Expired carbon dioxide: a noninvasive monitor of cardiopulmonary resuscitation

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ABSTRACT  End-tidal CO₂ concentration (ETCO₂) may serve as a simple noninvasive measurement of the blood flow generated by precordial compression during cardiopulmonary resuscitation (CPR). In a mechanically ventilated porcine preparation of ventricular fibrillation, onset of fibrillation was associated with a rapid decrease in ETCO₂ from 4.0 ± 0.2% to less than 0.7 ± 0.2%. With precordial compression, it increased to 1.9 ± 0.3%. Animals that were successfully defibrillated after 12 min of CPR demonstrated an immediate increase in ETCO₂. The ETCO₂ increased from 1.9 ± 0.3% to 4.9 ± 0.3% over an interval of between 30 and 60 sec. These changes in ETCO₂ were closely related to proportionally similar decreases and increases in cardiac output (CO), and a close correlation between ETCO₂ and CO was demonstrated (r = .92). A similar highly significant correlation between ETCO₂ and CO was also demonstrated during open-chest cardiac massage (r = .95). ETCO₂ therefore serves as a noninvasive measure of pulmonary blood flow and therefore CO. In 17 successfully resuscitated animals, ETCO₂ during precordial compression averaged 1.7 ± 0.2%, whereas it was only 0.5 ± 0.1% in five animals in whom resuscitation procedures were unsuccessful (p<.001). Accordingly, ETCO₂ prognosticates outcome during CPR and immediately identifies restoration of spontaneous circulation. Circulation 77, No. 1, 234–239, 1988.

PRIMARY INTERVENTIONS during cardiopulmonary resuscitation (CPR) include external ventilation after establishing airway patency, and precordial compression.¹ It is precordial compression that maintains forward flow of blood in amounts that temporarily sustain the viability of major organs and especially the heart and the brain. The cardiac output measured during experimental closed-chest cardiac massage has ranged between 17% and 27% of prearrest values.²⁻⁵ Except for arterial or intracardiac pressure measurements, there are currently no reliable options for continuously monitoring the efficacy of precordial compression in terms of the blood flow that is generated. We therefore searched for practical, and preferably noninvasive, options with which the efficacy of precordial compression could be quantitatively monitored.

In prior studies in a porcine preparation of cardiac arrest and subsequently on human patients, measurements of arterial blood gases demonstrated hypercarbia in mixed venous blood and hypocarbia in arterial blood during CPR.⁶⁻⁹ There was venous acidemia and arterial alkalemia. A large vena arterial Pco₂ gradient was associated with decreases in end-tidal CO₂ concentration (ETCO₂). We hypothesized that this was related to a critical reduction in pulmonary blood flow during CPR accounting for a critical curtailment of CO₂ excretion.¹⁰¹¹ In the present study, we observed a close relationship between ETCO₂ and cardiac output. We further demonstrated the potential usefulness of ETCO₂ as a prognosticator of resuscitability. Moreover, ETCO₂ was an immediate indicator of successful resuscitation. These studies served as a basis for human application of ETCO₂ measurements during cardiac arrest, which confirmed its clinical applicability.¹²

Methods

Animal preparation. Minnesota minipigs weighing between 20 and 35 kg were fasted for 12 hr. Anesthesia was induced after intramuscular injection of between 10 and 15 mg/kg body weight of ketamine followed by slow intravenous injection of 20 to 30 mg/kg pentobarbital sodium into an ear vein. Neuro-muscular blockade was induced after intravenous injection of 0.09 mg/kg pancuronium bromide. A cuffed endotracheal tube was advanced
into the trachea and each animal was ventilated with a Bennett MA-1 (volume controlled) ventilator at a frequency of 12 to 15/min, a tidal volume of 10 to 15 ml/kg, a maximal flow rate 40 liters/min, and FIO2 of 0.5. Minute volume was adjusted to maintain Paco2 in the range of 35 to 45 mm Hg and then held constant throughout the experiment. Anesthesia and neuromuscular blockade were maintained with additional intravenous doses of pentobarbital given at 30 min intervals and 0.05 mg/kg pancuronium at 1 hr intervals as needed.

The experimental preparation is diagrammatically illustrated in figure 1. With an aseptic technique, the right femoral vein was surgically exposed. A flow-directed thermodilution catheter (Allied Instrumentation Laboratory 7F Model 44166-05 Lexington, MA) was advanced into the vein and, under oscillographic guidance, it was flow directed into the pulmonary artery. Through the right femoral artery, a Cordis Ducov 7F catheter (Model 521-735-7F) was inserted into the descending thoracic aorta and secured. The right internal jugular vein was then surgically isolated; a 5F balloon-tipped catheter (Cook CPV 4.8-50-56A Bloomington, IN) was inserted through an introducer sheath and flow directed into the pulmonary artery under oscillographic control. It was subsequently withdrawn into the right ventricle. The 7F introducer sheath, 25 cm in length, was then inserted over the balloon-tipped catheter into the right ventricle and secured. The right ventricular balloon-tipped catheter was then removed and the introducer sheath was capped. This sheath provided the entry point for a wire electrode for ventricular fibrillation. All catheter positions were confirmed with fluoroscopic image intensification. Patency of catheters was maintained with minimal pressure flushes (Intraflow, Gould Inc. Oxnard, CA.,) with saline containing 10 IU of heparin per milliliter.

**Blood flow measurement.** Cardiac output was measured by the constant infusion thermodilution technique described by Pavek et al. and Ganz and Swan. Physiologic salt solution, maintained at a temperature of approximately 4°C with slushed ice, was infused into the right atrium at a rate of 40 ml/min with a peristaltic pump (Baxter Travenol Model 4-6901A, Deerfield, IL) that was calibrated to deliver this volume with an accuracy of ± 1%. During the infusion period, the injectate temperature was continuously measured by a thermistor (Injectate Sensor, Allied Instrumentation Laboratory Model 38560, Lexington, MA) located in line with the right atrial port of the pulmonary artery catheter. The temperature of the blood and subsequently the blood-indicator mixture was measured in the pulmonary artery. The accuracy of this method was established by studies in vitro on three isolated porcine hearts in which directly measured flow and measurements of flow with the constant infusion thermodilution technique were compared. Over ranges of 100 to 1500 ml/min, the directly measured and thermodilution flow measurements correlated very highly (r = .99, p<.001).

**Expired gas measurement.** Expired CO2 concentration was continuously measured with an infrared absorption CO2 analyzer (Model 200 Allied Instrumentation Laboratories, Lexington, MA) and tidal volume was measured with a Fleisch pneumotachometer (Model 7319, Dynasences Corp., Huntington Beach, CA).

The CO2 analyzer was calibrated with precision-analyzed gases containing 0%, 5%, and 10% CO2 (Air Products, Allentown, PA). Separate experiments demonstrated maximum differences of 0.2% over the range of 0.1% to 6.0% CO2 concentration. The side-wall sample manifold of the CO2 analyzer was adapted to the endotracheal tube. Gas was analyzed at a flow rate of 200 ml/min. The pneumotachometer was connected to the expiratory port of the ventilator tubing to confirm constancy of minute volume.

**Experimental CPR.** Before ventricular fibrillation, cardiac output was measured by continuous infusion technique. ETCO2 and aortic and right atrial pressures were monitored together with pulmonary arterial and aortic blood gases. Ventricular fibrillation was induced by a 5 mA alternating current delivered to the right ventricular endocardium. Cardiac arrest was confirmed when electrocardiographic ventricular fibrillation was accompanied by a decline in aortic systolic pressure to less than 25 mm Hg and a decline in pulse pressure to less than 5 mm Hg. The FIO2 was increased to 1.0 and the volume-controlled ventilator was synchronized to the chest compressor with a 5:1 compression/ventilation ratio. Chest compression was initiated after 1

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**FIGURE 1.** Diagram of experimental procedure.
min of ventricular fibrillation with a commercial piston device (Thumper 1003, Michigan Instruments, Grand Rapids, MI) at a rate of 60/min, an equal compression/relaxation interval (i.e., 50% duty cycle), and a compression depth between 25% to 30% of the animal’s anterior-posterior chest width. Cardiac output was measured at 1, 5, and 9 min during CPR and related to continuously measured ETCO₂. After 12 min of CPR, i.e., 13 min after ventricular fibrillation had been induced, direct-current countershocks were delivered to the anterior chest in power increments of 40, 80, 160, and 320 J with a direct-current defibrillator (Model 911 Physio-Control, Redmond, WA). In animals that were successfully resuscitated, cardiac output measurements were repeated at 6 min after resuscitation. Surviving animals were killed after 24 hr by injection of pentobarbital. Autopsy was performed on all animals. Autopsy revealed no visceral injury in either resuscitated or unresuscitated animals, except that rib fractures without gross hemorrhage were almost uniformly noted.

In separate experiments, laparotomy was performed after a midline incision. Anesthesia, mode of ventilation, tidal volumes, and the frequency of both ventilation and cardiac compression were identical to those already described. A large window was surgically created with the aid of electrocautery in the tendinous portion of the diaphragm (figure 2). After 1 min of electrically induced ventricular fibrillation, direct cardiac massage was performed through the diaphragmatic window for 5 min. Electrical conversion with direct-current countershock was then attempted. ETCO₂ was continuously monitored and cardiac index was measured at 1 and 5 min after start of direct cardiac massage.

**Statistical analysis.** The differences in cardiac index and ETCO₂ between resuscitated and nonresuscitated animals were analyzed by the Student t test for unpaired measurements. ETCO₂ in resuscitated and nonresuscitated animals was analyzed by repeated measurement analysis of variance by Wilk’s method. The effects of time and die-by-time were not significant. Linear regression analyses were used for computation of the correlation between ETCO₂ and cardiac index. Measurements are reported as the mean ± SEM.

**Results**

**End-tidal CO₂.** The results of a typical experiment in a 23 kg female minipig are shown in figure 3. Arterial and intracardiac pressures and the electrocardiogram, together with ETCO₂, were continuously monitored. From a precardiac arrest value of 3.3%, ETCO₂ decreased to less than 0.2% immediately after onset of ventricular fibrillation. When precordial compression was started, ETCO₂ immediately increased to 1.7%, reaching a plateau level within 90 sec. After electrical
TABLE 1
Observations in 22 pigs (mean ± SEM)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (-5 min)</th>
<th>During CPR</th>
<th>After resusc. (+6 min of resusc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+1 min</td>
<td>9 min</td>
</tr>
<tr>
<td>Aortic PCO₂ (mm Hg)</td>
<td>40±1.0</td>
<td>31±1.0</td>
<td>34±2.0</td>
</tr>
<tr>
<td>PvCO₂ (mm Hg)</td>
<td>47±1</td>
<td>52±1</td>
<td>49±2</td>
</tr>
<tr>
<td>PvCO₂ - aortic PCO₂ (mm Hg)</td>
<td>7±0.6</td>
<td>20±2.0</td>
<td>15±2.0</td>
</tr>
<tr>
<td>CI (ml/kg/min)</td>
<td>69±4</td>
<td>18.4±2^</td>
<td>26±2^</td>
</tr>
<tr>
<td>ETCO₂ (%)</td>
<td>4.0±0.2</td>
<td>1.0±0.2</td>
<td>1.87±0.3</td>
</tr>
</tbody>
</table>

Cl = cardiac index.
Except where shown, values are based on measurements in 22 animals.
^16 animals; ^18 animals; ^17 animals.

defibrillation and return of spontaneous circulation, ETCO₂ rapidly increased. After a transient overshoot, the ETCO₂ returned to approximately the baseline value. The ETCO₂ overshoot was associated with simultaneous increases in both aortic PCO₂ and PvCO₂ (table 1).

Cardiac index. The relationship between cardiac index and ETCO₂ in a representative study is shown in figure 4. As the cardiac index decreased to 30% of prearrest values, there was a corresponding decrease in ETCO₂ from 100% to 32%. After successful resuscitation, cardiac index increased to 67% and ETCO₂ increased to 118% of precardiac arrest levels.

Cardiac index, measured at 1 and 9 min after the beginning of precordial compression in 22 animals, averaged 27 ± 1% and 38 ± 4% of prearrest values, respectively. ETCO₂ was 27 ± 5% and 43 ± 8% of the precardiac arrest value at 1 and 9 min after beginning precordial compression. Six minutes after spontaneous circulation was reestablished, cardiac index increased to 88 ± 5% and ETCO₂ increased to 121 ± 80% of precardiac arrest values (table 1). The correlation between ETCO₂ and cardiac index for the 22 individual animals based on four or five paired measurements, one of which was obtained before ventricular fibrillation, three of which were obtained during CPR, and one of which was obtained at 6 min in successfully resuscitated animals, ranged from 0.75 to 0.99 and averaged 0.92 ± 0.07 (p<.001). Accordingly, there was good predictability of cardiac index from ETCO₂ [ETCO₂ = (0.069)CI - 0.167].

Effect on resuscitability. Highly significant differences in ETCO₂ (p<.007) measured at 1, 3, 5, 9, and 11 min during CPR in resuscitated and nonresuscitated animals were also observed (figure 5). ETCO₂ exceeded 1% after 12 min of CPR in 15 animals and each of these animals was successfully resuscitated. Among seven animals in which ETCO₂ was less than 1%, only two animals were successfully resuscitated.

The cardiac index measured 5 min after start of precordial compression for resuscitated animals averaged 31 ± 2 ml/kg/min. In animals that were not successfully defibrillated, it was only 19 ± 4 ml/kg/min (p<.02).

Open-chest cardiac massage. In a separate study of five animals, measurements were obtained during direct
manual compression of the heart, i.e., open-chest cardiac massage. ETCO₂ and cardiac index were measured before cardiac arrest, 1 and 5 min after beginning direct cardiac massage, and after restoration of spontaneous circulation (figure 6). Proportional changes in ETCO₂ and cardiac index were also demonstrated in open-chest animals during direct cardiac compression. The correlation coefficients for the relationship between ETCO₂ and cardiac index for the five individual animals during direct cardiac compression ranged from .91 to .98 and averaged .95 ± .014.

**Discussion**

Smalhout and Kalenda\(^1\) and Kalenda\(^2\) recorded capnograms during cardiac arrest and CPR in three patients. They observed decreases in ETCO₂ when the resuscitator became fatigued. When resuscitation was continued by another operator, there was an impressive increase in ETCO₂. After spontaneous circulation was established, a rapid rise in ETCO₂ was observed. Kalenda speculated that ETCO₂ was related to pulmonary blood flow and therefore cardiac output. Wiklund et al.\(^1\) also observed decreases in ETCO₂ during cardiac arrest. When epinephrine was administered during CPR, an increase in ETCO₂ was frequently observed. These investigators speculated that the increases in ETCO₂ were related to either improvement in cardiac output or increased CO₂ production.

Our own studies were performed without awareness of these reports. We were led to examine ETCO₂ because we observed increased mixed venous (PvCO₂) and decreased aortic PCO₂ during CPR. We hypothesized that the increases in PvCO₂ were due to a critical reduction in cardiac output and therefore a critical reduction in pulmonary blood flow such that CO₂ clearance was critically reduced.\(^1\) In the present study we confirmed that there was a highly significant relationship between cardiac output and therefore pulmonary blood flow and ETCO₂ during both external precordial compression and open-chest cardiac massage.

Sanders et al.\(^2\) observed a high correlation between ETCO₂ and coronary perfusion pressure. Coronary perfusion pressure was computed as the difference between aortic diastolic and right atrial pressure. Ditchey et al.\(^2\) had previously demonstrated that with increasing force of precordial compression during CPR, both systemic and coronary blood flow increased. This would explain the observed correlation between ETCO₂, cardiac output, and coronary perfusion pressure.

According to the current standards of CPR, palpation of carotid pulses is cited as the only option for monitoring of the adequacy of blood flow generated by precordial or direct cardiac compression. In the setting of CPR, palpable pulses represent the maximum (compression systolic) pressures only. However, MacKenzie et al.,\(^2\) in studies on three patients, found that compression systolic arterial pressures during CPR failed to correlate with cardiac output. Del Guercio et al.\(^3\) also demonstrated poor correlations between systolic pressure and cardiac output during CPR. Errors stem, at least in part, from mechanical transmission of pulse waves that do not reflect arterial blood flow. The presence of a palpable pulse therefore confirms continuity of a fluid-filled vessel but not necessarily blood flow, because an artery pulsates even at its site of ligation.\(^2\) Accordingly, current evidence does not support the assumption that palpable carotid systolic pressure pulses serve as a reliable indication of viable systemic flow.

Consequently, there is an important need for an objective monitor that reflects systemic blood flow generated during CPR. The present study demonstrated that ETCO₂ serves as such a monitor during experimental CPR. Preliminary observations in our center on human patients during CPR confirm its clinical applicability. ETCO₂ has the additional advantage of being a noninvasive monitor. As speculated some 11 years ago by Smalhout and Kalenda,\(^1\) the ETCO₂ may then serve to moderate the CPR procedures such as to ensure that precordial compression produces viable blood flow. Under the controlled conditions of our studies on pigs, the frequency of ventilation, tidal volumes, and a 5:1 compression/ventilation ratio were kept constant. However, it may be difficult to maintain comparable consistency in the clinical setting such that distribution of ventilation, the airway impedance, and the frequency of ventilation may vary and thereby alter
ETCO₂ independently of pulmonary blood flow. We have also documented that some pharmacologic interventions, and especially buffer agents, may transiently alter ETCO₂. Increases follow administration of NaHCO₃ and decreases follow administration of the organic, CO₂-consuming buffer tromethamine.* Nevertheless, striking increases in ETCO₂ to levels that exceed prearrest values provide unequivocal evidence that spontaneous circulation has been restored such that precordial compression need not be interrupted to assess whether there has been a return of spontaneous circulation.

We observed marked increases in ETCO₂ together with increases in aortic PaCO₂ and PvCO₂ immediately after successful resuscitation. However, the venoarterial gradient for PaCO₂ was simultaneously decreased. This ETCO₂ overshoot and the concurrent increases in both PvCO₂ and especially aortic PaCO₂ are well explained by washout of CO₂ from poorly perfused tissues.

The success of resuscitation during CPR depends on the efficacy of precordial compression and the cardiac output that is generated by it.24-26 Since these studies demonstrate that ETCO₂ is closely related to cardiac output, ETCO₂ like cardiac output predicts outcome. In the present experiments, when ETCO₂ was maintained at levels that exceeded 25% of precardiac arrest value with ETCO₂ exceeding 1%, all animals were successfully resuscitated.

We conclude that ETCO₂ provides a competent and technically simple, noninvasive monitor that highly correlates with cardiac output under conditions of constant ventilation during experimental CPR. Preliminary data in the clinical setting of CPR validate our observations about the usefulness of ETCO₂ during CPR.12


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