Perioperative Precision Medicine
eISSN: 2957-5443

Zentime

Review Article

Progress of end-tidal carbon dioxide monitoring in non-intubated patients

Yue Wang[1], Miao Zhou[1], Pengxin Li[2], Lianbing Gu[2]

[1]Department of Anesthesiology, The Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, Nanjing Medical University, Nanjing 210009, Jiangsu, China. [2]Xuzhou Medical University, Jiangsu Province Key Laboratory of Anesthesiology, Jiangsu Province Key Laboratory of Anesthesia and Analgesia Application Technology, Xuzhou 221002, Jiangsu, China.

Acknowledgment: This work was supported by Jiangsu Cancer Hospital Excellent Talent Program (YC201805).

Declaration of conflict of interest: None.

Received March 15, 2023; Accepted April 27, 2023; Published June 30, 2023

Highlights

- This review focuses on literature regarding end-tidal carbon dioxide monitoring for non-intubated patients.
- Partial pressure of carbon dioxide monitoring can benefit non-intubated patients.
- As carbon dioxide detection technology continues to improve, end-tidal carbon dioxide monitoring is expected to be used in more medical scenarios.

Abstract

End-tidal carbon dioxide ($ETCO_2$) monitoring is an important tool for assessing respiratory and circulatory status of patients. It has become an integral component of perioperative anesthesia care in patients undergoing general anesthesia with endotracheal intubation. $ETCO_2$ monitoring can also benefit non-intubated patients. This review covers the basics of $ETCO_2$ and methods of partial pressure of $ETCO_2$ ($P_{ET}CO_2$) monitoring and focuses on the literature regarding $P_{ET}CO_2$ monitoring for non-intubated patients. Most studies explored the superiority of $P_{ET}CO_2$ monitoring in patients under sedation outside operating room, while others investigated the potential advantages of $P_{ET}CO_2$ monitoring in other scenarios such as post-anesthesia care unit, cardiopulmonary resuscitation, and patient-controlled analgesia. As carbon dioxide detection technology and sampling circuits continue to improve, $P_{ET}CO_2$ monitoring is expected to be used in more medical scenarios.

Keywords: End-tidal carbon dioxide, monitoring, non-intubated patients, airway management, anesthesia

Introduction

End-tidal carbon dioxide ($ETCO_2$) monitoring measures the partial pressure of $ETCO_2$ ($P_{ET}CO_2$) or concentration of $ETCO_2$ ($C_{ET}CO_2$) at the end of an exhaled breath. $ETCO_2$ monitoring often relies on capnography, which measures carbon dioxide concentrations over time. Due to its simplicity, non-invasiveness, continuous monitoring capability, and strong timeliness, $ETCO_2$ monitoring has been widely used for evaluating patients' respiratory and circulatory conditions in clinical practice [1]. In clinical anesthesia, $ETCO_2$ monitoring can indicate the respiratory and circulatory conditions of patients, and can help detect respiratory failure, pulmonary embolism, and other conditions during surgery [2, 3]. With the progress of technology and social advancements, the application of $ETCO_2$ monitoring has expanded to non-intubated patients, such as those in endoscopy rooms, catheterization labs, intensive care units (ICU), post-anesthesia care units (PACU), and emergency departments, with $P_{ET}CO_2$ monitoring being the most common [4]. This article primarily reviews the clinical applications of $ETCO_2$ monitoring in non-intubated patients.

$P_{ET}CO_2$ monitoring

Pathophysiology of $P_{ET}CO_2$

Carbon dioxide (CO_2) is present in the blood, with one-third being carried by red blood cells and the remaining two-thirds in plasma. CO_2 produced in the tissues diffuses into the blood

Address correspondence to: Lianbing Gu, The Affiliated Cancer Hospital of Nanjing Medical University, Department of Anesthesiology, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research, Nanjing Medical University, Nanjing 210009, Jiangsu, China. E-mail: 13951947684@163.com.

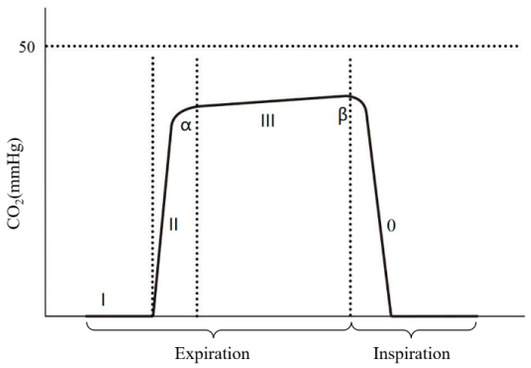

Figure 1. Time capnogram displays segments, phases and angles. Inspiratory segment is phase 0, and expiratory segment is divided into three phases: I, II, and III. Maximum value of CO_2 at the end of the breath is designated as $P_{ET}CO_2$. The angle between phase II and phase III is angle α, and between phase III and inspiratory downstroke is angle β. $P_{ET}CO_2$, partial pressure of end-tidal carbon dioxide.

through tissue cells, is carried by red blood cells through the bloodstream to the lungs, and undergoes diffusion in the pulmonary capillaries to be exhaled from the body via the alveolar air. Therefore, $P_{ET}CO_2$ is typically measured at the peak of the respiratory cycle and is affected by three factors, namely CO_2 production, lung gas exchange, and alveolar ventilation.

In healthy adults, $P_{ET}CO_2$ ranges between 35 and 45 mmHg, and arterial to endtidal partial pressure CO_2 ($P_{(a\text{-}ET)}CO_2$) is between 2 and 5 mmHg due to matching of alveolar ventilation and perfusion [5]. For patients without apparent cardio-pulmonary dysfunction, $P_{ET}CO_2$ values can be used to estimate $PaCO_2$. When the ratio of ventilation to perfusion ($\dot{V}_A/\dot{Q}$) is imbalanced, $P_{(a\text{-}ET)}CO_2$ increases [6]. At this point, arterial blood gas analysis is necessary to obtain a more accurate $PaCO_2$ value. A stable $P_{(a\text{-}ET)}CO_2$ usually indicates relative stability of alveolar ventilation and perfusion, while an increased $P_{(a\text{-}ET)}CO_2$ gradient may hold clinical value in the diagnosis of pulmonary embolism [7].

$P_{ET}CO_2$ values increase in conditions characterized by high CO_2 production and transportation to the lungs, such as high metabolic crises, malignant hyperthermia, thyrotoxic crisis, sodium bicarbonate infusion, venous CO_2 embolism, and increased cardiac output. On the other hand, $P_{ET}CO_2$ values decrease in conditions characterized by low CO_2 production and transportation to the lungs, such as in hypothermia, inadequate pulmonary perfusion, cardiac arrest, pulmonary embolism, and hypotension. When there is inadequate alveolar ventilation, such as in chronic obstructive pulmonary disease or partial airway obstruction, $\dot{V}_A/\dot{Q}$ decreases, and $PaCO_2$ increases, leading to a corresponding increase in $P_{ET}CO_2$. Conversely, when there is excessive ventilation, $\dot{V}_A/\dot{Q}$ increases, and $PaCO_2$ decreases, leading to a corresponding decrease in $P_{ET}CO_2$.

Waveforms of $P_{ET}CO_2$

The time capnogram of $P_{ET}CO_2$ can be divided into two phases: the inspiratory phase (phase 0) and the expiratory phase [8, 9]. The $P_{ET}CO_2$ waveform during the expiratory phase can be further divided into three phases: phase I corresponds to dead space gas; phase II corresponds to alveolar gas elimination, where the PCO_2 rises rapidly to a plateau; phase III corresponds to the plateau period (**Figure 1**). Typically, the CO_2 concentration during phase III shows a slight upward slope over time, as the latest emptied or smallest alveoli contain relatively more CO_2, resulting in a higher PCO_2 level. Therefore, the height and slope of the alveolar plateau can provide information about ventilation and perfusion. The maximum PCO_2 obtained during phase III is known as $P_{ET}CO_2$. When there is a significant change in airway caliber, such as under asthma or chronic obstructive pulmonary disease (COPD), the rising of phase III becomes steeper, and the α angle between phases II and III increases. At the end of phase III, the inspiration begins, and the $P_{ET}CO_2$ drops rapidly to 0. The angle between phase III and the inspiratory phase is usually 90° (β angle), which increases with each subsequent breath.

Under normal conditions, mechanical ventilation waveforms have a trapezoidal appearance, as shown in **Figure 1** [10]. A decrease in airway diameter, such as in cases of asthma, COPD, or partial obstruction of the respiratory circuit, can result in an increase in the slope of the III phase. At the end of exhalation, the decrease to zero flow and the influence of cardiac pulsations can cause oscillations between emptying of different lung regions and the movement of exhaled and fresh gases, resulting in a wave pattern of cardiac origin. The presence of gaps in phase III waveform indicates spontaneous breathing during mechanical ventilation. In the event of an endotracheal tube misplacement into the esophagus, the concentration of CO_2 drops rapidly, causing a decrease in the waveform. Additionally, if CO_2 is repeatedly inhaled, the baseline value will not be zero. A sudden shortening of the plateau period in phase III indicates air leakage from the endotracheal tube

Table 1. The characteristics of three methods of the partial pressure of carbon dioxide monitoring

Types	Location of sensor	Methods of quantifying CO_2 concentration	Spectral range	Characteristics
Mainstream	In breathing circuits	Infrared radiation	Around 4.26 μm, filter required	Potential increase in dead space, generally faster rise time
Sidestream	Away from breathing circuits	Infrared radiation	Around 4.26 μm, filter required	Gas withdrawal rate of 30-500ml/min, long response time, large sample cell
Microstream	Away from breathing circuits	Molecular correlation spectroscopy	4.2 - 4.35 μm, no filter required	Gas withdrawal rate of 50ml/min, short response time, 15ul sample cell

cuff during mechanical ventilation.

Methods of $P_{ET}CO_2$ monitoring

In 1864, John Tyndall first proposed the use of infrared absorption spectroscopy to measure CO_2. According to Beer-Lambert law, the amount of infrared radiation (IR) absorbed by a sensor during IR detection is directly proportional to the concentration of CO_2 absorbed in the sample. With advances in CO_2 monitoring technology in the 1980s, $P_{ET}CO_2$ monitoring gradually became common in clinical practice. **Table 1** shows the characteristics of three methods of $P_{ET}CO_2$ monitoring: mainstream, sidestream and microstream [11].

Mainstream monitoring involves placing an infrared sensor directly in the patient's breathing circuit. Its advantages include fast response time, high accuracy, and minimal waveform distortion. However, the drawback is that it can only be used in relatively closed breathing circuits. Currently, a new type of tube-based mainstream capnography is available for non-intubated patients (cap-ONE; Nihon Kohden, Tokyo, Japan). It is small in size and weighs only 10g, making it suitable for nasal cannula channel [12].

Sidestream monitoring involves connecting a gas sampling tube to the patient's breathing circuit and using a suction pump to draw gas from the breathing circuit into the infrared measurement chamber for analysis. It can be used in both closed and non-closed breathing circuits, making it suitable for patients with spontaneous breathing [5]. The sidestream $P_{ET}CO_2$ sensors generally use conventional infrared radiation techniques, which have a wide absorption spectrum and require filtering, resulting in a low accuracy. Additionally, a large gas sampling volume and flow rate are required, which lead to a longer response time. Although it can be used for patients with spontaneous breathing, it has a higher loss of tidal volume during sampling, making it difficult to be used in newborns [13, 14]. To prevent water vapor blockage, a water trap must be installed, but it is easily damaged.

Currently, the microstream technology (Oridion Capnography Inc.) sensor uses molecular correlation spectroscopy, which operates within a small spectral range (4.2-4.35 μm) and does not require filtering. The gas sample demand can be as low as 15 μL, allowing for a very low sampling flow rate (50 ml/min). Additionally, microstream technology uses innovative small diameter and low dead space sampling tubes, which accelerate the delivery of gas and increase the sensitivity for recognizing events such as respiratory pauses [15]. This has expanded the use of $P_{ET}CO_2$ monitoring in populations with low tidal volumes, such as newborns [16]. The micrometer-level filter in the sampling tube can filter out particles down to the 0.2μm level, and the use of Nafion drying tube can adsorb condensate in the sampling tube and prevent water vapor blockage, eliminating the need for a water trap. Zhang et al. found that two types of sampling tubes using microstream technology (Smart CapnoLine (Oridion Capnography Inc., A) and Filterline H Set (Oridion Capnography Inc., B)) were utilized to collect $P_{ET}CO_2$ via nasal or pharyngeal routes in non-intubated patients who underwent digital subtraction cerebral angiography (DSA). The $P_{ET}CO_2$ and $PaCO_2$ were significantly correlated (0.832 vs. 0.836, $P<0.001$), which provides valuable clinical references [17].

$P_{ET}CO_2$ monitoring in specific populations

Obesity is considered as a risk factor for postoperative respiratory depression, and obese patients with respiratory system complications and obstructive sleep apnea (OSA) may benefit from $P_{ET}CO_2$ monitoring [18, 19]. However, there are some challenges in measuring $P_{ET}CO_2$ in OSA patients, as mouth breathing and low tidal volume can result in greater dilution of the sample by ambient air. The cap-ONE (Nihon Kohden, Tokyo, Japan) sensor was designed to

monitor respiratory pauses and measure $P_{ET}CO_2$ in OSA patients, as it can better accommodate mouth breathing [20]. Latham applied $P_{ET}CO_2$ monitoring to postoperative high-risk OSA patients in the PACU as a part of hospital continuous quality improvement program. Latham et al. reported that $P_{ET}CO_2$ monitoring allowed for timely detection of postoperative respiratory complications in patients and provided a better understanding of their conditions, enabling them to provide better care for the patients [21].

Gupta reviewed 13 studies and reported that advanced age, COPD, and heart disease are important risk factors for opioid-induced respiratory depression (OIRD) [22]. Older patients are more sensitive to the central inhibitory effects of opioid drugs, and they also have higher rates of comorbidities, leading to decreased plasma clearance of medications by the liver and kidneys [23]. Therefore, monitoring respiratory function in elderly patients after surgery is vital for their respiratory function.

Taylor et al. conducted a retrospective case-control analysis of 62 adult patients who experienced respiratory events (defined as respiratory rate <10 breaths/min and/or SpO_2 <90%) after surgery and found that patients aged 65 years and above had an increased risk of respiratory events (OR: 2.34; 95% CI: 1.14 - 4.82) [24]. Overdyk et al. evaluated respiratory function in 205 adult patients receiving PCA analgesia after surgery. The results showed that the rates of respiratory depression (respiratory rate <10 breaths/min) lasting for more than 2 or 3 minutes were 77.8% and 66.7%, respectively, in patients aged 65 years and above, which were higher than the mean occurrence rates (58.4% and 41.0%, respectively) [25].

$P_{ET}CO_2$ monitoring is critical in children because respiratory depression is prone to occur due to their larger tongue. In 1997, Hart et al. used relatively advanced $P_{ET}CO_2$ equipment to monitor children and found that $P_{ET}CO_2$ monitoring provided earlier indications of respiratory depression than pulse oximetry during procedural sedation with preserved spontaneous breathing [26]. Langhan et al. conducted a study on children aged 1-20 years in the PACU and found that the intervention group had higher rate of hypoventilation per minute (5% (95% CI: 2% - 8%) vs. 1% (95% CI: -1% - 3%); P=0.040], and higher apnea rate (11% (95% CI: 8% - 14%) vs. 1.5% (95% CI: -2% - 5%); P<0.001), as well as a faster rate of respiratory depression (5% (95% CI: 2% - 8%) vs. 1% (95% CI: 0% - 4%); P=0.050] compared to the control group, indicating that $P_{ET}CO_2$ monitoring in the PACU could better protect the postoperative respiratory function of children [27]. Yarchi et al. included 57 patients aged 4-62 years in a study on painless endoscopy and used $P_{ET}CO_2$ monitoring with $SpO_2 \leq 90\%$ or changes in heart rate or respiratory rate greater than 20% from baseline as an event. They found that $P_{ET}CO_2$ monitoring increased the probability of event occurrence in patients with lower average $P_{ET}CO_2$ values, higher $P_{ET}CO_2$ variability, and younger age [28]. Singh tested the correlation between $P_{ET}CO_2$ measured using microcapillary technology and $PaCO_2$ in newborns in the neonatal intensive care unit. The r value between $P_{ET}CO_2$ and $PaCO_2$ was 0.73 in 204 blood samples from very low birth weight (VLBW) infants (birth weight<1,500 g) and 0.82 in 82 blood samples from non-VLBW infants [29].

The identification of respiratory events and accurate estimation of $PaCO_2$ in patients with OSA, elderly individuals, and children through non-invasive means are the ongoing issues. The development of new measurement methods and sensors may provide us with more options to address this challenge.

$P_{ET}CO_2$ monitoring in non-intubated patients

$P_{ET}CO_2$ monitoring in patients under sedation outside operating room

With the advancements in endoscopy, interventional therapy, and radiological examination techniques, the number of procedures requiring sedation outside the operating room has significantly increased. The anesthesia plan for such procedures often requires moderate sedation, involving general anesthesia with preservation of spontaneous breathing [30]. During moderate sedation, patients are able to respond purposefully to verbal commands and respond to light tapping or verbal stimulation, usually without any intervention to maintain airway patency; their cardiovascular function is almost unaffected. However, in examination rooms for painless endoscopy, cholangioscopy, and DSA, the ambient light level is generally low, and internal medicine doctors and anesthesiologists often cannot detect respiratory impairment in patients in a timely manner, leading to respiratory depression [31]. In 2015, the Association of Anaesthetists of Great Britain and Ireland recommended $P_{ET}CO_2$ monitoring for all patients undergoing procedural sedation, especially for those requiring oxygen [32]. The American Society of Anesthesiologists also revised its basic anesthesia monitoring standards to include

$P_{ET}CO_2$ monitoring during moderate and deep sedation [33].

In recent years, multiple clinical studies have demonstrated that monitoring $P_{ET}CO_2$ can effectively detect respiratory events and reduce the incidence of hypoxemia during sedation in various non-operating room settings. Qadeer et al. reported that in 247 patients undergoing endoscopy, 69% of the patients experienced hypoxemia without $P_{ET}CO_2$ monitoring, and this proportion decreased to 46% after $P_{ET}CO_2$ monitoring (P<0.001) [34]. Similarly, Beitz et al. conducted a randomized trial and found that $P_{ET}CO_2$ monitoring during routine colonoscopy reduced the incidence of hypoxemia by 50% [35]. Ishiwata's study exhibited that the incidence of respiratory events during tracheal surgery was as high as 48.8%, and $P_{ET}CO_2$ monitoring could detect respiratory events earlier (30 seconds earlier than pulse oximetry), with a shorter duration of hypoxemia (20.4 vs. 41.7 seconds, P=0.029), a lower incidence of severe hypoxemia (SpO_2<85%) (16 (17%) vs. 29 (32%), P=0.019), and a higher mean lowest SpO_2 value (90.5 vs. 87.6, P=0.002) [36, 37]. Study of Schlag et al. confirmed that $P_{ET}CO_2$ monitoring during sedation for percutaneous transhepatic cholangiography drainage revealed significantly more respiratory events than clinical observation alone (113 vs. 7; P=0.012) [38]. Jiang et al. demonstrated that $P_{ET}CO_2$ monitoring in the painless abortion room was able to reveal a higher rate of respiratory events or abnormal ventilation (55.1%, 95% CI: 39.4% - 62.3% vs. 3.0%, 95% CI: 1.1% - 4.2%, P<0.001), leading to a lower incidence of hypoxemia (37.8%, 95% CI: 33.8% - 45.2% vs. 54.2%, 95% CI: 47.8% - 58.2%, P<0.001) [39]. It is indicated that $P_{ET}CO_2$ monitoring can also be used to identify early changes in ventilation parameters in the painless abortion room.

From an evidence-based medicine perspective, Waugh et al. conducted a meta-analysis on procedural sedation and analgesia (PSA) and demonstrated that $P_{ET}CO_2$ monitoring during PSA increased the detection rate of respiratory events by 17.6 times compared to no $P_{ET}CO_2$ monitoring (95% CI: 2.50 - 122.10; P<0.004) [40]. Similarly, Askar et al. carried out a meta-analysis on dental procedural sedation and found that $P_{ET}CO_2$ monitoring during sedation reduced the incidence of hypoxemia (RR 0.76, 95%CI: 0.70 - 0.83, P<0.001) and decreased oxygen saturation (RR 0.79, 95%CI: 0.71 - 0.87, P<0.001) [41]. These studies support the benefits of $P_{ET}CO_2$ monitoring during sedation in non-operating room settings.

In summary, the use of $P_{ET}CO_2$ monitoring during sedation and anesthesia procedures performed outside the operating room can improve the detection efficiency of respiratory pauses, enabling clinical physicians to provide timely intervention, and can reduce the incidence of hypoxemia in patients. Thus, $P_{ET}CO_2$ monitoring provides an effective safety guarantee for sedation and anesthesia procedures performed outside the operating room.

$P_{ET}CO_2$ monitoring in PACU

The PACU is a vital location for the monitoring of patients who have undergone general anesthesia and intubation. During the recovery period, the patient's vital signs and respiratory function need to be closely monitored [42]. $P_{ET}CO_2$ monitoring is an effective tool for evaluating the patient's respiratory and circulatory conditions [43]. The fourth national audit project of the National Audit Project of the Royal College of Anesthetists and the Difficult Airway Society indicates that around 30% of anesthesia-related airway complications occur during the recovery period [44]. Kawanishi et al. reported that airway adverse events exhibited an incidence of 16% in the PACU and about one-fourth of these events occurred at the end of anesthesia or in the recovery room [45]. Chung et al. conducted a study to monitor the respiratory function with microstream technology in 250 adult patients during the recovery period after general anesthesia and found that approximately 55% of patients experienced at least one episode of hypoxemia [46]. In addition, Potvin et al. discovered that $P_{ET}CO_2$ monitoring before tracheal extubation or removal of a laryngeal mask airway significantly reduced the proportion of patients with $P_{ET}CO_2$>45 mmHg in the minute before extubation (83.3% and 54.1%, respectively, P = 0.029) [43].

Although there is limited research in this area at present, future studies can explore whether monitoring vital signs such as respiratory rate, depth, and CO_2 concentration with $P_{ET}CO_2$ during the recovery period can improve the detection rate of adverse events such as airway obstruction, pulmonary embolism, respiratory distress, respiratory failure, and pneumothorax, with the aim of improving the safety of clinical anesthesia.

$P_{ET}CO_2$ monitoring in patients under non-invasive ventilation (NIV)

Patients with COPD, acute respiratory distress

syndrome, severe asthma, respiratory failure, congestive heart failure, OSA/hypopnea syndrome, and other respiratory conditions often require NIV [47]. NIV can correct alveolar hypoventilation, improve sleep quality and survival rate, and capnography can be used to monitor the respiratory and circulatory functions of these patients [48, 49]. Sakuraya et al. found that mainstream and sidestream $P_{ET}CO_2$ monitoring during NIV could effectively predict $PaCO_2$ levels in adults (mainstream: r=0.92, P<0.001 vs. sidestream: r=0.79, P<0.001) [50]. Duggal et al. conducted a systematic review on the safety and efficacy of NIV for blunt chest trauma patients without respiratory failure and concluded that early use of NIV could prevent intubation events [51]. Aarrestad et al. monitored $PtCO_2$ in 67 patients with chronic respiratory failure receiving long-term NIV, and reported a significant correlation between $PaCO_2$ and $PtcCO_2$ (r=0.9, P<0.0001) [52].

Currently, there is limited research on capnography for NIV. Hence, further studies are needed to support its benefits for non-invasive ventilation.

$P_{ET}CO_2$ monitoring in cardiopulmonary resuscitation

In 1978, Dr. Kalenda proposed to use CO_2 monitoring for the evaluation of pulmonary blood flow during cardiac resuscitation, which would help assess systemic circulation [53]. The 2015 Resuscitation Council UK guidelines identified the role of capnography in cardiopulmonary resuscitation (CPR), including endotracheal tube placement, monitoring ventilation rate during CPR to avoid hyperventilation, assessing the quality of chest compressions during CPR, and monitoring the return of spontaneous circulation after CPR [54]. In a retrospective analysis of 14,504,809 internal medicine and 6,771,882 surgical patients, Izrailtyan et al. identified 96,554 cases of cardiac arrest, with surgical patients experiencing twice as many events as internal medicine patients (6.17 vs. 3.77 events per 1000 cases) [55]. Independent predictors of cardiac arrest following opioid treatment included hispanic ethnicity, obesity, mild liver disease, and COPD. Baldi's study showed that changes in $P_{ET}CO_2$ before and within 10 minutes after intubation during cardiac arrest were independent predictors of CPR outcomes (OR 1.83, 95% CI: 1.02 - 3.30; P=0.040 and OR 3.9, 95% CI: 1.97 - 7.74; P<0.001) [56]. Murphy's study found that increasing chest compression depth by 10mm was associated with a 4.0% increase in $P_{ET}CO_2$ (P<0.001), increasing compression rate by 10 per minute was associated with a 1.7% increase in $P_{ET}CO_2$ (P=0.020), and increasing chest compression recoil speed by 10mm per second was associated with a 2.8% increase in $P_{ET}CO_2$ (P=0.030) [57]. Additionally, Gutiérrez et al. demonstrated that the average percentage change in $P_{ET}CO_2$ during chest compressions could be used to differentiate spontaneous circulation recovery (sensitivity: 95.4%, 95% CI: 90.10 - 98.10; specificity: 94.9%, 95% CI: 91.40 - 97.10) [58].

Although $P_{ET}CO_2$ monitoring can aid in monitoring spontaneous breathing and circulation recovery during cardiopulmonary resuscitation, there is currently limited evidence to suggest that the use of $P_{ET}CO_2$ monitoring during CPR can improve patient outcomes [59].

$P_{ET}CO_2$ monitoring and patient-controlled analgesia (PCA)

The implementation of the enhanced recovery after surgery concept has led to the widespread use of PCA for postoperative pain management in the ward. However, the use of opioid analgesics can lead to OIRD, which is a significant risk factor [22]. The Anesthesia Patient Safety Foundation recommends monitoring SpO_2 and respiratory rate, especially after extubation and when using opioid analgesics for pain management [60]. Lee et al. conducted a claims analysis on postoperative OIRD and reported that among 92 claims (κ=0.690), the majority of respiratory depression events (88%) occurred within 24 hours after surgery, and 97% were considered preventable with better monitoring [61]. Therefore, $P_{ET}CO_2$ monitoring is necessary when patients are using PCA pumps. In a survey of 178 patients using PCA pumps conducted by Overdyk et al., $P_{ET}CO_2$ monitoring detected a sustained decrease in pulse oxygen saturation (SpO_2<90%) in 12% of patients and a slow respiratory rate (RR<10 breaths/min) in 41% of patients, highlighting the need for $P_{ET}CO_2$ monitoring in the population using PCA pumps [25].

Despite the frequent occurrence of OIRD in clinical practice, most clinicians in hospitals rely on intermittent assessments to monitor PCA patients. However, there is currently limited research on real-time monitoring and timely intervention to reduce the occurrence of respiratory depression. $P_{ET}CO_2$ monitoring can provide real-time monitoring of a patient's respiratory status and promptly detect respiratory events, allowing for timely intervention.

Conclusion

In conclusion, $P_{ET}CO_2$ monitoring could be used not only in patients undergoing general anesthesia with endotracheal incubation, but also in many other medical settings such as endoscopy rooms, catheterization labs, ICU, PACU and emergency departments. Multiple studies have confirmed that $P_{ET}CO_2$ monitoring can also benefit non-intubated patients. As CO_2 detection technology and sampling circuits continue to improve, $P_{ET}CO_2$ monitoring is expected to better reflect respiratory and circulatory functions of patients, thereby expanding its use in non-intubated patients. Presently, $P_{ET}CO_2$ monitoring is primarily employed in non-intubated patients for PSA, while more research is required to investigate its application in post-extubation after general anesthesia, cardiopulmonary resuscitation, as well as the diagnosis and management of respiratory and circulatory system disorders.

References

[1] Selby ST, Abramo T, Hobart-Porter N. An Update on End-Tidal CO2 Monitoring. Pediatr Emerg Care 2018;34(12):888-892.

[2] Ortega R, Connor C, Kim S, et al. Monitoring ventilation with capnography. N Engl J Med 2012;367(19):e27.

[3] Rackley CR. Monitoring During Mechanical Ventilation. Respir Care 2020;65(6):832-846.

[4] Kodali BS. Capnography outside the operating rooms. Anesthesiology 2013;118(1):192-201.

[5] Kreit JW. Volume Capnography in the Intensive Care Unit: Potential Clinical Applications. Ann Am Thorac Soc 2019;16(4):409-420.

[6] Restrepo RD, Nuccio P, Spratt G, et al. Current applications of capnography in non-intubated patients. Expert Rev Respir Med 2014;8(5):629-639.

[7] Park CI, Bendjelid K, Bonvini RF. Arterial to end-tidal CO2 pressure gradient: a bedside parameter to monitor patients with massive pulmonary embolism. Am J Emerg Med 2013;31(3):1-3.

[8] Bhavani-Shankar K, Kumar AY, Moseley HS, et al. Terminology and the current limitations of time capnography: a brief review. J Clin Monit 1995;11(3):175-182.

[9] Bhavani-Shankar K, Philip JH. Defining segments and phases of a time capnogram. Anesth Analg 2000;91(4):973-977.

[10] Krauss B, Hess DR. Capnography for procedural sedation and analgesia in the emergency department. Ann Emerg Med 2007;50(2):172-181.

[11] Mogue L R, Rantala B. Capnometers. J Clin Monit 1988;4(2):115-121.

[12] Kasuya Y, Akça O, Sessler DI, et al. Accuracy of postoperative end-tidal Pco2 measurements with mainstream and sidestream capnography in non-obese patients and in obese patients with and without obstructive sleep apnea. Anesthesiol 2009;111(3):609-615.

[13] Williams EE, Greenough A. Lung Protection During Mechanical Ventilation in the Premature Infant. Clin Perinatol 2021;48(4):869-880.

[14] Schmalisch G. Basic principles of respiratory function monitoring in ventilated newborns: A review. Paediatr Respir Rev 2016;20:76-82.

[15] Colman Y, Krauss B. Microstream Capnography Technology: A New Approach to an Old Problem. J Clin Monit Comput 1999;15(6):403-409.

[16] Williams E, Dassios T, Greenough A. Carbon dioxide monitoring in the newborn infant. Pediatr Pulmonol 2021;56(10):3148-3156.

[17] Zhang C, Wang M, Wang R, et al. Accuracy of end-tidal CO2 measurement through the nose and pharynx in nonintubated patients during digital subtraction cerebral angiography. J Neurosurg Anesthesiol 2013;25(2):191-196.

[18] Laporta ML, Sprung J, Weingarten TN. Respiratory depression in the post-anesthesia care unit: Mayo Clinic experience. Bosn J Basic Med Sci 2021;21(2):221-228.

[19] Maddox RR, Williams CK, Oglesby H, et al. Clinical experience with patient-controlled analgesia using continuous respiratory monitoring and a smart infusion system. Am J Health Syst Pharm 2006;63(2):157-164.

[20] Yamamori S, Takasaki Y, Ozaki M, et al. A flow-through capnometer for obstructive sleep apnea. J Clin Monit Comput 2008;22(3):209-220.

[21] Latham K, Bird T, Burke J. Implementing Microstream End-Tidal CO2 in the PACU. J Perianesth Nurs 2018;33(1):23-27.

[22] Gupta K, Prasad A, Nagappa M, et al. Risk factors for opioid-induced respiratory depression and failure to rescue: a review. Curr Opin Anaesthesiol 2018;31(1):110-119.

[23] van der Schrier R, Roozekrans M, Olofsen E, et al. Influence of Ethanol on Oxycodone-induced Respiratory Depression: A Dose-escalating Study in Young and Elderly Individuals. Anesthesiology 2017;126(3):534-542.

[24] Taylor S, Kirton OC, Staff I, et al. Postoperative day one: a high risk period for respiratory events. Am J Surg 2005;190(5):752-756.

[25] Overdyk FJ, Carter R, Maddox RR, et al. Continuous oximetry/capnometry monitoring reveals frequent desaturation and bradypnea during patient-controlled analgesia. Anesth Analg 2007;105(2):412-418.

[26] Hart LS, Berns SD, Houck CS, et al. The value of end-tidal CO2 monitoring when comparing

three methods of conscious sedation for children undergoing painful procedures in the emergency department. Pediatr Emerg Care 1997;13(3):189-193.
[27] Langhan ML, Li FY, Lichtor JL. The impact of capnography monitoring among children and adolescents in the postanesthesia care unit: a randomized controlled trial. Paediatr Anaesth 2017;27(4):385-393.
[28] Yarchi D, Cohen A, Umansky T, et al. Assessment of end-tidal carbon dioxide during pediatric and adult sedation for endoscopic procedures. Gastrointest Endosc 2009;69(4):877-882.
[29] Singh BS, Gilbert U, Singh S, et al. Sidestream microstream end tidal carbon dioxide measurements and blood gas correlations in neonatal intensive care unit. Pediatr Pulmonol 2013;48(3):250-256.
[30] Parker W, Estrich CG, Abt E, et al. Benefits and harms of capnography during procedures involving moderate sedation: A rapid review and meta-analysis. J Am Dent Assoc (1939) 2018;149(1):38-50.
[31] Whitaker DK, Benson JP. Capnography standards for outside the operating room. Curr Opin Anaesthesiol 2016;29(4):485-492.
[32] Checketts MR, Alladi R, Ferguson K, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia 2016;71(1):85-93.
[33] American Society of Anesthesiologists. Standards for Basic Anesthetic Monitoring. Available at: www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring.
[34] Qadeer MA, Vargo JJ, Dumot JA, et al. Capnographic monitoring of respiratory activity improves safety of sedation for endoscopic cholangiopancreatography and ultrasonography. Gastroenterol 2009;136(5):1568-1576.
[35] Beitz A, Riphaus A, Meining A, et al. Capnographic monitoring reduces the incidence of arterial oxygen desaturation and hypoxemia during propofol sedation for colonoscopy: a randomized, controlled study (ColoCap Study). Am J Gastroenterol 2012;107(8):1205-1212.
[36] Ishiwata T, Tsushima K, Fujie M, et al. End-tidal capnographic monitoring to detect apnea episodes during flexible bronchoscopy under sedation. BMC Pulm Med 2017;17(1):7.
[37] Ishiwata T, Tsushima K, Terada J, et al. Efficacy of End-Tidal Capnography Monitoring during Flexible Bronchoscopy in Nonintubated Patients under Sedation: A Randomized Controlled Study. Respiration 2018;96(4):355-362.
[38] Schlag C, Wörner A, Wagenpfeil S, et al. Capnography improves detection of apnea during procedural sedation for percutaneous transhepatic cholangiodrainage. Can J Gastroenterol 2013;27(10):582-586.
[39] Jiang ZM, Chen ZH, Fang XM. Sidestream capnographic monitoring reduces the incidence of arterial oxygen desaturation during propofol ambulatory anesthesia for surgical abortion. Med Sci Monit 2014;20:2336-2342.
[40] Waugh JB, Epps CA, Khodneva YA. Capnography enhances surveillance of respiratory events during procedural sedation: a meta-analysis. J Clin Anesth 2011;23(3):189-196.
[41] Askar H, Misch J, Chen Z, et al. Capnography monitoring in procedural intravenous sedation: a systematic review and meta-analysis. Clin Oral Investig 2020;24(11):3761-3770.
[42] McNeill MM, Hardy Tabet C. The Effectiveness of Capnography Versus Pulse Oximetry in Detecting Respiratory Adverse Events in the Postanesthesia Care Unit (PACU): A Narrative Review and Synthesis. J Perianesth Nurs 2022;37(2):264-269.
[43] Potvin J, Etchebarne I, Soubiron L, et al. Effects of capnometry monitoring during recovery in the post-anaesthesia care unit: a randomized controlled trial in adults (CAPNO-SSPI). J Clin Monit Comput 2022;36(2):379-385.
[44] Cook TM, Woodall N, Frerk C. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: Anaesthesia. Br J Anaesth 2011;106(5):617-631.
[45] Kawanishi H, Inoue S, Kawaguchi M. A Retrospective Analysis of Oxygen Desaturation during Acoustic Respiratory Rate Monitoring in Non-ICU Patients following Tracheal Extubation after General Anesthesia. Anesthesiol Res Pract 2017;2017:1-6.
[46] Chung F, Wong J, Mestek ML, et al. Characterization of respiratory compromise and the potential clinical utility of capnography in the post-anesthesia care unit: a blinded observational trial. J Clin Monit Comput 2020;34(3):541-551.
[47] Contal O, Adler D, Borel JC, et al. Impact of different backup respiratory rates on the efficacy of noninvasive positive pressure ventilation in obesity hypoventilation syndrome: a randomized trial. Chest 2013;143(1):37-46.
[48] Duiverman ML, Wempe JB, Bladder G, et al. Two-year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: a randomized controlled trial. Respir Res 2011;12(1):112.

[49] Köhnlein T, Windisch W, Köhler D, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. Lancet Respir Med 2014;2(9):698-705.

[50] Sakuraya M, Douno E, Iwata W, et al. Accuracy evaluation of mainstream and sidestream end-tidal carbon dioxide monitoring during noninvasive ventilation: a randomized crossover trial (MASCAT-NIV trial). J Intensive Care 2022;10(1):17.

[51] Duggal A, Perez P, Golan E, et al. Safety and efficacy of noninvasive ventilation in patients with blunt chest trauma: a systematic review. Crit Care 2013;17(4):142.

[52] Aarrestad S, Tollefsen E, Kleiven AL, et al. Validity of transcutaneous PCO2 in monitoring chronic hypoventilation treated with non-invasive ventilation. Respir Med 2016;112:112-118.

[53] Kalenda Z. The capnogram as a guide to the efficacy of cardiac massage. Resuscitation 1978;6(4):259-263.

[54] Lloyd G. Resuscitation Council (UK) basic and advanced life support guidelines 2015. Br J Hosp Med 2015;76(12):678-680.

[55] Izrailtyan I, Qiu J, Overdyk FJ, et al. Risk factors for cardiopulmonary and respiratory arrest in medical and surgical hospital patients on opioid analgesics and sedatives. PloS One 2018;13(3):e0194553.

[56] Baldi E, Caputo ML, Klersy C, et al. End-tidal carbon dioxide (ETCO2) at intubation and its increase after 10 minutes resuscitation predicts survival with good neurological outcome in out-of-hospital cardiac arrest patients. Resusc 2022;181:197-207.

[57] Murphy RA, Bobrow BJ, Spaite DW, et al. Association between Prehospital CPR Quality and End-Tidal Carbon Dioxide Levels in Out-of-Hospital Cardiac Arrest. Prehosp Emerg Care 2016;20(3):369-377.

[58] Gutiérrez JJ, Leturiondo M, Ruiz de Gauna S, et al. Assessment of the evolution of end-tidal carbon dioxide within chest compression pauses to detect restoration of spontaneous circulation. PLoS One 2021;16(5):e0251511.

[59] Nolan JP, Soar J, Cariou A, et al. European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care. Intensive Care Med 2015;41(12):2039-2056.

[60] Maddox RR, Williams CK. Clinical Experience with Capnography Monitoring for PCA Patients. Anesthesia Patient Safety Foundation. 2012. Available at: www.apsf.org/article/clinical-experience-with-capnography-monitoring-for-pca-patients/.

[61] Lee LA, Caplan RA, Stephens LS, et al. Postoperative opioid-induced respiratory depression: a closed claims analysis. Anesthesiology 2015;122(3):659-665.