Application of End-tidal Carbon Dioxide Concentration During Cardiopulmonary Resuscitation: A Review of the Literature

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In 2005, the American Heart Association guidelines for advanced cardiac life support emphasized that cardiopulmonary resuscitation (CPR) should include effective chest compression and reasonable ventilation to provide the patient a higher coronary artery perfusion pressure and adequate oxygenation. Therefore, these two indicators became the main factors determining whether CPR was successful. The measurement of the partial pressure of end-tidal CO₂ (PetCO₂) is a non-invasive primary method; it is used to monitor the patient's cardiac output, coronary perfusion pressure, ventilation and systemic metabolic function during resuscitation. In 1999, the National Association of Emergency Medical Service Physicians recommended that PetCO₂ monitoring be standard in pre-hospital care and in emergency departments. We will review the literature on the measurement of PetCO₂ and the evolution of monitoring as well as the use of PetCO₂ for monitoring efficacy in CPR. This information is used to substantiate the clinical utilization and predict the probability of success of endotracheal tube placement in the emergency department.

Key words: cardiac output, cardiopulmonary resuscitation, endotracheal intubation, partial pressure of end-tidal carbon dioxide, prognosis

Introduction

During cardiac arrest, capnometry and capnography can safely and conveniently monitor cardiac output and respiratory function changes in a non-invasive, randomized way. In terms of ease and accuracy of data reading, capnography has many advantages.

Here we will review current laboratory and clinical studies of the evolution of CO₂ (carbon dioxide) monitoring in experimental animals and clinical usage and prospects of continuous PetCO₂ (partial pressure of end-tidal CO₂) monitoring with a capnograph to observe alterations in cardiopulmonary circulation in a patient being resuscitated.

Breathing CO₂ Measurement

In 1943, Luft used infrared absorption spectra to develop a device that measures and records breathing CO₂ (1). After 1970, capnometry was used to investigate anesthesia accidents or injury by anesthesiologists (2-4). Later, in 1985, Weil et al
found a close correlation between end-tidal CO$_2$ partial pressure and the cardiac output index$^6$; thereafter, it was applied widely in animal and human CPR (cardiopulmonary resuscitation) studies$^{(1,6-9)}$. A device is used to measure the partial pressure of CO$_2$ during the last period of the breathing, called the end-tidal CO$_2$ pressure (PetCO$_2$) (Fig. 1). This value is used to assess the function between pulmonary vascular plexus perfusion and pulmonary alveolar diffusion, the actual cardiac output volume, and whether the ventilation pathway from the mouth and nose to the alveoli is clear$^{10}$. Furthermore, PetCO$_2$ monitors may detect an anoxic crisis before clinical symptoms appear and earlier than the frequently used pulse oximeter$^{11}$.

Breathing CO$_2$ measurement

There are two systems that can be used to measure the breathing CO$_2$$^3$: (1) Chemical measurement using the carbonic acid produced by CO$_2$, in which the pH value changes the color of the reagent; this is called a colorimeter$^{(3,12)}$. (2) Physical measurement using infrared spectrophotoscopy is widely accepted. Furthermore, there are two measuring methods. A single measurement of PetCO$_2$ is called capnometry$^{(10,12-14)}$ and a continuous measurement with a CO$_2$ rhythmic wave graph is called capnography (capnogram)$^{(3,10,12)}$ (Fig. 2).

Normal breathing capnogram/capnography

CO$_2$ detected by a capnograph is visualized by plotted wave changes. The graph is divided into four phases and an end-tidal point (Fig. 2)$^{(10,12)}$. In the figure, the lower flat region from points A to B is called phase I or the basic phase. This means there is nearly no CO$_2$ detected in the expired air from the tracheal space or the anatomical and functional dead spaces of the bronchial and alveolar cavity. The slope from points B to C is phase II or the ascending phase. When CO$_2$ expired

![Fig. 1](image-url)
End-tidal carbon dioxide in cardiopulmonary resuscitation

by the alveoli mixes into the air in the bronchi and trachea, the measurable CO$_2$ partial pressure in the capnograph increases rapidly, leading to a steep upstroke on the graph. Near the end of exhalation, the detected gas gradually becomes the simple alveolar CO$_2$ concentration, and the curve gradually flattens, forming a plateau from points C to D, which is phase III or the plateau phase. The peak point D in this phase is situated at the end point of expiration called the end-tidal point. The partial pressure of CO$_2$ detected at this point is called the PetCO$_2$. The value should be close to the partial pressure of alveolar CO$_2$ (PACO$_2$). When the patient starts inspiration, from points D to E, a large amount of fresh air rapidly enters the alveoli and the CO$_2$ concentration curve drops nearly perpendicularly in phase IV or the downstroke phase$^{(10,12)}$.

The Evolution from PetCO$_2$ Monitoring to Clinical Application

When the total metabolic rate, cardiovascular circulation and respiration are all normal in an individual, the breathing CO$_2$ production should be a constant value. If the breathing CO$_2$ concentration changes suddenly, at least one of three criteria have caused an alteration$^6$.

The relationship with cardiac output

Weil et al.$^9$ in 1985 and Gudipati et al.$^{15}$ in 1988 proved that PetCO$_2$ and cardiac output were positively correlated in pigs. When the cardiac output returned during resuscitation, the PetCO$_2$ showed an overshoot phenomenon, increasing to a level higher than the reference value$^{15}$ (Fig. 3). Falk et al observed the records of 10 severely ill patients who experienced 13 episodes of CPR and found the PetCO$_2$ dropped during cardiac arrest and recovered rapidly with a re-beating heart, followed by a PetCO$_2$ overshoot phenomenon$^9$. There are two explanations for this phenomenon: (1) Persistently low arterial perfusion produces acidemia which leads to pulmonary vascular plexus dilation and decreases the functional dead space in the alveoli in the pulmonary cavity followed by flare-up of the PetCO$_2$. (2) A large amount of CO$_2$ accumulates in the tissues. It diffuses into the blood in the veins, is brought to the pulmonary vascular plexus, and diffuses into the alveoli where it brings out a temporary CO$_2$ concentration peak.

The relationship between chest compression efficiency and PetCO$_2$

In 2005 at the University of Chicago Hospitals,
Abella et al studied 67 cardiac arrest patients who received CPR and discovered that the artificial chest compression rate was tremendously uneven. In the first 5 minutes of the compression, on average patients received less than 80 chest compressions per minute for 39 seconds and more than 110 chest compressions per minute for 109 seconds. Also, within these 5 minutes, the chest compression did not reach the required depth of 38mm for about 2 minutes. Hence, clinically, it is very difficult to achieve standard, effective external cardiac massage. In 1975, Kalanda observed three consecutive capnographs in patients who received CPR with non-stop external cardiac compression from different medical personnel. It was found that when a staff member was exhausted, the PetCO$_2$ value dropped significantly; when a new staff member began compression, the cardiac output increased again and the PetCO$_2$ value also significantly increased. Therefore, he suggested that continuous capnography monitoring be used for all patients under resuscitation. Sander et al also performed 35 episodes of CPR (one patient experienced 2 cardiac arrest events) on 34 patients with cardiac arrest. It was found that the average PetCO$_2$ value for the 9 patients with successful resuscitation was 15±4mmHg and for the 26 patients with failed procedures was 7±5mmHg.

These clinical data demonstrate that the cardiac output of patients with different body types who receive CPR from different medical personnel should be monitored and a fixed standard emergency procedure should not be followed. PetCO$_2$ detected by capnography should be a main parameter to monitor the rapid variation in cardiopulmonary circulation volume during CPR to evaluate whether chest compression generates enough cardiac output for a patient under resuscitation; it may be more reasonable and effective than counting the frequency and looking at the depth of external cardiac compression.

**As a blood circulation recovery index**

During cardiac arrest, the cardiac output
provided by chest compression is about 1/3 of normal\(^{15,20}\). When chest compression is effective, the patient's heartbeat increases, pulmonary blood perfusion markedly increases, the ventilation/perfusion ratio moves toward the normal value (V/Q=1), and the detected PetCO\(_2\) rises\(^{9,15}\). Once the body has obtained a sufficient cardiac output, the PetCO\(_2\) will significantly elevate and the overshoot phenomenon appears within a few seconds (Fig. 3)\(^{8,9,15}\). The PetCO\(_2\) goes to an unusually high level within seconds after the heartbeat returns on the electrocardiogram and it returns earlier than the blood pressure or the oxygen concentration in the arterial blood. Therefore, PetCO\(_2\) can be the first accurate, rapid index to monitor whether cardiopulmonary blood perfusion has adequately recovered\(^{8,9,15,21}\).

**Identifying asphyxia-induced cardiac arrest or fatal arrhythmia- associated cardiac arrest**

Grmec et al. found that when patients with asphyxia-induced cardiac arrest received CPR, the average PetCO\(_2\) at the start was 66.4±17.3mmHg; but, for patients with life threatening arrhythmias, the PetCO\(_2\) dropped to 16.5±9.2mmHg. After
performing CPR for a minute, the average PetCO\textsubscript{2} of the former was 29.1±4.9mmHg and the latter, 24.2±5.1mmHg; at this time, no statistically significant difference was found between them\textsuperscript{(22)}.

In asphyxia-induced cardiac arrest, respiratory failure occurs earlier than in cardiac arrest; therefore, when the cause of asphyxia is excluded, the alveolar gas rapidly exchanges with the external air and a massive amount of CO\textsubscript{2} is washed out of the respiratory tract, leading to a PetCO\textsubscript{2} overshoot\textsuperscript{(22,23)}. It can even rise to double the normal value\textsuperscript{(22,24)} (the normal value is about 40mmHg). When a life threatening arrhythmia stops the heart, the respiratory tract still functions normally, but the cardiac output is low and the PetCO\textsubscript{2} is usually half the normal value\textsuperscript{(22,24)}\textsuperscript{.} Therefore, one minute before performing CPR, the abnormal PetCO\textsubscript{2} value may already identify whether the arrest is associated with asphyxia or an arrhythmia.

**Prediction of CPR successful rate**

The majority of clinical researchers agree that the PetCO\textsubscript{2} can be the survival index for a patient receiving CPR\textsuperscript{(8,15,21,25-28)}\textsuperscript{.} Mally et al. observed 600 cardiac arrest patients; multivariate analysis found that patients with higher PetCO\textsubscript{2} values and higher average arterial pressures tended to have better outcomes\textsuperscript{(29)}\textsuperscript{.} Levine et al. studied 150 patients who presented with only cardiac electrical activity without a pulse; after 20 minutes of advanced cardiac life support, the final average PetCO\textsubscript{2} value of the survivors was 32.8±7.4mmHg; for non-survivors the value was 4.4±2.9mmHg. The researchers concluded that for those who receive more than 20 minutes of advanced cardiac life support, a PetCO\textsubscript{2} ≤ 10mmHg may be the lowest threshold predicting patient survival. Its sensitivity, specificity, positive predictive value and negative predictive value all reached 100%\textsuperscript{(27)}\textsuperscript{.} Other researchers also agreed with that if the PetCO\textsubscript{2} stays between 10 and 15mmHg or goes even lower during CPR\textsuperscript{(26,28)}, the patient will definitely not survive. If cardiac electrical activity is seen but no pulse is detected and the PetCO\textsubscript{2} value stays ≤ 10mmHg in spite of continuous resuscitation, stopping CPR should be seriously considered\textsuperscript{(26, 27)}.

**Application of PetCO\textsubscript{2} Monitoring in the Emergency Department**

**Verifying endotracheal tube position**

Usually, endotracheal intubation must be done quickly. If the endotracheal tube is wrongly inserted into the esophagus, further hypoxia may lead to irreversible brain damage or death. Under noisy, busy conditions, the rate of insertion the endotracheal tube into the esophagus is as high as 8.7% in ordinary procedures in the emergency room\textsuperscript{(30)}\textsuperscript{.} Therefore, conventional methods to assure correct positioning of the endotracheal tube, such as auscultation, are not absolutely reliable, and portable chest radiography investigation is limited by manpower and time.

Li investigated 10 reports on emergency intubation from 1966 to 1999 and found that the sensitivity for PetCO\textsubscript{2} recorded by capnometry or capnography in identifying the position of an endotracheal tube was 93% (CI 92-94%), the specificity was 97% (CI 93-99%), the false negative rate (correct positioning wrongly assumed to be esophageal intubation) was 7%, and the false positive rate (esophageal intubation wrongly thought to be correct) was 3%\textsuperscript{(31)}\textsuperscript{.} In contrast, in cases in which colorimeters were used to check the position of the endotracheal tube, false negatives were found in 13-28% of cardiac arrest patients, especially in those with long cardiac arrests\textsuperscript{(32-34)}\textsuperscript{.}

The PetCO\textsubscript{2} detected by capnogram has 100% sensitivity even under low cardiovascular perfusion\textsuperscript{(10,32)}\textsuperscript{.} For a long cardiac arrest, the specificity of the graph in recognizing an
esophageal intubation has not been confirmed. Although the presence of the four phases of the PetCO\textsubscript{2} wave may ensure a tracheal intubation, absence of the four phases could indicate either esophageal intubation or tracheal intubation with a long absence of cardiopulmonary circulation with no CO\textsubscript{2} exchange in the alveoli. The patient could have already died\textsuperscript{(5)} (Fig. 4). Currently, there is no single tool with 100% sensitivity and specificity. Objective comparison with other tools shows that a capnogram is a beneficial, efficient instrument to identify the position of the endotracheal tube.

**Monitoring of CPR Quality**

The final outcome of CPR will decide if a patient lives or dies, and becomes healthy or bedridden. Finding a safe, accurate method to monitor CPR quality is an important undertaking. Researchers have accepted PetCO\textsubscript{2} in monitoring cardiopulmonary efficiency (1) as an index of automatic circulation recovery\textsuperscript{(9,15,21)}; (2) to predict the survivorship of resuscitated patients\textsuperscript{(8,21,25-27)}; (3) to identify whether the cause of the problem is respiratory failure or cardiac arrest\textsuperscript{(22,23)}; and (4) to monitor chest compression quality\textsuperscript{(6,9,15)} and adequacy for cardiac output during CPR\textsuperscript{(1,35)}.

A PetCO\textsubscript{2} graph provides a rapid, accurate and identifiable conclusion on whether CPR actions are appropriate.

**Limitations of PetCO\textsubscript{2} Monitoring**

False negative false positive problems warrant attention when measuring PetCO\textsubscript{2} to ascertain the endotracheal tube position.

Garnett\textsuperscript{(36)} et al. found that esophageal intubated dogs fed a carbonated drink were wrongly thought to have successful endotracheal intubation because of a high PetCO\textsubscript{2}, a false positive result. The PetCO\textsubscript{2} wave did not present the typical four phase picture and the rapidly released CO\textsubscript{2} had a dropping curve instead\textsuperscript{(5)}. Intravenous injection of NaHCO\textsubscript{3} may produce a temporary rise in the PetCO\textsubscript{2}\textsuperscript{(12)}, so care must be taken to identify this misleading capnography result.

Clinically, pulmonary vascular plexus perfusion is reduced in shock, pulmonary embolism and cardiac arrest. The denominator of the ventilation/perfusion ratio decreases and the ratio increases (V/Q>1), meaning that the functional dead space in the lungs is getting larger\textsuperscript{(5)}. Under those circumstances, the detected PetCO\textsubscript{2} is significantly lower than the PaCO\textsubscript{2} and the CO\textsubscript{2} gap is usually greater than 5mmHg\textsuperscript{(14)}, causing a false negative interpretation. This problem must be remembered when PetCO\textsubscript{2} is used to differentiate tracheal from esophageal intubation in these patients.

Experimental mice given an epinephrine injection during CPR were found to have an increased arteriovenous shunt in the pulmonary vascular plexus that impaired the effective pulmonary perfusion. The pulmonary functional dead space became larger, the ventilation/perfusion ratio increased, and the PetCO\textsubscript{2} dropped temporarily, which resulted in a significant gap compared with the PaCO\textsubscript{2}\textsuperscript{(38)}. The phenomenon described above has also been shown in a pig model\textsuperscript{(39)}. However, would a human patient under resuscitation have the same reaction when epinephrine is applied? A 2007 report found that vasopressin combined with epinephrine resulted in lower PetCO\textsubscript{2} levels and poorer outcomes\textsuperscript{(40)}; however, during the resuscitation many other drugs were used, which may have obscured the single effect of epinephrine in the study.

**Conclusion**

PetCO\textsubscript{2} monitoring from pre-hospital emergency care until arrival at the emergency department has been widely discussed. It is thought to be the fifth vital sign for patients.
In the latest guidelines for Advanced Cardiac Life Support (ACLS)\(^{(19)}\), PetCO\(_2\) measuring instruments and methods such as colorimeters, capnometry and capnography are all reported useful in checking the position of the endotracheal tube and are all thought to be Class IIa evidence by a majority of clinicians. The National Association of Emergency Medical Service Physicians recommends that, with normal blood circulation, capnometry is the best method to check the position of the endotracheal tube; however, for patients who have lost normal blood circulation, capnography would be the better choice. Capnography is a convenient and reliable monitoring tool in continuously monitoring the accuracy and efficacy of CPR and is widely accepted. The use of this technique can improve the CPR success rate\(^{(8,9,21,37)}\).

Academic units and clinical departments of emergency and critical care medicine in Taiwan should reevaluate the importance of non-invasive PetCO\(_2\) monitoring. It is hoped that the current review article may lead clinicians to use non-invasive PetCO\(_2\) capnogram monitoring to ensure suitable treatment during resuscitation, and thus improve the survival, life quality, and living efficacy of patients.

References

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潮氣末二氧化碳濃度於心肺復甦的應用

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2005年美國心臟醫學會於新版高級救命術(ACLS)中強調：高品質心肺復甦術必需包含高效率的胸部按壓以及合理的換氣量，維持較高的冠狀動脈灌注壓和充足的血氧含量。非侵襲性潮氣末二氧化碳分壓 (partial pressure of end- tidal CO₂, PetCO₂)可立即評估心輸出量及間接瞭解冠狀動脈灌注量和病人的呼吸系統及代謝功能，所以被列為必要之監測工具。1999年國際緊急醫療醫師協會亦建議：將PetCO₂監測列為院前及急診中緊急照護必備的標準程序。我們將回顧PetCO₂的測量，潮氣末二氧化碳分壓監測至臨床運用的演進。寄望藉此提醒我們：PetCO₂於進行院外或急診室心肺復甦時，用來監測體外心臟按壓的有效性及確認氣管內插管的位置，有其重要受到重視的特色。

關鍵詞：心輸出量，心肺復甦術，氣管內插管，潮氣末二氧化碳分壓，預後