

Efficacy of Chest Compressions Directed by End-Tidal CO₂ Feedback in a Pediatric Resuscitation Model of Basic Life Support

Jennifer L. Hamrick, MD; Justin T. Hamrick, MD; Jennifer K. Lee, MD; Benjamin H. Lee, MD; Raymond C. Koehler, PhD; Donald H. Shaffner, MD

Background—End-tidal carbon dioxide (ETCO₂) correlates with systemic blood flow and resuscitation rate during cardiopulmonary resuscitation (CPR) and may potentially direct chest compression performance. We compared ETCO₂-directed chest compressions with chest compressions optimized to pediatric basic life support guidelines in an infant swine model to determine the effect on rate of return of spontaneous circulation (ROSC).

Methods and Results—Forty 2-kg piglets underwent general anesthesia, tracheostomy, placement of vascular catheters, ventricular fibrillation, and 90 seconds of no-flow before receiving 10 or 12 minutes of pediatric basic life support. In the optimized group, chest compressions were optimized by marker, video, and verbal feedback to obtain American Heart Association-recommended depth and rate. In the ETCO₂-directed group, compression depth, rate, and hand position were modified to obtain a maximal ETCO₂ without video or verbal feedback. After the interval of pediatric basic life support, external defibrillation and intravenous epinephrine were administered for another 10 minutes of CPR or until ROSC. Mean ETCO₂ at 10 minutes of CPR was 22.7±7.8 mm Hg in the optimized group (n=20) and 28.5±7.0 mm Hg in the ETCO₂-directed group (n=20; *P*=0.02). Despite higher ETCO₂ and mean arterial pressure in the latter group, ROSC rates were similar: 13 of 20 (65%; optimized) and 14 of 20 (70%; ETCO₂ directed). The best predictor of ROSC was systemic perfusion pressure. Defibrillation attempts, epinephrine doses required, and CPR-related injuries were similar between groups.

Conclusions—The use of ETCO₂-directed chest compressions is a novel guided approach to resuscitation that can be as effective as standard CPR optimized with marker, video, and verbal feedback. (*J Am Heart Assoc.* 2014;3:e000450 doi: 10.1161/JAHA.113.000450)

Key Words: CPR • end-tidal carbon dioxide • pediatrics • resuscitation

Successful cardiopulmonary resuscitation (CPR) requires the rapid and effective implementation of infrequently used skills in tense, high-stakes situations. During cardiac arrest, high-quality CPR is essential to generate blood flow to vital organs and to achieve return of spontaneous circulation (ROSC).¹ The most critically important CPR skill is the delivery of optimal chest compressions. If chest compression performance is inadequate, resuscitative efforts may fail or

survivors may have permanent neurologic injury. The delivery of effective closed-chest compressions has remained an active area of resuscitation research and the foundation of basic life support since its description >50 years ago.²

Survival to discharge from out-of-hospital cardiac arrest in infants (3%) and children (9%) remains low despite 20 years of research.³ Current American Heart Association (AHA) pediatric resuscitation guidelines emphasize high-quality CPR and recommend chest-compressions at a rate of at least 100 compressions/minute, a depth of at least one-third of the anteroposterior (AP) diameter, minimization of interruptions, and avoidance of excessive ventilation.¹ Unfortunately, adherence to the guidelines for adequate chest compression depth is difficult because the victim's prearrest AP chest diameter is not known and is hard to determine during CPR and because compression depth is difficult to estimate when viewed from above. These and other factors contribute to the delivery of inadequate compression depth by resuscitators.^{4,5} The recommended chest compression rate is also inconsistently achieved by rescuers without the aid of a timing device or invasive monitoring.⁶ The current AHA mantra of “push

From the Department of Pediatric Anesthesiology and Pain Medicine, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, Little Rock, AR (J.L.H., J.T.H.); Department of Anesthesiology/Critical Care Medicine, Johns Hopkins University, Baltimore, MD (J.K.L., B.H.L., R.C.K., D.H.S.).

Correspondence to: Jennifer L. Hamrick, MD, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, 1 Children's Way, Slot 203, Little Rock, AR 72202. E-mail: jlhamrick@uams.edu

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hard, push fast” underscores the difficulty rescuers have in estimating the depth and rate for chest compressions in real-life situations^{5,6} and pediatric simulations.⁴ Given the difficulties described here, it is not surprising that up to 90% of chest compressions have been shown to be inadequate in simulation models⁴ and clinical studies.^{5,6}

The current AHA recommendations for children regarding hand placement, depth, and rate during chest compressions are based on consensus interpretation of the literature⁷ and extrapolation from adult and animal data. A direct correlation between compression depth and CPR effectiveness has not been established in children, and, in some instances, the one-third AP compression depth exceeds that recommended for adults.^{8,9} Even if pediatric studies were available, recommendations would be based on generalizations that fail to account for the victim’s physical and physiologic variability. Chest geometry is not uniform among pediatric patients and may change as a result of ongoing chest compressions. An ideal method for the delivery of chest compressions would take into account patient-specific geometry and hemodynamic realities and would allow for rescuer adaptation as these variables change during resuscitation efforts.

A technically simple, widely available, noninvasive method of real-time physiologic feedback that helps rescuers optimize the delivery of CPR could improve rates of both ROSC and neurologically intact survival after cardiac arrest. End-tidal carbon dioxide (ETCO₂) monitoring is readily available, easily used, and a standard of care in the operating suite and in the critical care setting. When a capnometer is available and the machine is warmed-up, connection to the ventilatory circuit takes <3 seconds.¹⁰ ETCO₂ can be measured during CPR whether ventilating via bag-mask, laryngeal mask airway, or endotracheal tube.^{11–13} In 1978, Kalenda¹⁴ proposed that ETCO₂ could assess pulmonary and, therefore, systemic, blood flow during CPR. Since that time, ETCO₂ has been shown to correlate well with cardiac output,^{15–17} coronary perfusion pressure,^{10,18} and successful resuscitation^{10,15,19–21} in animal models and clinical trials. ETCO₂ monitoring during CPR indicates ROSC without the need to interrupt resuscitative efforts^{14,16,22} and has been used to evaluate the efficacy of different modalities of chest compressions.^{23,24} Despite its potential advantages and suggestions that it can be of benefit when assessing the adequacy of CPR, ETCO₂ monitoring has not been evaluated as a physiologically responsive guide for the delivery of chest compressions.^{3,14} In this study, we compared outcomes of ETCO₂-directed chest compression to those of compressions optimized with a depth marker and video and verbal feedback to ensure compliance with AHA pediatric basic life support (PBLs) guidelines.¹ Outcomes included the ETCO₂ (a surrogate for cardiac output), systemic perfusion pressure (SPP), and the rate of ROSC.

Methods

Animal Preparation

All animal studies were performed with approval from the Animal Care and Use Committee of Johns Hopkins University and all procedures followed were in accordance with institutional guidelines. A total of 40 male piglets 3 to 6 days of age and weighing 2.1±0.38 kg were anesthetized via inhalational induction with 5% isoflurane and a 50:50 mixture of oxygen and nitrous oxide. Pulse oximetry and a 4-lead ECG were placed on the piglet and monitored for the duration of the experiment. After induction of general anesthesia and basic monitor placement, the piglet received 2% isoflurane and a 30:70 mixture of oxygen/nitrous oxide for the duration of the surgical interventions. With the piglet spontaneously breathing anesthesia gas, a tracheostomy was performed and a 3.0- to 3.5-cuffed endotracheal tube was placed in the trachea and secured. The piglet was then placed on pressure-controlled ventilation, and ventilatory parameters were adjusted to maintain an ETco₂ of 35 to 45 mm Hg. The bilateral femoral vessels were then surgically exposed. On one side, catheters were placed in the femoral artery and vein and threaded 12 to 15 cm into the intrathoracic descending aorta and inferior vena cava, respectively. On the contralateral side, a fibrillation wire was advanced until ectopy was observed on the ECG tracing. At the conclusion of surgery, the inspired concentration of isoflurane was decreased to 0.8%. A D5 0.45% normal saline infusion was started at a rate of 10 mL/h through the femoral central venous line, and fentanyl 10 µg/kg and pancuronium 0.3 mg/kg were administered for analgesia and neuromuscular blockade, respectively. The arterial and central venous lines were connected to pressure transducers and zeroed; thereafter, continuous blood pressure and central venous pressure (CVP) were monitored. An arterial blood gas sample was drawn and the ETco₂ was calibrated with the Paco₂; ventilatory parameters were again adjusted to ensure a Paco₂ of approximately 40 mm Hg. Baseline vital signs, including ETCO₂, mean arterial blood pressure (MAP), mean CVP (mCVP), diastolic blood pressure (DBP), heart rate, and rectal temperature, were recorded before initiation of the experimental protocol and at 15-second intervals after the initiation of CPR.

Experimental Protocol

At minimum, 2 piglet experiments were performed per day. The first piglet of the day was randomly assigned to either the ETCO₂-directed or the optimized group, and subsequent piglets were assigned to the alternate group. The piglets were placed on our resuscitation board, and the initial AP diameter was measured by placing the bottom of a rubber band across 2 poles at the maximal sternal height. The measurement was made when the rubber band was parallel to the backboard

and its height on the 2 poles was equal. After the piglets were prepared as described earlier, ventricular fibrillation was induced with a 50-mA alternating current delivered to the right ventricular endocardium. Cardiac arrest was confirmed by a dramatic decrease in ETco₂, electrographic evidence of ventricular fibrillation, and a loss of aortic blood pressure. Ventilation and inhalational anesthesia were discontinued after cardiac arrest was confirmed. After a no-flow interval of 90 seconds, ventilation was resumed at the previous settings with a fractional inspired O₂ of 1.0, and PBLs was started via either the optimized or the ETco₂-directed protocol. Both protocols included an unblinded recorder, who noted the aforementioned vital signs every 15 seconds during resuscitation, and 2 dedicated resuscitators who alternated administration of chest compressions every 2 minutes per AHA recommendations. The same 2 resuscitators administered compressions on any given day. The blinding of the 2 resuscitators depended on the protocol group.

Optimized group

Immediately before induction of ventricular fibrillation, a depth marker was placed at one-third the AP diameter, and a high-fidelity video camera was positioned so that the resuscitator could view chest compressions from the side and ensure that the desired depth was being reached consistently (Figure 1A and 1B). The pulse oximeter and arterial line monitor provided heart rate feedback. Depth feedback was provided with the high-fidelity video monitor and the depth marker. Verbal feedback was also provided by the second resuscitator, who had a lateral view of the chest and depth marker during compression. Chest compressions were performed with 2 thumbs over the sternum and fingers wrapped around the chest, compressing to a depth of one-third the initial AP diameter and rate of 100 per minute (consistent with the minimum recommendations of the AHA). Resuscitators were blinded to the ETco₂ during optimized CPR.

ETco₂-directed group

In the ETco₂-directed group, the resuscitators also placed 2 thumbs over the sternum and the fingers wrapped around the chest, but they modified compression depth, rate, and/or thumb position in real time to obtain maximal ETco₂. No depth marker was present, and the resuscitator's efforts were guided only by the ETco₂ reading. They were blinded to all other monitors and had no video or verbal feedback about compression rate or depth (Figure 1C).

Advanced Life Support

Our initial protocol called for 10 minutes of PBLs before beginning advanced life support (ALS); however, due to a

large number of ROSC piglets in both groups after 10 minutes of PBLs (20 animals, 10 in each group, 75% ROSC), we extended our basic resuscitation time midway through the study to 12 minutes (an additional 20 animals, 10 in each group, 60% ROSC) in hopes of finding lower rates of ROSC and increasing potential differences between techniques. After either 10 or 12 minutes of PBLs, we began ALS, which included external defibrillation (20 J) every 2 minutes and intravenous epinephrine (300 µg) every 4 minutes. Chest compressions were continued as previously described. For analysis, the ROSC group consisted of piglets that, at any point during resuscitation, had ROSC sustained for 20 minutes without intervention. Non-ROSC piglets failed to obtain ROSC after a maximum of 5 defibrillations and 3 doses of epinephrine (10 minutes of ALS). In both groups, arterial blood gases were drawn at baseline, at 8 minutes of PBLs, postresuscitation, and at 20 minutes post-ROSC (when applicable). General inhalational anesthesia was restarted at the time of ROSC.

Postmortem Examination

At the conclusion of each experiment, the ROSC piglets were euthanized with potassium chloride. To determine compression-induced deformity, the same investigators who had measured the prearrest AP diameter measured the postarrest AP diameter. The abdominal and thoracic cavities were examined for internal injuries, catheter location, and tracheostomy tube placement. Traumatic injuries to the heart, lungs, major vessels, and liver were noted.

Statistical Analysis

Data were collected and stored in Microsoft Excel. SPP was calculated as MAP minus mCVP. ETco₂, DBP, MAP, mCVP, and SPP were reported in mm Hg. The MAP and mCVP measurements were recorded from the digital readout of a monitor that uses area under the curve divided by time interval to calculate invasive mean pressures. Relaxation (diastolic) pressures traditionally used to calculate coronary perfusion pressure and to evaluate CVP between compressions during CPR were not available during the basic life support period of most experiments as they were below the detectable limit of the monitor. The calculated SPP would be higher than the actual coronary perfusion pressure. For analysis of the resuscitation statistics and injury statistics, we compared means with an unpaired, 2-sided Student *t* test and binary variables via χ^2 analysis in Microsoft Excel. We analyzed ETco₂, MAP, mCVP, and SPP by using repeated-measures ANOVA with Greenhouse-Geisser correction with 2009 SPSS software. All values are expressed as mean±SD. Missing data points were replaced by the average of the

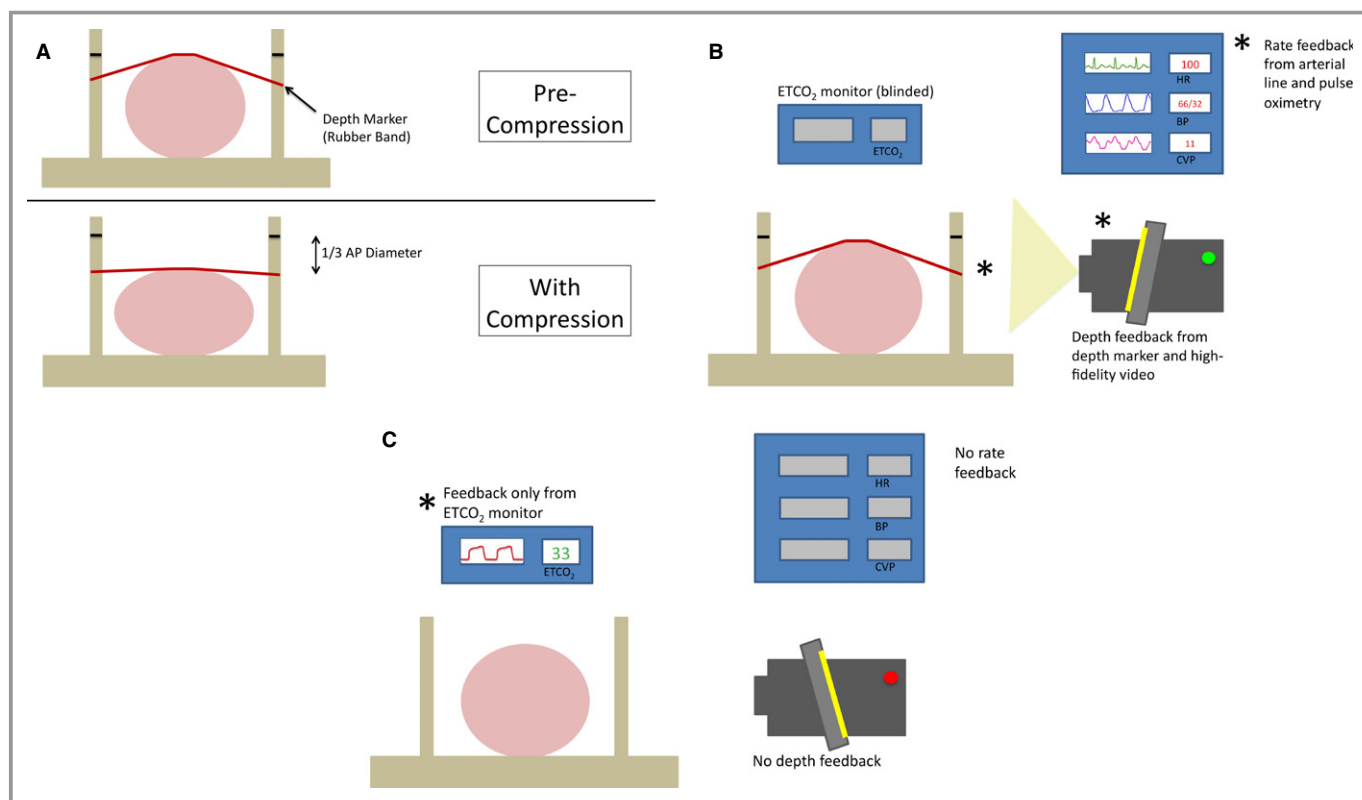


Figure 1. Illustration of experimental setup. A, Optimized CPR model. A piglet is depicted in cross section lying on the resuscitation board. The red line across the anterior chest indicates a rubber band, which served as one depth marker during chest compressions in the optimized standard group. The anteroposterior (AP) chest diameter was measured prearrest, and the rubber band was secured at a depth of one-third of the AP diameter. With compressions, the AHA-recommended compression depth was reached when the rubber band became horizontal across the chest wall. B, The setup to ensure that AHA guidelines were met during resuscitation in the optimized group. Rate feedback was supplied by pulse oximetry and invasive arterial monitoring. Depth feedback was supplied by the depth marker, the high-fidelity video monitor, and verbal feedback from an observer with a view of the lateral chest wall. Resuscitators were blinded to the ET_{CO₂} monitor. Compressions were performed at a depth of one-third of the initial AP diameter at a rate of 100 per minute; compressors were alternated every 2 minutes. C, The setup for resuscitation of piglets in the ET_{CO₂}-directed group. Compression depth, rate, and/or thumb position were modified by resuscitators in real-time to obtain maximal ET_{CO₂}. Resuscitation efforts were guided only by the ET_{CO₂} reading without rate or depth feedback. ECG, pulse oximeter, pressure monitor, and video screen were turned away from resuscitators. Chest compression depth was not measured, and no verbal feedback was provided for this group. AHA indicates American Heart Association; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; ET_{CO₂}, end-tidal carbon dioxide.

values for that parameter from 4 adjacent time points. Any subject who had >10% of total time points with missing data was excluded from analysis. We set statistical significance at $\alpha < 0.05$. No adjustment was made for multiplicity of comparisons when reporting the *P*-values associated with individual time points.

Results

ET_{CO₂} During CPR

The pre-CPR ET_{CO₂} were similar in the optimized and ET_{CO₂}-directed groups (53.0±4.3 versus 53.8±4.2 mm Hg, respectively). Figure 2A illustrates ET_{CO₂} by group. At the onset of

PBLS, both groups started with an ET_{CO₂} of 31.5±2 mm Hg. After 6 minutes of PBLS, ET_{CO₂} values were maintained in the ET_{CO₂}-directed group but steadily declined in the optimized group. The overall difference in ET_{CO₂} between the ET_{CO₂}-directed and optimized groups was not statistically significant (*P*=0.16). Detailed analysis after 6 minutes of CPR showed that the ET_{CO₂}-directed group maintained greater ET_{CO₂} through 10 minutes (6 minutes: 29.1±6.7 versus 26.8±6.1, *P*=0.26; 7 minutes: 29.3±6.7 versus 24.8±7.3, *P*=0.05; 8 minutes: 28.0±7.0 versus 23.0±7.9, *P*=0.04; 9 minutes: 28.3±6.5 versus 23.5±8.4, *P*=0.05; 10 minutes: 28.5±7.0 versus 22.7±7.8, *P*=0.02, *n*=40 for all time points). Figure 2B shows the ET_{CO₂} for both groups by ROSC status. In the ET_{CO₂}-directed group, both the ROSC and

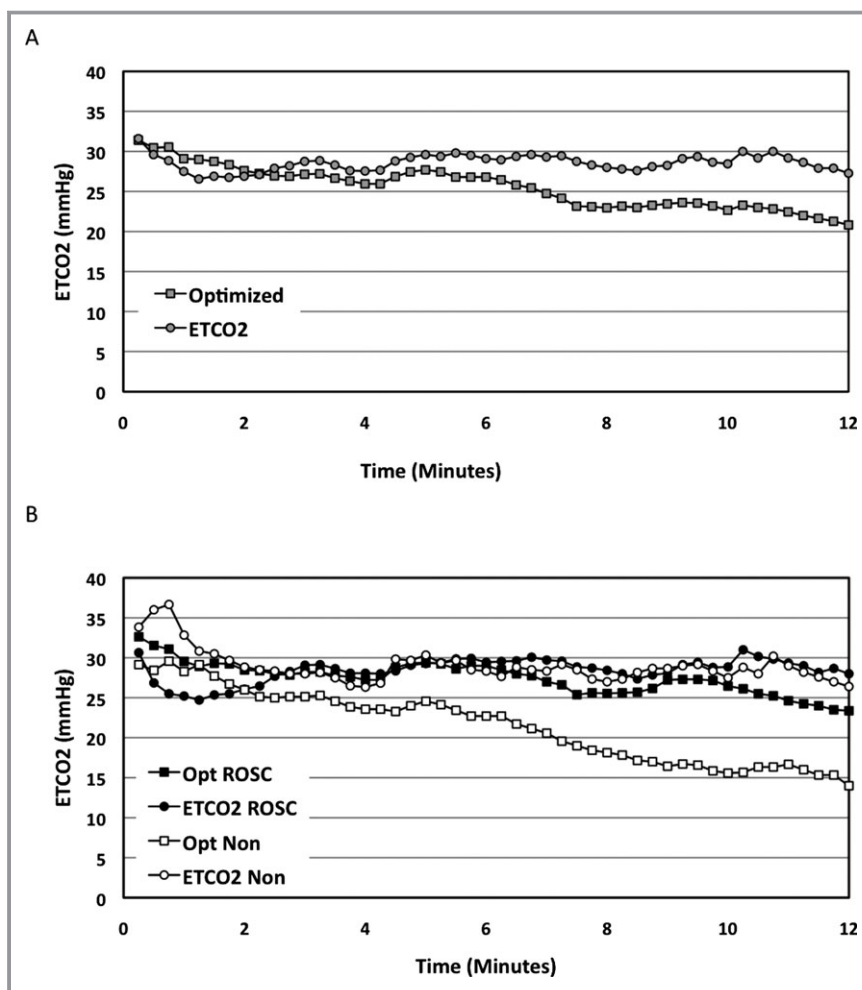


Figure 2. End-tidal CO₂ (ETCO₂) by group and by group and ROSC. A, ETCO₂ versus duration of compressions by group. B, ETCO₂ versus duration of compressions by group and ROSC. Each data point represents the mean ETCO₂ of the piglets at 15-second intervals. CPR indicates cardiopulmonary resuscitation; ETCO₂ Non, non-ROSC piglets of the ETCO₂-directed group; ETCO₂ ROSC, ROSC piglets of the ETCO₂-directed group; ETCO₂, ETCO₂-directed group; Opt Non, non-ROSC piglets of the optimized CPR group; Opt ROSC, ROSC piglets of the optimized CPR group; Optimized, optimized CPR group; ROSC, return of spontaneous circulation.

non-ROSC piglets maintained ETCO₂ in the upper 20s throughout PBLs. In the optimized group, the ROSC piglets produced ETCO₂ in the upper 20s, but non-ROSC piglets exhibited a steady decline in ETCO₂ after 6 minutes of PBLs. The ROSC rate was not significantly different among groups ($P=0.26$), and there was no interaction between group and ROSC ($P=0.12$). The 10-minute ETCO₂ were greater for ROSC piglets than for non-ROSC piglets in the optimized group ($P=0.0002$).

Hemodynamic Parameters and Patterns

The pre-CPR MAP values were 66.6 ± 10.1 and 71.7 ± 13.8 mm Hg in the optimized and ETCO₂-directed groups, respec-

tively. MAP values were similar at the onset of PBLs (32.9 ± 6.2 versus 30.0 ± 7.3) and, like ETCO₂, were better maintained in the ETCO₂-directed group through 10 minutes of PBLs (21.5 ± 6.4 versus 27.7 ± 5.4 at 10 minutes, $P=0.002$; Figure 3A). This better maintenance of MAP for the ETCO₂-directed group was significant ($P=0.04$). MAP was greater in the ROSC piglets and non-ROSC piglets of the ETCO₂-directed group than in those of the optimized groups (Figure 3B). MAP in the ETCO₂-directed non-ROSC piglets was similar to that in optimized ROSC piglets. The non-ROSC piglets in the optimized CPR group exhibited a steady decline in MAP throughout CPR. The difference in MAP between ROSC piglets and non-ROSC piglets was statistically significant ($P=0.001$); however, there was no difference in MAP with respect to

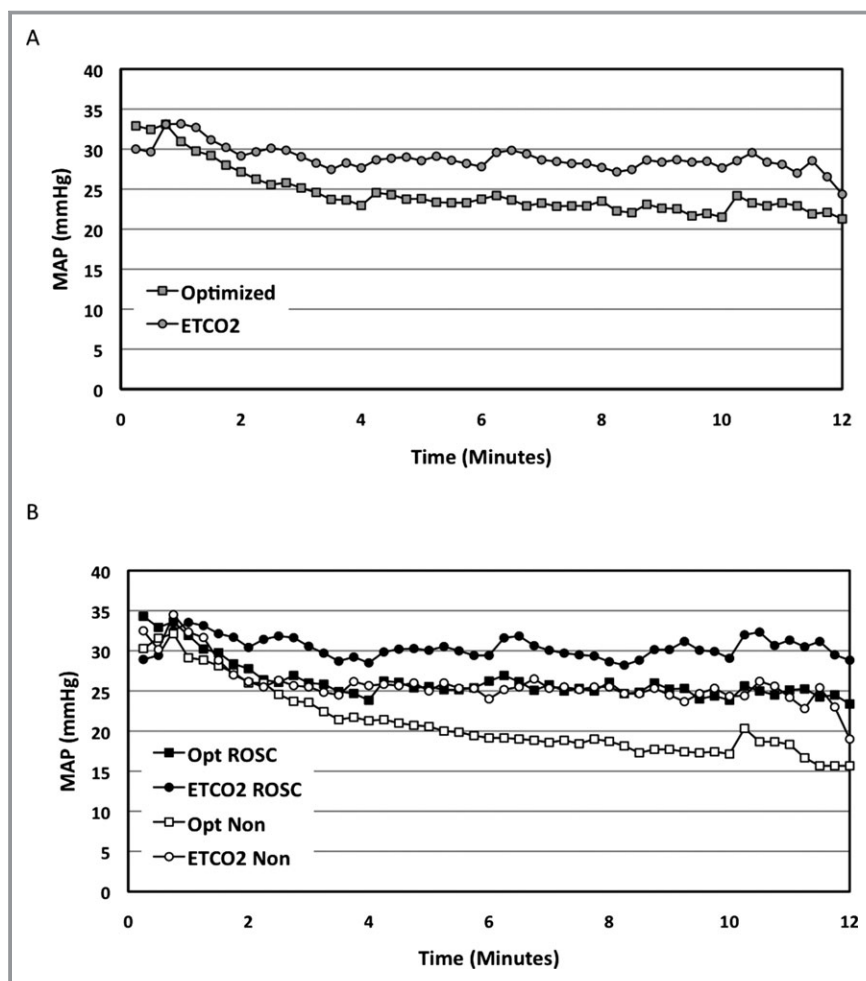


Figure 3. Mean arterial pressure (MAP) by group and by group and ROSC. A, MAP versus duration of compressions by group. B, MAP versus duration of compressions by group and ROSC. Each data point represents the mean MAP value of the piglets at 15-second intervals. CPR indicates cardiopulmonary resuscitation; ETco₂ Non, non-ROSC piglets of the ETco₂-directed group; ETco₂ ROSC, ROSC piglets of the ETco₂-directed group; ETco₂, ETco₂-directed group; Opt Non, non-ROSC piglets of the optimized CPR group; Opt ROSC, ROSC piglets of the optimized CPR group; Optimized, optimized CPR group; ROSC, return of spontaneous circulation.

group and ROSC ($P=0.97$) because of the similarity in the curves of the ETco₂-directed non-ROSC piglets and optimized ROSC piglets. At 10 minutes, MAP was higher in the ETco₂-directed ROSC piglets than in the optimized ROSC piglets ($P=0.02$).

The pre-CPR mCVPs were similar in the optimized and ETco₂-directed groups (6.2 ± 1.4 versus 5.9 ± 1.2 mm Hg, respectively). Like MAP, mCVP was better maintained in the ETco₂-directed group than in the optimized group ($P=0.04$; Figure 4A). mCVP was equivalent among ROSC piglets and appears to be lowest in the non-ROSC piglets of the optimized group and highest in the non-ROSC piglets of the ETco₂-directed group (Figure 4B). The difference in mCVP between ROSC piglets and non-ROSC piglets was not significant

($P=0.41$), nor was there a difference in the mCVP with respect to group and ROSC ($P=0.099$). The difference between the ETco₂-directed and optimized non-ROSC piglets was not significant at 10 minutes of PBLs (16.4 ± 3.5 versus 12.4 ± 2.4 , respectively; $P=0.07$).

The pre-CPR SPP values were similar in the optimized and ETco₂-directed groups (60.4 ± 10.4 versus 65.3 ± 15.1 mm Hg, respectively). Overall, SPP was not different between the 2 groups ($P=0.373$; Figure 5A). A detailed analysis of the 2 groups at 10 minutes of PBLs did not show a difference ($P=0.07$). Figure 5B highlights the fact that ROSC piglets in both groups maintained SPP values >10 mm Hg throughout PBLs resuscitation, whereas the non-ROSC piglets consistently had SPP values <10 mm Hg after 5 to 6 minutes of

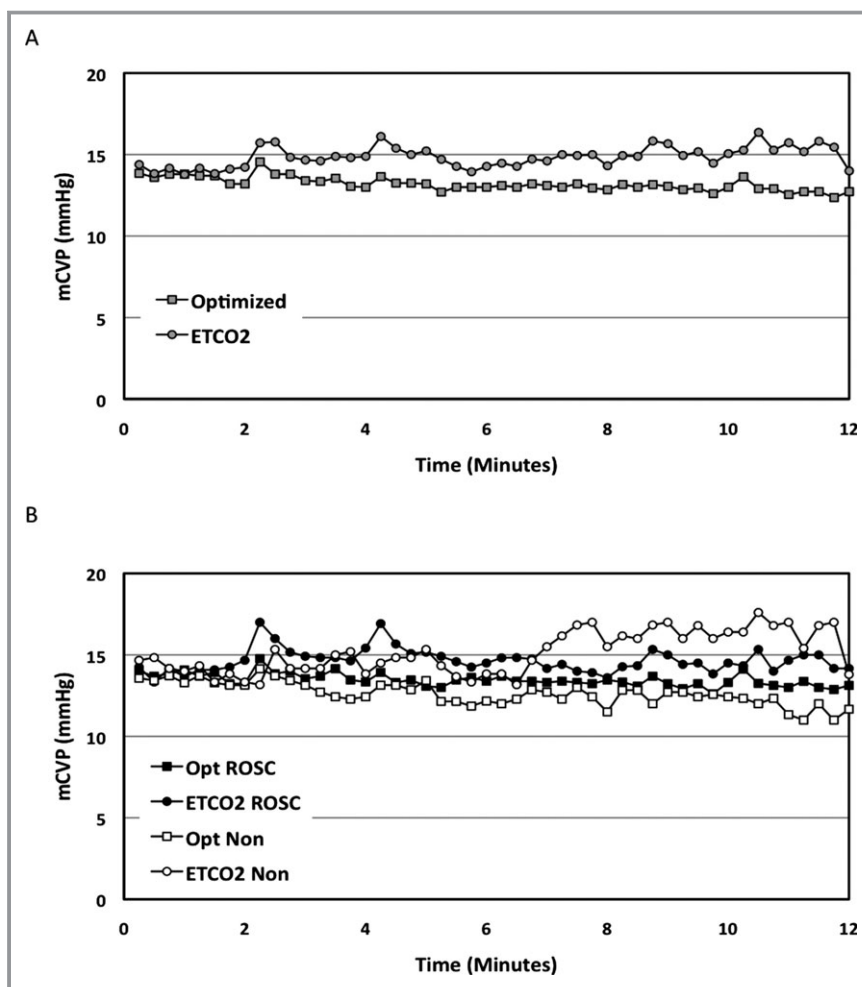


Figure 4. Mean central venous pressure (mCVP) by group and by group and ROSC. A, mCVP versus duration of compressions by group. B, mCVP versus duration of compressions by group and ROSC. Each data point represents the mean CVP value of the piglets at 15-second intervals. CPR indicates cardiopulmonary resuscitation; ETco₂ Non, non-ROSC piglets of the ETco₂-directed group; ETco₂ ROSC, ROSC piglets of the ETco₂-directed group; ETco₂, ETco₂-directed group; Opt Non, non-ROSC piglets of the optimized CPR group; Opt ROSC, ROSC piglets of the optimized CPR group; Optimized, optimized CPR group; ROSC, return of spontaneous circulation.

CPR; this difference in SPP was related to ROSC ($P=0.02$). This effect of SPP on ROSC for combined groups was significant at 6 minutes of CPR (12.2 ± 5.6 versus 6.4 ± 4.1 , $P=0.001$) and at 10 minutes (13.8 ± 3.9 versus 8.5 ± 4.2 , $P=0.001$). Among non-ROSC piglets, the maintenance of ETco₂ in the ETco₂-directed group (Figure 2B) failed to correlate with SPP (Figure 5B), whereas the decline in ETco₂ correlated with the decline in SPP in the optimized group. There was no statistically significant difference in SPP with respect to group and ROSC ($P=0.64$).

The pre-CPR heart rates were 216 ± 38 and 207 ± 36 beats per minute in the optimized and ETco₂-directed groups, respectively. The goal rate of chest compressions in the optimized group was 100 per minute. Resuscitators modified

the compression rate in the ETco₂-directed group to optimize ETco₂. Because piglets in this group had periods of slower and faster compressions, the average rate was similar in the 2 groups (ETco₂ directed: 104 ± 6 , optimized: 101 ± 2).

Effectiveness of CPR

The rates of ROSC did not differ significantly between the optimized CPR group and the ETco₂-directed group ($P=0.74$). Additionally, resuscitation requirements did not differ significantly between groups as indicated by the mean number of defibrillations ($P=0.83$), mean doses of epinephrine ($P=0.47$), time to defibrillation ($P=0.50$), or the time to ROSC ($P=0.18$) (Table 1). The occurrence and severity of injuries secondary

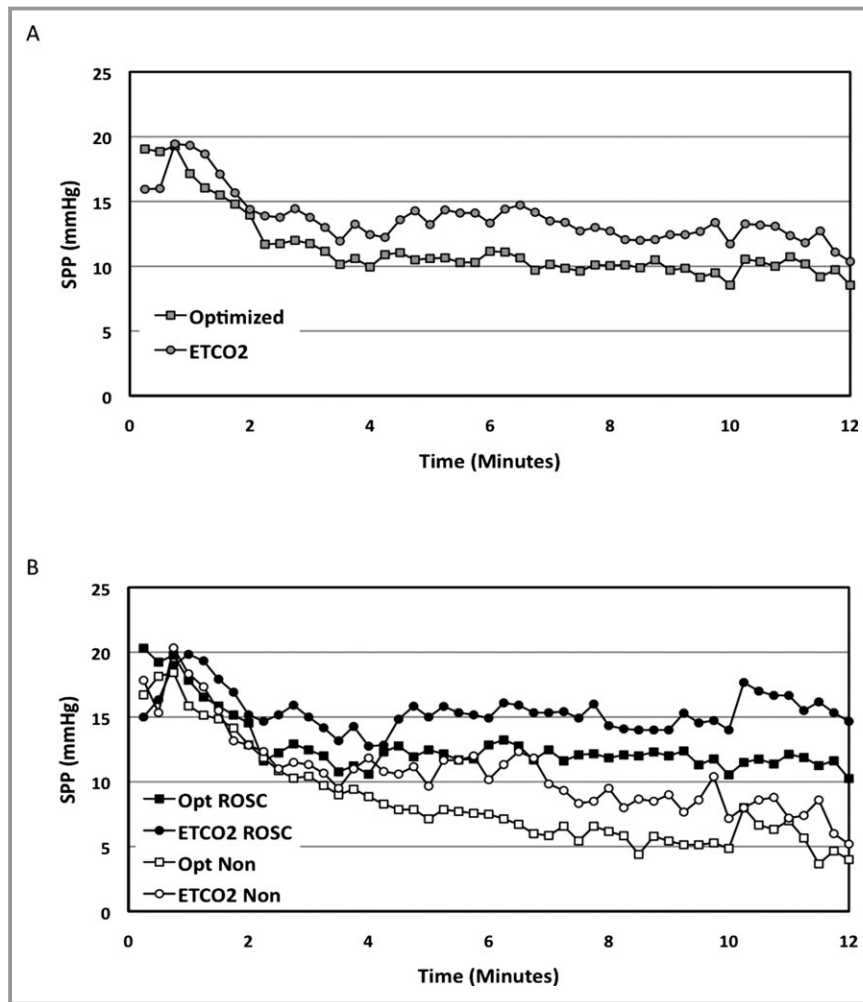


Figure 5. Systemic perfusion pressure (SPP) by group and by group and ROSC. A, SPP versus duration of compressions by group. B, SPP versus duration of compressions by group and ROSC. Each data point represents the mean SPP value of the piglets at 15-second intervals. CPR indicates cardiopulmonary resuscitation; ETCO₂ Non, non-ROSC piglets of the ETCO₂-directed group; ETCO₂ ROSC, ROSC piglets of the ETCO₂-directed group; ETCO₂, ETCO₂-directed group; Opt Non, non-ROSC piglets of the optimized CPR group; Opt ROSC, ROSC piglets of the optimized CPR group; Optimized, optimized CPR group; ROSC, return of spontaneous circulation.

Table 1. Resuscitation Statistics

Variable	ETCO ₂ -Directed	Optimized	P Value
Successful ROSC	14/20 (70%)	13/20 (65%)	0.736*
Time to ROSC, min	12.0±1.4 (n=14)	13.2±2.8 (n=13)	0.184†
Successfully defibrillated	17/20 (85%)	19/20 (95%)	0.292*
Time to defibrillation, min	12.2±2.3 (n=17)	12.8±2.8 (n=19)	0.502†
Defibrillation attempts	2.3±1.6 (n=20)	2.2±1.4 (n=20)	0.834†
Doses of epinephrine required	1.5±1.1 (n=17)	1.7±1.1 (n=18)	0.473†

Data are reported as either percentage or mean±SD. ETCO₂ indicates end-tidal carbon dioxide; ROSC, return of spontaneous circulation.

*χ².

†Student *t* test.

Table 2. Injury Statistics

Variable	ETCO ₂ -Directed	Optimized	P Value
Epicardial hemorrhage	6/20 (30%)	11/20 (55%)	0.110*
Liver laceration	3/20 (15%)	5/20 (25%)	0.430*
Hemothorax	3/20 (15%)	0/20	0.072*
Change in AP diameter, cm	0.7±0.2 (n=12)	0.9±0.3 (n=18)	0.018†

Data are reported as either percentage or mean±SD. ETCO₂ indicates end-tidal carbon dioxide; AP, anteroposterior.

* χ^2 .

†Student *t* test.

to closed-chest CPR were also similar (Table 2). However, permanent deformation of AP diameter (initial minus final AP diameter) at the end of CPR was slightly greater in the optimized group (Table 2). Arterial blood gas and electrolytes did not differ between groups (Table 3).

Discussion

In this study, we present the first comparison of chest compressions directed only by ETCO₂ with gold-standard chest compressions optimized according to AHA guidelines for PBLs. We found that ETCO₂ provides continuous, real-time feedback that is as effective as the use of depth markers and video and verbal feedback for optimizing chest compressions. Resuscitators used ETCO₂ feedback to modify chest compression depth, rate, and hand position during CPR to produce maximal ETCO₂. In our comparison, ETCO₂-directed compressions produced hemodynamic measurements and a resuscitation rate comparable to AHA-optimized CPR with no difference in compression-induced injuries.

ETCO₂ During CPR

CPR is a low cardiac output state during which ETCO₂ becomes less dependent on CO₂ production and ventilation and more linearly related to cardiac output.^{25–27} Flow of systemic venous blood to the pulmonary vasculature becomes rate-limiting for the elimination of CO₂ and a surrogate for blood flow produced by chest compressions.^{16,28} After ventricular fibrillation, the ETCO₂ decreases to zero during the no-flow period and increases again with effective CPR.^{16,26} The inability to produce significant of ETCO₂ during CPR is a prognostic indicator for lack of ROSC in adults,^{19–21} whereas an abrupt increase in ETCO₂ during CPR can be an indicator of ROSC.^{16,22} ETCO₂ production during CPR has been used to compare CPR techniques²⁴ and to show that increasing chest compression force, but not rate, increases blood flow production.²³

In this study, ETCO₂-directed CPR produced significantly higher ETCO₂ than did optimized CPR from 6 to 10 minutes of PBLs. Surprisingly, the expected relationship between ROSC and ETCO₂ was present for optimized but not for ETCO₂-

Table 3. Blood Gas, pH, Electrolytes, and Glucose Values

Variable	Baseline		8-Minute		Post-ALS		20-Minute Post-ROSC	
	ETCO ₂ (n=20)	Optimized (n=20)	ETCO ₂ (n=18)	Optimized (n=20)	ETCO ₂ (n=19)	Optimized (n=17)	ETCO ₂ (n=13)	Optimized (n=12)
pH	7.41±0.06	7.41±0.07	7.18±0.07	7.19±0.09	6.99±0.09	6.96±0.11	6.92±0.18	6.98±0.19
Paco ₂	37±5	37±4	46±8	44±13	59±17	57±17	77±31	63±27
PaO ₂	143±62	143±38	70±24	70±45	172±117	174±112	214±139	190±124
BE	−1.2±3.5	−1.6±2.8	−10.2±3.1	−11.0±3.8	−16.6±2.0	−17.2±4.4	−16.4±4.7	−16.8±5.0
Hb	7.2±1.4	6.7±1.4	8.4±1.4	7.9±1.4	7.3±1.3	7.0±1.2	8.6±1.2	7.8±1.7
Na ⁺	148±5	148±5	147±4	148±5	149±6	147±5	146±4	143±13
K ⁺	4.1±0.6	4.2±0.3	5.6±0.7	5.5±0.6	5.7±1.0	5.5±0.7	4.8±0.6	5.2±1.0
Cl [−]	110±6	110±6	113±6	114±7	115±6	113±6	111±4	112±6
iCa	1.31±0.18	1.35±0.15	1.35±0.16	1.39±0.10	1.31±0.16	1.34±0.12	1.40±0.12	1.39±0.15
Glucose	127±39	136±32	209±59	216±54	290±93	273±101	258±108	291±60

Data are reported as mean±SD. ALS indicates advanced life support; BE, base excess; ETCO₂, end-tidal carbon dioxide; Hb, hemoglobin; iCa, ionized calcium; ROSC, return of spontaneous circulation.

directed CPR. Others have shown that an ETco₂ of <10 mm Hg is a threshold below which ROSC is unlikely,^{19,20} but we found that maintaining of ETco₂ above this threshold level does not ensure ROSC. Our results indicate that although ETco₂-directed CPR maintains levels of ETco₂ above those produced by optimized CPR, it was not associated with a greater likelihood of ROSC than optimized CPR.

Hemodynamic Parameters and Patterns

We found that ETco₂-directed chest compressions maintained higher values of MAP during CPR than did optimized CPR but not higher levels of mCVP or SPP. As expected, MAP values were higher in ROSC piglets for both methods, but MAP was not predictive of ROSC. ETco₂-directed non-ROSC piglets had MAP values similar to those of optimized group ROSC piglets. The fact that ETco₂ and MAP were greater in the ETco₂-directed group late in PBLs is encouraging for the production of greater systemic blood flow during PBLs, but it is disappointing that these higher levels were not associated with improved ROSC. The increase in mCVP above baseline in the ETco₂-directed non-ROSC piglets as PBLs progressed is an unwelcome finding. The rise in mCVP may have been caused by more forceful compressions as resuscitation progressed and ETco₂ was harder to maintain; however, the elevated mCVP may also indicate incomplete chest recoil between compressions. Such incomplete chest recoil will reduce venous return to the heart, cardiac output, and cardiac perfusion pressure and may explain why the increase in mCVP was observed in the piglets that did not achieve ROSC. The resuscitators were aware of the effects of leaning and tried to allow complete chest recoil for both compression techniques, but the lack of verbal feedback may have contributed to this finding in the ETco₂ group while preventing it in the optimized group.

Unlike ETco₂, SPP corresponded with ROSC for both chest-compression methods. This difference in SPP between ROSC piglets and non-ROSC piglets became more prominent as CPR continued, with ROSC piglets from both groups maintaining a higher SPP over time. The lack of difference in ROSC despite higher MAP in the ETco₂-directed group may be due to a higher mCVP in non-ROSC piglets, resulting in SPP values of <10 mm Hg (10-minute MAP, mCVP, and SPP for ETco₂-directed non-ROSC piglets: 24.3±3.1, 16.4±3.5, and 7.2±4.8; for optimized group ROSC piglets: 23.8±5.6, 13.3±1.7, and 10.5±5.8; n=40). As noted previously, if the elevation in mCVP resulted chiefly from inadequate chest recoil between compressions, the resulting compromise in venous return to the heart and reduction in cardiac output and coronary perfusion pressure would explain the link between the high mCVP and failure to achieve ROSC in the ETco₂-guided piglets. Prior studies have found a direct link

between ETco₂ and coronary perfusion pressure.^{10,18} We were not able to demonstrate a connection between ETco₂ and SPP, but because the SPP is higher than coronary perfusion pressure, the coronary perfusion pressure may have been very low in this study. Ornato and colleagues²³ demonstrated that the applied pressure during resuscitation is linearly related to the systolic pressure and to the ETco₂ concentration, but they found no increase in coronary blood flow.

The finding that better maintenance of MAP did not result in improved SPP in the ETco₂-directed non-ROSC piglets raises several questions. The first question is whether brain perfusion is improved with ETco₂-directed chest compressions. SPP in the non-ROSC piglets and overall ROSC may not have improved because the coronary perfusion was not enhanced enough to increase the effectiveness of defibrillation. If brain perfusion is improved during prolonged PBLs with the ETco₂-directed method, then, despite unchanged ROSC rates, the ROSC piglets may have better neurologic and extrathoracic organ (brain, liver, renal) outcomes than those receiving optimized CPR.

The second question is whether the medications used in ALS would help prevent the deterioration in SPP in the ETco₂-directed non-ROSC piglets. Vasopressor administration is reported to improve coronary perfusion during cardiac arrest.³ We specifically chose a basic life support model to begin our studies of physiology-based resuscitation. The effects of ALS on ETco₂ and the response of resuscitators will require further investigation.

The third question raised is whether extrathoracic perfusion can be modified as ETco₂-directed CPR progresses. For example, would a slower compression rate and/or shorter duty cycle increase venous return and improve systemic circulation? We found no overall difference in chest-compression rates between the ETco₂-directed and optimized groups. However, some piglets in the ETco₂-directed group had periods of slower compression rates with improved ETco₂ whereas other piglets improved with faster rates, and the overall effect balanced out. The compression rate and duty cycle were not systematically addressed, as they were varied in real time at the discretion of the resuscitator.

Effectiveness of CPR

The depth for chest compressions should be based on anatomical realities and physiologic responses (hemodynamic measurements).⁹ The ideal depth surpasses the minimum needed to achieve optimal blood flow and avoids the maximum that does not generate additional blood flow and may cause chest deformity and vital organ injury.^{9,29,30} In addition to depth and rate, proper hand position is an essential factor for the delivery of high-quality compressions.

The role of proper hand position may be accentuated in pediatric patients, as variations in the chest anatomy alter the compression point relative to the heart.⁹ Additionally, the method of delivering CPR in children is based on age and may influence chest-compression effectiveness. The 2-finger technique and the 2-thumb-encircling-hands technique have been shown to produce different hemodynamic profiles and consistencies in depth and force of compressions.^{1,31} Even when AHA guidelines for depth, rate, and hand position are followed, the force of closed-chest compression varies among rescuers and diminishes as the rescuer fatigues.^{30,32} Such variations among methods and rescuers, as well as the risk of injury from excessive chest compression depth, underscore the need for a continuous, physiologic, real-time, and adaptive feedback mechanism during CPR. Hemodynamic measurements such as SPP would provide this information, but arterial and central venous access may not be present. In contrast, ETco₂ monitors are available throughout most hospitals, and portable versions are available that can be used easily for in- and out-of-hospital locations.

The comparable rate of ROSC and the resuscitation requirements (epinephrine doses and defibrillation attempts) suggest that the 2 methods provide similar cardiac perfusion for defibrillation and effective myocardial contraction. CPR-related injuries were not different between the 2 methods, despite the generation of a higher MAP and mCVP by ETco₂-directed PBLs. The only significant finding was the decrease in AP diameter from baseline, which paradoxically showed more chest wall deformity (flattening) with the optimized CPR method. The observed difference is unlikely to be clinically significant. It does not appear that the presence of a hemothorax, epicardial hemorrhage, or liver laceration either consistently or significantly resulted in an inability to achieve ROSC.

Ventricular fibrillation is a common etiology of cardiac arrest in adults, whereas infants and children are more likely to have cardiac arrest from an asphyxial event.³ We chose a ventricular fibrillation model because it provides tight control over the arrest and no-flow durations and a consistent model for initial studies. Asphyxial arrest may present a different physiologic profile, as patients with asphyxial arrest have 2 to 4 times the ETco₂ at intubation as patients who experience dysrhythmic arrest.²⁷ In asphyxial arrest, the ETco₂ is markedly elevated for the first minute of CPR but decreases to subnormal levels until ROSC.²¹ The use of ETco₂-directed CPR in an asphyxial model of cardiac arrest should be applicable after the first minute of resuscitation.²¹

There are several limitations to our study. In this study, we were unable to determine the pressures during various phases of closed-chest compressions (direct compression versus relaxation). While blood flow is not likely to be uniform during

these phases of chest compression, the pressures reported (MAP, mCVP, and calculated SPP) are representative of clinically available data. Our inability to identify diastolic aortic and central venous pressures (ie, pressures between compressions) prevented calculation of coronary perfusion pressure and detection of incomplete chest recoil.

In addition, we did not evaluate the benefits or effects of ALS on the use of ETco₂ to direct chest compressions. The effect of vasopressors, specifically epinephrine, on ETco₂ during CPR remains controversial. Epinephrine has been postulated to increase, decrease, or have no effect on the concentration of ETco₂. If the reported 50% decrease in ETco₂ occurs with epinephrine administration, it could affect the usefulness of ETco₂-directed chest compressions.^{18,33} After 10 to 12 minutes of PBLs, we did use epinephrine during the continued CPR while attempting defibrillation. During ALS, the ETco₂ in the non-ROSC piglets was declining but was not noticeably depressed by the administration of intravenous epinephrine. ETco₂ increased markedly as the piglets achieved ROSC, and with the numerous ROSC piglets, it is difficult to draw any conclusions about the administration of epinephrine during this stage of the protocol. Additional investigation is required to delineate the effects of early epinephrine use (ALS) on ETco₂-directed resuscitation.

Another practical consideration is the impact of pulmonary disease on the interpretation of ETco₂. None of our animals had known pulmonary disease, and none developed obvious pulmonary edema during the resuscitation. This is an important issue when considering the use of ETco₂-directed resuscitation, as the initial cause of arrest in children is frequently a respiratory complication.

Finally, the use of supplemental oxygen in a ventricular fibrillation model is a limitation, as in the clinical arena ventricular fibrillation often occurs in patients breathing room air or, in the pediatric population, in arrests that are hypoxic in origin. This study provides groundwork for a future study that focuses on a hypoxic model of pediatric arrest.

Conclusions

Consistently achieving AHA guidelines for the depth and rate of chest compression is difficult in simulation and in clinical practice. Additional equipment to provide optimal CPR (video cameras, depth markers, invasive arterial monitoring, and rate counters) is often impractical or unavailable. Monitoring the ETco₂ concentration is a commonly available, noninvasive, continuous, real-time method of obtaining physiologic feedback during CPR that correlates with cardiac output and successful resuscitation. Using only ETco₂ monitoring, we were able to gauge the effectiveness of chest compressions and provide resuscitation that was as

effective as AHA-optimized CPR. The ET_{CO₂}-directed method of CPR can help rescuers bring typical CPR up to the level of optimized CPR with the hope of improving rates of ROSC and neurologically intact survival for children who have cardiac arrest.

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Disclosures

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