanugula, S. Solanki, S. Chugh, Telemedicine, the current COVID-19 pandemic and the future: a narrative review and perspectives moving forward in the USA, Fam Med Community Health 8 (2020) e000530. https://doi.org/10.1136/fmch-2020-000530

[6] E. Mehraeen, S. SeyedAlinaghi, M. Heydari, A. Karimi, A. Mahdavi, M. Mashoufi, A. Sarmad, P. Mirghaderi, A. Shamsabadi, K. Qaderi, P. Mirzapour, A. Fakhfouri, H.A. Cheshmekabodi, K. Azad, S. Bagheri Zargande, S. Oliaei, P. Yousefi Konjdar, F. Vahedi, T. Noori, Telemedicine technologies and applications in the era of COVID-19 pandemic: A systematic review, Health Informatics J 29 (2023) 146045822311674. https://doi.org/10.1177/14604582231167431

[7] D.C. Parish, H. Goyal, F.C. Dane, Mechanism of death: there's more to it than sudden cardiac arrest, J Thorac Dis 10 (2018) 3081–3087. https://doi.org/10.21037/jtd.2018.04.113

[8] S. Intagliata, A. Rizzo, W. Gossman, Physiology, Lung Dead Space, 2024. http://www.ncbi.nlm.nih.gov/pubmed/30908313

[9] H.Y. Reynolds, Respiratory Structure and Function, in: Goldman's Cecil Medicine, Elsevier, 2012: pp. e14–e20. https://doi.org/10.1016/B978-1-4377-1604-7.00553-4

[10] S. Coppola, S. Froio, A. Marino, M. Brioni, B.M. Cesana, M. Cressoni, L. Gattinoni, D. Chiumello, Respiratory Mechanics, Lung Recruitability, and Gas Exchange in Pulmonary and Extrapulmonary Acute Respiratory Distress Syndrome, Crit Care Med 47 (2019) 792–799. https://doi.org/10.1097/CCM.0000000000003715

[11] B. Huang, D. De Vore, C. Chirinos, J. Wolf, D. Low, R. Willard-Grace, S. Tsao, C. Garvey, D. Donesky, G. Su, D.H. Thom, Strategies for recruitment and retention of underrepresented populations with chronic obstructive pulmonary disease for a clinical trial, BMC Med Res Methodol 19 (2019) 39. https://doi.org/10.1186/s12874-019-0679-y

[12] M. Kiefmann, S. Tank, M.-O. Tritt, P. Keller, K. Heckel, L. Schulte-Uentrop, C. Olotu, S. Schrepfer, A.E. Goetz, R. Kiefmann, Dead space ventilation promotes alveolar hypocapnia reducing surfactant secretion by altering mitochondrial function, Thorax 74 (2019) 219–228. https://doi.org/10.1136/thoraxjnl-2018-211864

[13] H.M. Coleridge, J.C.G. Coleridge, Reflexes Evoked from Tracheobronchial Tree and Lungs, in: Compr Physiol, Wiley, 1986: pp. 395–429. https://doi.org/10.1002/cphy.cp030212

[14] T.J. Biscoe, M.J. Purves, S.R. Sampson, The frequency of nerve impulses in single carotid body chemoreceptor afferent fibres recorded *in vivo* with intact circulation, J Physiol 208 (1970) 121–131. https://doi.org/10.1113/jphysiol.1970.sp009109

[15] E.R. Weibel, Morphometry of the Human Lung, Springer Berlin Heidelberg, Berlin, Heidelberg, 1963. https://doi.org/10.1007/978-3-642-87553-3

[16] B. Haut, A. Nonclercq, A. Buess, J. Rabineau, C. Rigaut, B. Sobac, Comprehensive Analysis of Heat and Water Exchanges in the Human Lungs, Front Physiol 12 (2021). https://doi.org/10.3389/fphys.2021.649497

[17] Déry R., J. Pelletier, A. Jacques, M. Clavet, J.J. Houde, Humidity in anaesthesiology III. Heat and moisture patterns in the respiratory tract during anaesthesia with the semi-closed system, Can Anaesth Soc J 14 (1967) 287–298. https://doi.org/10.1007/BF03003698

[18] E. Ortiz-Prado, J.F. Dunn, J. Vasconez, D. Castillo, G. Viscor, Partial pressure of oxygen in the human body: a general review., Am J Blood Res 9 (2019) 1–14.

[19] E. Zeserson, B. Goodgame, J.D. Hess, K. Schultz, C. Hoon, K. Lamb, V. Maheshwari, S. Johnson, M. Papas, J. Reed, M. Breyer, Correlation of Venous Blood Gas and Pulse Oximetry With Arterial Blood Gas in the Undifferentiated Critically Ill Patient, J Intensive Care Med 33 (2018) 176–181. https://doi.org/10.1177/0885066616652597

[20] G.J. Arthurs, M. Sudhakar, Carbon dioxide transport, Continuing Education in Anaesthesia Critical Care & Pain 5 (2005) 207–210. https://doi.org/10.1093/bjaceaccp/mki050
[21] I. Tyuma, The Bohr effect and the Haldane effect in human hemoglobin., Jpn J Physiol 34 (1984) 205–216. https://doi.org/10.2170/jjphysiol.34.205
[22] H. Malte, G. Lykkeboe, The Bohr/Haldane effect: a model-based uncovering of the full extent of its impact on $O_2$ delivery to and $CO_2$ removal from tissues, J Appl Physiol 125 (2018) 916–922. https://doi.org/10.1152/japplphysiol.00140.2018
[23] J. Hodgkinson, R. Smith, W.O. Ho, J.R. Saffell, R.P. Tatam, Non-dispersive infra-red (NDIR) measurement of carbon dioxide at 4.2μm in a compact and optically efficient sensor, Sens Actuators B Chem 186 (2013) 580–588. https://doi.org/10.1016/j.snb.2013.06.006
[24] M.B. Jaffe, Infrared Measurement of Carbon Dioxide in the Human Breath: "Breathe-Through" Devices from Tyndall to the Present Day, Anesth Analg 107 (2008) 890–904. https://doi.org/10.1213/ane.0b013e31817ee3b3
[25] T.A. Vincent, J.W. Gardner, A low cost MEMS based NDIR system for the monitoring of carbon dioxide in breath analysis at ppm levels, Sens Actuators B Chem 236 (2016) 954–964. https://doi.org/10.1016/j.snb.2016.04.016
[26] Hwan-Joo Lee, Do-Eok Kim, Dae-Hyuk Kwon, Seung-Ha Lee, Shin-Won Kang, Development of non-invasive optical transcutaneous pCO2 gas sensor and analytic equipment, in: Proceedings of IEEE Sensors, 2004., IEEE, 2004: pp. 730–733. https://doi.org/10.1109/ICSENS.2004.1426271
[27] J. Yang, B. Chen, K. Burk, H. Wang, J. Zhou, A mainstream monitoring system for respiratory CO2 concentration and gasflow, J Clin Monit Comput 30 (2016) 467–473. https://doi.org/10.1007/s10877-015-9739-y
[28] M.D. McCue, K.C. Welch, 13C-Breath testing in animals: theory, applications, and future directions, Journal of Comparative Physiology B 186 (2016) 265–285. https://doi.org/10.1007/s00360-015-0950-4
[29] J. Yang, B. Chen, J. Zhou, Z. Lv, A Low-Power and Portable Biomedical Device for Respiratory Monitoring with a Stable Power Source, Sensors 15 (2015) 19618–19632. https://doi.org/10.3390/s150819618
[30] O.H.G. Diniz, Volumetric Capnography: History, Function and Clinical Uses, Open Access Library Journal 09 (2022) 1–7. https://doi.org/10.4236/oalib.1109175
[31] G. van Weerden, Some clinical applications of capnography., Am J Med Electron 1 (1962) 199–207.
[32] A. Koziorowski, L. Radwan, [Use of the capnograph in the determination of partial pressure of carbon dioxide in mixed venous and in arterial blood with the aid of repeated respiration]., Pol Arch Med Wewn 32 (1962) 1543–52.
[33] B.K. Walsh, D.N. Crotwell, R.D. Restrepo, Capnography/Capnometry During Mechanical Ventilation: 2011, Respir Care 56 (2011) 503–509. https://doi.org/10.4187/respcare.01175
[34] Endler Gerhard C., Capnography or Capnometry?, Anesthesiology 72 (1990) 214–214. https://doi.org/10.1097/00000542-199001000-00046
[35] R. Canelli, R. Ortega, Colorimetric capnography: a misnomer worth correcting, J Clin Monit Comput 35 (2021) 951–951. https://doi.org/10.1007/s10877-021-00665-5
[36] C. Hällsjö Sander, M. Hallbäck, M. Wallin, P. Emtell, A. Oldner, H. Björne, Novel continuous capnodynamic method for cardiac output assessment during mechanical ventilation, Br J Anaesth 112 (2014) 824–831. https://doi.org/10.1093/bja/aet486
[37] T.S. Sigmundsson, T. Öhman, M. Hallbäck, E. Redondo, F.S. Sipmann, M. Wallin, A. Oldner, C. Hällsjö-Sander, H. Björne, Performance of a capnodynamic method estimating cardiac output during respiratory failure - before and after lung recruitment, J Clin Monit Comput 34 (2020) 1199–1207. https://doi.org/10.1007/s10877-019-00421-w
[38] J. Karlsson, P. Lönnqvist, Capnodynamics—Measuring cardiac output via ventilation, Pediatric Anesthesia 32 (2022) 255–261. https://doi.org/10.1111/pan.14329
[39] F.E. Block, J.S. McDonald, Sidestream versus mainstream carbon dioxide analyzers, J Clin Monit 8 (1992) 139–141. https://doi.org/10.1007/BF01617434
[40] E. Lopez, S. Grabar, A. Barbier, B. Krauss, P.-H. Jarreau, G. Moriette, Detection of carbon dioxide thresholds using low-flow sidestream capnography in ventilated preterm infants, Intensive Care Med 35 (2009) 1942–1949. https://doi.org/10.1007/s00134-009-1647-5
[41] M. Pekdemir, O. Cinar, S. Yılmaz, E. Yaka, M. Yuksel, Disparity Between Mainstream and Sidestream End-Tidal Carbon Dioxide Values and Arterial Carbon Dioxide Levels, Respir Care 58 (2013) 1152–1156. https://doi.org/10.4187/respcare.02227
[42] Y. Colman, B. Krauss, Microstream capnograpy technology: a new approach to an old problem., J Clin Monit Comput 15 (1999) 403–9. https://doi.org/10.1023/a:1009981115299
[43] S. Humphreys, A. Schibler, B.S. von Ungern-Sternberg, Carbon dioxide monitoring in children—A narrative review of physiology, value, and pitfalls in clinical practice, Pediatric Anesthesia 31 (2021) 839–845. https://doi.org/10.1111/pan.14208

[44] E.K. Murray, C.X. You, G.C. Verghese, B.S. Krauss, T. Heldt, Low-Order Mechanistic Models for Volumetric and Temporal Capnography: Development, Validation, and Application, IEEE Trans Biomed Eng 70 (2023) 2710–2721. https://doi.org/10.1109/TBME.2023.3262764
[45] K. Bhavani-Shankar, J.H. Philip, Defining Segments and Phases of a Time Capnogram, Anesth Analg 91 (2000) 973–977. https://doi.org/10.1097/00000539-200010000-00038
[46] K. Bhavani-Shankar, A.Y. Kumar, H.S.L. Moseley, R. Ahyee-Hallsworth, Terminology and the current limitations of time capnography: A brief review, J Clin Monit 11 (1995) 175–182. https://doi.org/10.1007/BF01617719
[47] C.A. Manifold, N. Davids, L.C. Villers, D.A. Wampler, Capnography for the Nonintubated Patient in the Emergency Setting, J Emerg Med 45 (2013) 626–632. https://doi.org/10.1016/j.jemermed.2013.05.012
[48] M.B. Jaffe, Using the features of the time and volumetric capnogram for classification and prediction, J Clin Monit Comput 31 (2017) 19–41. https://doi.org/10.1007/s10877-016-9830-z
[49] M.B. Jaffe, Respiratory Gas Analysis—Technical Aspects, Anesth Analg 126 (2018) 839–845. https://doi.org/10.1213/ANE.0000000000002384
[50] P. Bourgoin, F. Baudin, D. Brossier, G. Emeriaud, M. Wysocki, P. Jouvet, Assessment of Bohr and Enghoff Dead Space Equations in Mechanically Ventilated Children, Respir Care 62 (2017) 468–474. https://doi.org/10.4187/respcare.05108
[51] B. You, R. Peslin, C. Duvivier, V. Vu, J. Grilliat, Expiratory capnography in asthma: evaluation of various shape indices, European Respiratory Journal 7 (1994) 318–323. https://doi.org/10.1183/09031936.94.07020318
[52] T.A. Howe, K. Jaalam, R. Ahmad, C.K. Sheng, N.H. Nik Ab Rahman, The Use of End-Tidal Capnography to Monitor Non-Intubated Patients Presenting with Acute Exacerbation of Asthma in the Emergency Department, J Emerg Med 41 (2011) 581–589. https://doi.org/10.1016/j.jemermed.2008.10.017
[53] S.H. Böhm, S. Maisch, A. von Sandersleben, O. Thamm, I. Passoni, J.M. Arca, G. Tusman, The Effects of Lung Recruitment on the Phase III Slope of Volumetric Capnography in Morbidly Obese Patients, Anesth Analg 109 (2009) 151–159. https://doi.org/10.1213/ane.0b013e31819bcbb5
[54] N.A.R. Nik Hisamuddin, A. Rashidi, K.S. Chew, J. Kamaruddin, Z. Idzwan, A.H. Teo, Correlations between capnographic waveforms and peak flow meter measurement in emergency department management of asthma, Int J Emerg Med 2 (2009) 83–89. https://doi.org/10.1007/s12245-009-0088-9
[55] R.J. Mieloszyk, G.C. Verghese, K. Deitch, B. Cooney, A. Khalid, M.A. Mirre-Gonzalez, T. Heldt, B.S. Krauss, Automated Quantitative Analysis of Capnogram Shape for COPD–Normal and COPD–CHF Classification, IEEE Trans Biomed Eng 61 (2014) 2882–2890. https://doi.org/10.1109/TBME.2014.2332954
[56] G. Tusman, E. Gogniat, S.H. Bohm, A. Scandurra, F. Suarez-Sipmann, A. Torroba, F. Casella, S. Giannasi, E.S. Roman, Reference values for volumetric capnography-derived non-invasive parameters in healthy individuals, J Clin Monit Comput 27 (2013) 281–288. https://doi.org/10.1007/s10877-013-9433-x
[57] M.S. Siobal, H. Ong, J. Valdes, J. Tang, Calculation of Physiologic Dead Space: Comparison of Ventilator Volumetric Capnography to Measurements by Metabolic Analyzer and Volumetric CO2 Monitor, Respir Care 58 (2013) 1143–1151. https://doi.org/10.4187/respcare.02116.
[58] M. Kazemi, M. M. B., T. A. H., A Review on methods using capnogram signals for detecting asthmatic patients, J Teknol 62 (2013). https://doi.org/10.11113/jt.v62.1179
[59] O.P. Singh, T.A. Howe, M. Malarvili, Real-time human respiration carbon dioxide measurement device for cardiorespiratory assessment, J Breath Res 12 (2018) 026003. https://doi.org/10.1088/1752-7163/aa8dbd
[60] K.Z. Lukic, B. Urch, M. Fila, M.E. Faughnan, F. Silverman, A novel application of capnography during controlled human exposure to air pollution, Biomed Eng Online 5 (2006) 54. https://doi.org/10.1186/1475-925X-5-54
[61] F. Suárez-Sipmann, J. Villar, C. Ferrando, J.A. Sánchez-Giralt, G. Tusman, Monitoring Expired CO2 Kinetics to Individualize Lung-Protective Ventilation in Patients With the Acute Respiratory Distress Syndrome, Front Physiol 12 (2021). https://doi.org/10.3389/fphys.2021.785014
[62] S. Verscheure, P.B. Massion, F. Verschuren, P. Damas, S. Magder, Volumetric capnography: lessons from the past and current clinical applications, Crit Care 20 (2016) 184. https://doi.org/10.1186/s13054-016-1377-3
[63] F. Scholkmann, J. Boss, M. Wolf, An Efficient Algorithm for Automatic Peak Detection in Noisy Periodic and Quasi-Periodic Signals, Algorithms 5 (2012) 588–603. https://doi.org/10.3390/a5040588
[64] J.E. Thompson, M.B. Jaffe, Capnographic waveforms in the mechanically ventilated patient., Respir Care 50 (2005) 100–8; discussion 108-9.
[65] M. Mohamed El-Sayed, N. Maher Nour, M. Abd El Malik Hassan, H. Abd El Sabor Hashem, Clinical Applications of Capnography Among Mechanically Ventilated Children, Al-Azhar Medical Journal 45 (2016) 753–766. https://doi.org/10.12816/0034760
[66] K.R. Scully, J. Rickerby, J. Dunn, Implementation Science: Incorporating Obstructive Sleep Apnea Screening and Capnography Into Everyday Practice, Journal of PeriAnesthesia Nursing 35 (2020) 7–16. https://doi.org/10.1016/j.jopan.2019.06.004

[67] B. Vijayam, E. Supriyanto, M.B. Malarvili, Digitization and Analysis of Capnography Using Image Processing Technique, Front Digit Health 3 (2021). https://doi.org/10.3389/fdgth.2021.723204
[68] T. Koyama, M. Kobayashi, T. Ichikawa, Y. Wakabayashi, H. Abe, Application of Capnography Waveform Analyses for Evaluation of Recovery Process in a Patient with Heart Failure: A Case Report, Arch Clin Med Case Rep 04 (2020). https://doi.org/10.26502/acmcr.96550265
[69] R.J. Mieloszyk, G.C. Verghese, K. Deitch, B. Cooney, A. Khalid, M.A. Mirre-González, T. Heldt, B.S. Krauss, Automated Quantitative Analysis of Capnogram Shape for COPD–Normal and COPD–CHF Classification, IEEE Trans Biomed Eng 61 (2014) 2882–2890. https://doi.org/10.1109/TBME.2014.2332954
[70] M.B. Malarvili, M. Alexie, N. Dahari, A. Kamarudin, On Analyzing Capnogram as a Novel Method for Screening COVID-19: A Review on Assessment Methods for COVID-19, Life 11 (2021) 1101. https://doi.org/10.3390/life11101101
[71] A.L. Balogh, F. Petak, G.H. Fodor, J. Tolnai, Z. Csorba, B. Babik, Capnogram slope and ventilation dead space parameters: comparison of mainstream and sidestream techniques, Br J Anaesth 117 (2016) 109–117. https://doi.org/10.1093/bja/aew127
[72] B. Smalhout, The first years of clinical capnography, in: Capnography, Cambridge University Press, 2011: pp. 430–456. https://doi.org/10.1017/CBO9780511933837.042
[73] M.B. Jaffe, Using the features of the time and volumetric capnogram for classification and prediction, J Clin Monit Comput 31 (2017) 19–41. https://doi.org/10.1007/s10877-016-9830-z
[74] T.J. Abramo, R.A. Wiebe, S. Scott, C.S. Goto, D.D. McIntire, Noninvasive capnometry monitoring for respiratory status during pediatric seizures, Crit Care Med 25 (1997) 1242–1246. https://doi.org/10.1097/00003246-199707000-00029
[75] R. Alessandro, B. Gerardo, L. Alessandra, C. Lorenzo, P. Andrea, G. Keith, Z. Yang, P. Antonio, Effects of Twenty Days of the Ketogenic Diet on Metabolic and Respiratory Parameters in Healthy Subjects, Lung 193 (2015) 939–945. https://doi.org/10.1007/s00408-015-9806-7
[76] K. Ansarin, End-tidal CO2 levels lower in subclinical and overt hypothyroidism than healthy controls; no relationship to thyroid function tests, Int J Gen Med (2011) 29. https://doi.org/10.2147/IJGM.S16252
[77] C.E. Araujo-Preza, M.E. Melhado, F.J. Gutierrez, T. Maniatis, M.A. Castellano, Use of capnometry to verify feeding tube placement., Crit Care Med 30 (2002) 2255–9. https://doi.org/10.1097/00003246-200210000-00013
[78] L. Baudendistel, N. Goudsouzian, C. Cote, M. Strafford, End-tidal CO2 monitoring, Anaesthesia 39 (1984) 1000–1003. https://doi.org/10.1111/j.1365-2044.1984.tb08889.x
[79] F. Baudin, P. Bourgoin, D. Brossier, S. Essouri, G. Emeriaud, M. Wysocki, P. Jouvet, Noninvasive Estimation of Arterial Co 2 From End-Tidal Co 2 in Mechanically Ventilated Children: The GRAeDIENT Pilot Study*, Pediatric Critical Care Medicine 17 (2016) 1117–1123. https://doi.org/10.1097/PCC.0000000000000935
[80] T. Bradley, R. Walker, Capnography for bougie placement, Anaesthesia 70 (2015) 631–632. https://doi.org/10.1111/anae.13089
[81] K. Brat, N. Stastna, Z. Merta, L.J. Olson, B.D. Johnson, I. Cundrle, Cardiopulmonary exercise testing for identification of patients with hyperventilation syndrome, PLoS One 14 (2019) e0215997. https://doi.org/10.1371/journal.pone.0215997
[82] R.H. Brown, A. Brooker, R.A. Wise, C. Reynolds, C. Loccioni, A. Russo, T.H. Risby, Forced expiratory capnography and chronic obstructive pulmonary disease (COPD), J Breath Res 7 (2013) 017108. https://doi.org/10.1088/1752-7155/7/1/017108
[83] R. Bou Chebl, B. Madden, J. Belsky, E. Harmouche, L. Yessayan, Diagnostic value of end tidal capnography in patients with hyperglycemia in the emergency department, BMC Emerg Med 16 (2016) 7. https://doi.org/10.1186/s12873-016-0072-7
[84] P. Cruces, D. Moreno, S. Reveco, M. Améstica, P. Araneda, Y. Ramirez, P. Vásquez-Hoyos, F. Díaz, Capnometry after an inspiratory breath hold, PLAT CO2, as a surrogate for PaCO2 in mild to moderate pediatric acute respiratory distress syndrome: A feasibility study, Pediatr Pulmonol 58 (2023) 2899–2905. https://doi.org/10.1002/ppul.26610
[85] O.H.G. Diniz, M.C. Pereira, S.M.D. da Silva, M. Koenigkam-Santos, I.A. Paschoal, M.M. Moreira, Correlations between Volumetric Capnography and Automated Quantitative Computed Tomography Analysis in Patients with Severe COPD, Journal of Respiration 2 (2022) 13–24. https://doi.org/10.3390/jor2010002
[86] P. Dony, M. Dramaix, J.G. Boogaerts, Hypocapnia measured by end-tidal carbon dioxide tension during anesthesia is associated with increased 30-day mortality rate, J Clin Anesth 36 (2017) 123–126. https://doi.org/10.1016/j.jclinane.2016.10.028
[87] L. Eriksson, P. Wollmer, C.-G. Olsson, U. Albrechtsson, H. Larusdottir, R. Nilsson, A. Sjögren, B. Jonson, Diagnosis of Pulmonary Embolism Based upon Alveolar Dead Space Analysis, Chest 96 (1989) 357–362. https://doi.org/10.1378/chest.96.2.357

[88] T.A. Howe, K. Jaalam, R. Ahmad, C.K. Sheng, N.H. Nik Ab Rahman, The Use of End-Tidal Capnography to Monitor Non-Intubated Patients Presenting with Acute Exacerbation of Asthma in the Emergency Department, J Emerg Med 41 (2011) 581–589. https://doi.org/10.1016/j.jemermed.2008.10.017

[89] L. Jarenbäck, E. Tufvesson, J. Ankerst, L. Bjermer, B. Jonson, The Efficiency Index (EFFi), based on volumetric capnography, may allow for simple diagnosis and grading of COPD, Int J Chron Obstruct Pulmon Dis Volume 13 (2018) 2033–2039. https://doi.org/10.2147/COPD.S161345

[90] Y. Kasuya, O. Akça, D.I. Sessler, M. Ozaki, R. Komatsu, Accuracy of Postoperative End-tidal Pco2Measurements with Mainstream and Sidestream Capnography in Non-obese Patients and in Obese Patients with and without Obstructive Sleep Apnea, Anesthesiology 111 (2009) 609–615. https://doi.org/10.1097/ALN.0b013e3181b060b6

[91] Tan Teik Kean, M.B. Malarvili, Analysis of capnography for asthmatic patient, in: 2009 IEEE International Conference on Signal and Image Processing Applications, IEEE, 2009: pp. 464–467. https://doi.org/10.1109/ICSIPA.2009.5478699

[92] D. Kerklaan, M.E. Augustus, J.M. Hulst, J. van Rosmalen, S.C.A.T. Verbruggen, K.F.M. Joosten, Validation of ventilator-derived VCO2 measurements to determine energy expenditure in ventilated critically ill children, Clinical Nutrition 36 (2017) 452–457. https://doi.org/10.1016/j.clnu.2016.01.001

[93] J.-R. Lavillegrand, G. Offenstadt, E. Maury, B. Guidet, A. Galbois, Colorimetric Capnometry and Feeding Tube Placement, in: Diet and Nutrition in Critical Care, Springer New York, New York, NY, 2014: pp. 1–8. https://doi.org/10.1007/978-1-4614-8503-2_8-1

[94] H.-J. Lin, C.-T. Huang, H.-F. Hsiao, M.-C. Chiang, M.-J. Jeng, End-tidal carbon dioxide measurement in preterm infants with low birth weight, PLoS One 12 (2017) e0186408. https://doi.org/10.1371/journal.pone.0186408

[95] L.C. Luiz, F.A.L. Marson, C.C. Bresciani Almeida, A.A.D.C. Toro, A. Nucci, J.D. Ribeiro, Analysis of motor and respiratory function in Duchenne muscular dystrophy patients, Respir Physiol Neurobiol 262 (2019) 1–11. https://doi.org/10.1016/j.resp.2019.01.009

[96] M.M. Moreira, R.G.G. Terzi, I.A. Paschoal, L.C. Martins, E.P. da L. Oliveira, A.L.E. Falcão, Trombólise na embolia pulmonar maciça com base na capnografia volumétrica, Arq Bras Cardiol 95 (2010) e97–e100. https://doi.org/10.1590/S0066-782X2010001400025

[97] R.P. Neumann, R. Gerull, E. Zannin, S. Fouzas, S.M. Schulzke, Volumetric Capnography at 36 Weeks Postmenstrual Age and Bronchopulmonary Dysplasia in Very Preterm Infants, J Pediatr 241 (2022) 97-102.e2. https://doi.org/10.1016/j.jpeds.2021.10.019

[98] I. Nitzan, R. Abu Omar, F.B. Mimouni, D. Burshtein-Sorotzkin, N. Algavish-Landau, S. Attia-Reches, Capnography for catheter location confirmation in minimally invasive surfactant administration, Journal of Perinatology 43 (2023) 300–304. https://doi.org/10.1038/s41372-023-01624-5

[99] A.M. Norweg, A. Skamai, S.C. Kwon, J. Whiteson, K. MacDonald, F. Haas, E.G. Collins, R.M. Goldring, J. Reibman, Y. Wu, G. Sweeney, A. Pierre, A.B. Troxel, L. Ehrlich-Jones, N.M. Simon, Acceptability of capnography-assisted respiratory therapy: a new mind–body intervention for COPD, ERJ Open Res 7 (2021) 00256–02021. https://doi.org/10.1183/23120541.00256-2021

[100] P.J. Peyton, M. Kozub, Performance of a second generation pulmonary capnotracking system for continuous monitoring of cardiac output, J Clin Monit Comput 32 (2018) 1057–1064. https://doi.org/10.1007/s10877-018-0110-y

[101] K.M. Poon, C.T. Lui, K.L. Tsui, Prognostication of out-of-hospital cardiac arrest patients by 3-min end-tidal capnometry level in emergency department, Resuscitation 102 (2016) 80–84. https://doi.org/10.1016/j.resuscitation.2016.02.021

[102] M.Â.G.O. Ribeiro, M.T.N. Silva, J.D. Ribeiro, M.M. Moreira, C.C.B. Almeida, A.A. Almeida-Junior, A.F. Ribeiro, M.C. Pereira, G. Hessel, I.A. Paschoal, Volumetric capnography as a tool to detect early peripheric lung obstruction in cystic fibrosis patients, J Pediatr (Rio J) 88 (2012) 509–17. https://doi.org/10.2223/JPED.2233

[103] M. Shikama, M. Yamamoto, I. Osawa, T. Sato, I. Hirayama, N. Hayase, T. Matsubara, K. Doi, Monitoring the Resolution of Acute Exacerbation of Airway Bronchoconstriction in an Asthma Attack Using Capnogram Waveforms, Crit Care Explor 5 (2023) e0899. https://doi.org/10.1097/CCE.0000000000000899

[104] O.P. Singh, I. Bin Ahmed, M.B. Malarvili, Assessment of newly developed real-time human respiration carbon dioxide measurement device for management of asthma outside of hospital, Technology and Health Care 26 (2018) 785–794. https://doi.org/10.3233/THC-181288

[105] O. Szakál, Á. Király, D. Szűcs, M. Katona, D. Boda, G. Tálosi, Measurement of gastric-to-end-tidal carbon dioxide difference in neonates requiring intensive care, The Journal of Maternal-Fetal & Neonatal Medicine 25 (2012) 1791–1795. https://doi.org/10.3109/14767058.2012.663833

[106] S. Takaki, K. Mizutani, M. Fukuchi, T. Yoshida, M. Idei, Y. Matsuda, Y. Yamaguchi, T. Miyashita, T. Nomura, O. Yamaguchi, T. Goto, Deep Breathing Improves End-Tidal Carbon Dioxide Monitoring of an Oxygen Nasal Cannula-

Based Capnometry Device in Subjects Extubated After Abdominal Surgery, Respir Care 62 (2017) 86–91. https://doi.org/10.4187/respcare.04634

[107] L. Talker, D. Neville, L. Wiffen, A.B. Selim, M. Haines, J.C. Carter, H. Broomfield, R.H. Lim, G. Lambert, J. Winter, A. Gribbin, M. Chauhan, R. De Vos, P. Kalra, S. Begum, B. Robinson, B. Mundy, H. Rutter, K. Madronal, S.T. Weiss, G. Hayward, T. Brown, A. Chauhan, A.X. Patel, Machine diagnosis of chronic obstructive pulmonary disease using a novel fast-response capnometer, Respir Res 24 (2023) 150. https://doi.org/10.1186/s12931-023-02460-z

[108] L. Veronez, M.M. Moreira, S.T.P. Soares, M.C. Pereira, M.A.G.O. Ribeiro, J.D. Ribeiro, R.G.G. Terzi, L.C. Martins, I.A. Paschoal, Volumetric Capnography for the Evaluation of Pulmonary Disease in Adult Patients with Cystic Fibrosis and Noncystic Fibrosis Bronchiectasis, Lung 188 (2010) 263–268. https://doi.org/10.1007/s00408-009-9213-z

[109] B. Vijayam, M.B. Malarvili, M.F. Md Shakhih, N. Omar, A.A. Wahab, Effect of short-term ketogenic diet on end-tidal carbon dioxide, Clin Nutr ESPEN 42 (2021) 124–131. https://doi.org/10.1016/j.clnesp.2021.02.005

[110] V.J. Wang, B. Krauss, Carbon dioxide monitoring in emergency medicine training programs, Pediatr Emerg Care 18 (2002) 251–253. https://doi.org/10.1097/00006565-200208000-00005

[111] B. Long, A. Koyfman, M.A. Vivirito, Capnography in the Emergency Department: A Review of Uses, Waveforms, and Limitations, J Emerg Med 53 (2017) 829–842. https://doi.org/10.1016/j.jemermed.2017.08.026

[112] J.D. Pleil, L.E. Christensen, Rationale for developing tunable laser spectroscopy (TLS) technology for high resolution real-time carbon dioxide monitoring (capnography) in human breath, J Breath Res 15 (2021) 040201. https://doi.org/10.1088/1752-7163/ac2723

[113] I.E. Hoff, L.Ø. Høiseth, K.A. Kirkebøen, S.A. Landsverk, Volumetric and End-Tidal Capnography for the Detection of Cardiac Output Changes in Mechanically Ventilated Patients Early after Open Heart Surgery, Crit Care Res Pract 2019 (2019) 1–9. https://doi.org/10.1155/2019/6393649

[114] T. Citherlet, F. Crettaz von Roten, B. Kayser, K. Guex, Acute Effects of the Wim Hof Breathing Method on Repeated Sprint Ability: A Pilot Study, Front Sports Act Living 3 (2021). https://doi.org/10.3389/fspor.2021.700757

[115] A. Morais, A. Bugalho, M. Drummond, A.J. Ferreira, A.S. Oliveira, S. Sousa, J.C. Winck, J. Cardoso, Teleconsultation in respiratory medicine – A position paper of the Portuguese Pulmonology Society, Pulmonology 29 (2023) 65–76. https://doi.org/10.1016/j.pulmoe.2022.04.007

[116] D.F.T. Morais, G. Fernandes, G.D. Lima, J.J.P.C. Rodrigues, IoT-Based Wearable and Smart Health Device Solutions for Capnography: Analysis and Perspectives, Electronics (Basel) 12 (2023) 1169. https://doi.org/10.3390/electronics12051169

[117] M.R. Georgescu, A. Meslem, I. Nastase, Accumulation and spatial distribution of CO2 in the astronaut's crew quarters on the International Space Station, Build Environ 185 (2020) 107278. https://doi.org/10.1016/j.buildenv.2020.107278