Published in final edited form as:

Pediatr Crit Care Med. 2019 July ; 20(7): e352–e361. doi:10.1097/PCC.0000000000001968.

The Effect of Asphyxia Arrest Duration on a Pediatric End-Tidal Carbon Dioxide–Guided Chest Compression Delivery Model

Jennifer L. Hamrick, MD¹, Justin T. Hamrick, MD¹, Caitlin E. O'Brien, MD, MPH², Michael Reyes, BA², Polan T Santos, MD², Sophie E. Heitmiller, BA², Ewa Kulikowicz, MS², Jennifer K. Lee, MD², Sapna R. Kudchadkar, MD, PhD^{2,3,4}, Raymond C. Koehler, PhD², Elizabeth A. Hunt, MD, MPH, PhD^{2,3,5}, and Donald H. Shaffner, MD²

¹Department of Anesthesiology, Rady Children's Hospital, San Diego, California ²Department of Anesthesiology/Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland

³Department of Pediatrics, Johns Hopkins University School of Medicine ⁴Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine ⁵Division of Health Informatics, Johns Hopkins University School of Medicine

Abstract

Objective: To determine the effect of the duration of asphyxial arrest on the survival benefit previously seen with end-tidal carbon dioxide (ETCO₂)-guided chest compression delivery.

Design: Preclinical randomized controlled study.

Setting: University animal research laboratory.

Subjects: Two-week-old swine.

Interventions: After either 17 or 23 minutes of asphyxial arrest, animals were randomized to standard CPR or ETCO₂-guided chest compression delivery. Standard CPR was optimized by marker, monitor, and verbal feedback about compression rate, depth, and release. ETCO₂ guided delivery used adjustments to chest compression rate and depth to maximize ETCO₂ level without other feedback. CPR for both groups proceeded from 10 minutes of basic life support to 10 minutes of advanced life support or return of spontaneous circulation (ROSC).

Measurements and Main Results: After 17-minutes of asphyxial arrest mean ETCO₂ during 10 minutes of CPR was 18 ± 9 torr in the standard group and 33 ± 15 torr in the ETCO₂ group ($p=0.004$). The rate of ROSC was 3 / 14 (21%) in the standard group rate and 9/14 (64%) in the

Corresponding author: Donald H. Shaffner, MD, 6324 Bloomberg Children's Center, Johns Hopkins Hospital, 1800 Orleans Street, Baltimore, MD 21287, Phone: (410) 955-6412, Fax: (410) 502-5312, dshaffn1@jhmi.edu.

This work was performed in the research facilities of the Department of Anesthesiology/Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland.

Conflict of interest disclosure:

The remaining authors have disclosed that they do not have any potential conflicts of interest.

Copyright form disclosure: The remaining authors have disclosed that they do not have any potential conflicts of interest.

Article tweet: Survival benefit using ETCO₂-guided CPR confirmed after 17-min asphyxia arrest in pediatric swine model. 23-min asphyxia negates benefit.

ETCO₂ group ($p=0.05$). After a 23-minute asphyxial arrest, neither ETCO₂ values (20 vs 26) nor ROSC rate (3/14 vs 1/14) differed between the standard and ETCO₂-guided groups.

Conclusions: Our previously observed survival benefit of ETCO₂-guided chest compression delivery after 20 minutes of asphyxial arrest was confirmed after 17 minutes of asphyxial arrest. The poor survival after 23 minutes of asphyxia shows that the benefit of ETCO₂-guided chest compression delivery is limited by severe asphyxia duration.

Keywords

asphyxia; heart arrest; cardiopulmonary resuscitation; capnography; feedback; pediatrics

INTRODUCTION

Cardiopulmonary resuscitation (CPR) provides sub-physiologic blood flow during prolonged cardiopulmonary arrest (1). Despite the current emphasis on chest compression delivery, survival to discharge from out-of-hospital cardiac arrest in children remains <10% (2–6). The American Heart Association (AHA) guidelines provide a general approach to resuscitation but acknowledge that not all patients respond to basic and advanced life support (BLS, ALS) and they suggest monitoring the patient's physiologic response to interventions for titration of care (7, 8). Ideally, physiology-based titration of resuscitation would enable providers to maximize hemodynamic parameters, minimize CPR-related injuries, achieve return of spontaneous circulation (ROSC), and produce neurologically meaningful recovery (8, 9).

Several physiologic parameters have been investigated as guides for resuscitative efforts. End-tidal carbon dioxide (ETCO₂), coronary perfusion pressure, and arterial relaxation pressure correlate with cardiac output and myocardial blood flow during CPR (10). Hemodynamic-directed CPR uses arterial diastolic (relaxation) pressure to guide chest compression rate and force and epinephrine administration frequency in adults (11) and animal models (12–14). It requires invasive arterial blood pressure monitoring which may not be available outside the intensive care unit or operating room. Conversely, ETCO₂ monitoring is a widely available, noninvasive (can be used with invasive or noninvasive ventilation) method, which also provides continuous, real-time, physiologic feedback about chest compression efficacy during CPR (15–17).

The ETCO₂ level during CPR has correlates with cardiac output (18–20), coronary perfusion pressure (21, 22), and successful CPR (18, 21, 23–25) in animal models and clinical trials. Because CPR is a low cardiac output state, ETCO₂ becomes less dependent on CO₂ production and ventilation, more linearly related to pulmonary blood flow, and becomes a surrogate for cardiac output (7, 10, 18–20, 23, 26–35). An inadequate level of ETCO₂ during CPR is prognostic for failure to achieve ROSC (23–25). Despite this interest in ETCO₂ measurement during CPR, the AHA guidelines are unable to provide a specific ETCO₂ value to guide pediatric resuscitation (8).

Our previous study used ETCO₂ levels to guide chest compression delivery and compared results with optimal standard CPR after a 20-minute duration of asphyxial arrest (17). In that

study the 20-minute survival and hemodynamic parameters in animals that received ETCO₂-guided chest compressions were better than in those that received optimal standard CPR. The current study evaluates a shorter (17-minute) and a longer (23-minute) period of asphyxial arrest to determine if the improvements observed with ETCO₂-guided CPR are reproducible and if they are affected by duration of asphyxial arrest.

MATERIALS AND METHODS

All animal studies were performed with approval from the animal care and use committee of the Johns Hopkins University in accordance with institutional guidelines. Fifty-six neonatal, domestic, male swine weighing 3–4 kg each were randomized into four groups: 17-minute asphyxia/ETCO₂-guided and standard resuscitation groups, and 23-minute asphyxia/ETCO₂-guided and standard resuscitation groups. The piglets were anesthetized with isoflurane via inhalational induction, and general anesthesia was maintained with a mixture of 2% isoflurane, 70% nitrous oxide, and 30% oxygen during surgery. A cuffed 4.0 tracheal tube was secured via tracheostomy. The bilateral femoral vessels were surgically exposed. A femoral artery catheter was advanced to the mid-aorta for hemodynamic monitoring and blood gas determination. A femoral venous catheter was advanced to a mid-thoracic position to measure central venous pressure (CVP) and to administer fluids and medications. A pacing wire was placed via the contralateral femoral vein into the right ventricle; placement was confirmed by ventricular irritation on electrocardiogram. A sagittal sinus catheter was placed via a burr hole at the bregma to measure intracranial pressure (ICP) and cerebral venous blood gases. After surgical interventions were complete, the isoflurane was decreased to 0.8% and fentanyl (10 mcg/kg) and vecuronium (0.3 mg/kg) were administered. A heating pad beneath the piglet was adjusted to maintain a rectal temperature of 38–39°C (normal range for piglets). The FiO₂ was decreased from 30% to 21%, and peak inspiratory pressure in pressure-controlled ventilation mode was adjusted to maintain a PaCO₂ of 35–45 torr at a rate of 20 breaths per minute in the prearrest period. Vital signs, including ETCO₂, mean arterial blood pressure (MAP), mean CVP, arterial relaxation pressure (i.e., diastolic blood pressure, DBP), mean ICP, heart rate, and rectal temperature were recorded before experimental initiation (baseline) and at 30-second intervals during CPR.

Experimental Protocol

A timeline for the experimental protocol is provided in Figure 1. We induced 17-minute or 23-minute asphyxial arrest by clamping the tracheostomy tube. With the tracheostomy tube still clamped, we induced ventricular fibrillation at –6 minutes by applying 50 mA of alternating current to the right ventricular endocardium via the fibrillation wire. This asphyxia-then-fibrillation procedure was similar to the model used to study hemodynamic-directed CPR (12). The period of fibrillatory arrest is added to asphyxia in order to prevent ROSC during the subsequent 10-minute BLS interval. Piglets were randomized to either 17 or 23 minutes of asphyxial arrest. We induced fibrillation six minutes prior to the end of asphyxia in both asphyxia durations. After 17 or 23 minutes of arrest, BLS was initiated. Mechanical ventilation was resumed at the pre-arrest inspiratory pressures and a rate of 20 breaths per minute, but with an FiO₂ of 100%. The heating pad was adjusted to maintain a

rectal temperature of 38–39°C throughout CPR. In all groups, resuscitators performed chest compressions via the two-thumb, encircling hands technique at a rate that varied by study group. The resuscitators providing chest compressions alternated every 2 minutes.

Standard Group.—In this group, a marker was placed across the sternum to indicate 2/3 the anteroposterior diameter for chest compression depth (see Figure 1 in reference (16)). Guideline-based chest compression delivery was targeted as a rate of 100/min, a depth of 1/3 the anteroposterior diameter, and full release between compressions. A high-fidelity video monitor, the depth marker, and the second resuscitator provided real-time video and verbal feedback regarding depth, rate, and release. The resuscitators were blinded to the ETCO₂ value.

ETCO₂-Guided Group: In this group, resuscitators modified chest compression rate, depth, force, and hand position throughout BLS and ALS at their discretion in order to maintain the maximum obtainable level of ETCO₂. ETCO₂ was the only feedback available to guide resuscitation.

Both Groups: After 10 minutes of BLS, resuscitators began ALS. During compressor changes at 0, 2, 4, 6, and 8 minutes of ALS, a resuscitator administered 30 joules of biphasic defibrillation. In addition, 300 mcg of epinephrine was administered via the femoral central venous catheter at 0, 4, and 8 minutes of ALS. Doses of 10 joules/kg shock and 100 mcg/kg epinephrine are high for humans but have been most effective in this piglet model and were the same in both groups. Chest compressions were continued as previously described. ALS was terminated when ROSC occurred or after 10 minutes (20 total minutes of CPR). Survival was defined as sustained arterial pulsatility post-ROSC for 20 minutes, without further intervention. Non-survival was defined as a failure to achieve ROSC after 10 minutes of ALS (20 minutes of resuscitation) or ROSC that was not sustained for 20 minutes. No additional chest compressions, medications, or defibrillations were provided after ROSC occurred. Arterial and venous blood gases were examined at baseline, 10 minutes of asphyxia, 8 minutes of BLS, and 20 minutes of resuscitation (non-survivors) or 20 minutes of ROSC (survivors). Survivors were euthanized per animal care and use committee guidelines after 20 minutes of ROSC. We performed a postmortem examination on all animals to evaluate for resuscitation-induced injuries (hemopericardium, hemothorax, hemoperitoneum, liver laceration, atelectasis, or superficial cardiac injury).

Statistical Analysis

Baseline cardiorespiratory values are provided as descriptive data. All values are expressed as mean $\pm$ SD. Systemic perfusion pressure (SPP) was calculated as MAP – mean CVP. Myocardial perfusion pressure (MPP) was not calculated because diastolic CVP values were not available and aortic relaxation pressure is indicative of myocardial perfusion. Cerebral perfusion pressure (CPP) was calculated as MAP – mean ICP. Data from the 30-second interval during which ROSC was detected and all subsequent measurements were excluded from analysis. ROSC was detected during compressions by a sudden increase in arterial blood pressure and ETCO₂ levels or during the pre-shock pause at the 2-minute compressor change. If ROSC was detected only during the compressor change, the 30-second intervals

from the previous two minutes were analyzed and the 30-second intervals containing data that appeared to be elevated due to undetected ROSC were removed from analysis.

Resuscitation and injury differences between groups were compared with an unpaired, two-tailed *t* test for continuous variables and a chi-square or Fisher exact test for categorical variables, as appropriate. Two-tailed *p* values of less than 0.05 were considered statistically significant. Repeated-measures analysis of variance (ANOVA) was used to investigate the effect of time and group. All data were analyzed in Stata (Version 14; Statacorp LP, College Station, TX).

RESULTS

Baseline (pre-arrest) weight, blood gas, and physiologic variables were similar between study groups (Table 1). The hemodynamic results during CPR for the 17- and 23-minute durations of asphyxia are presented according to study group (ETCO₂-guided CPR or standard CPR) in Table 2 and Supplemental Figure 2 and according to survival in Table 3, Supplemental Figure 3 (17-minute asphyxia arrest), **and** Supplemental Figure 4 (23-minute asphyxia arrest). Outcomes, blood gas values, and autopsy results are presented by study group in Table 4.

End-tidal CO₂.

The precipitous washout of ETCO₂ expected during the first minute of BLS occurred for both asphyxia durations and in both CPR groups (Supplemental Figure 2A **and** B). After 17 minutes of asphyxial arrest, the mean ETCO₂ during CPR, after the washout period, could be successfully sustained at >30 torr using ETCO₂-guided chest compression delivery, whereas mean ETCO₂ fell to <20 torr with standard CPR. The mean ETCO₂ levels were significantly higher with ETCO₂-guided CPR than with standard CPR during both BLS and ALS (Table 2). The mean ETCO₂ levels were significantly higher in survivors of both groups than in non-survivors during both BLS (36 vs. 18) and ALS (43 vs. 21; Table 3, Supplemental Figure 3A). When evaluated for both CPR type and survival, the ETCO₂ level in the ETCO₂-guided non-survivors was >20 torr for the majority of resuscitation, but the elevated ETCO₂ did not always prognosticate ROSC (Supplemental Figure 3A1). The increase in ETCO₂ levels with ETCO₂-guided delivery after 17-minute asphyxia was lost with a 23-minute asphyxia duration. No significant difference in ETCO₂ was observed between CPR methods during BLS or ALS after 23 minutes of asphyxia (Table 2, Supplemental Figure 2B). The few survivors of 23-minute asphyxia had a late ETCO₂ response after epinephrine administration, whereas non-survivors exhibited no ETCO₂ response (Supplemental Figure 4A **and** A1). This response was not significant (*n* = 4; Table 3).

Return of spontaneous circulation.

The rate of ROSC after 17 minutes of asphyxia was greater in the ETCO₂-guided group than in the standard group (64% vs. 21%; Table 4). There was no difference between groups in time to ROSC, number of defibrillation attempts, time to defibrillation, or epinephrine doses administered. In the 23-minute asphyxia model, ETCO₂-guided chest compression provided

no benefit to ROSC (7% vs. 21%), time to ROSC, defibrillation attempts, time to defibrillation, or epinephrine doses (Table 4).

Chest compression rate.

For both the 17-minute and 23-minute asphyxia durations, the chest compression rate was significantly higher during ETCO₂-guided CPR than during standard CPR ($p < 0.0001$; Table 2, Supplemental Figure 2C and D). In the 17-minute asphyxia group, chest compression rates were higher among survivors than among non-survivors during BLS (140 vs. 115) and ALS (143 vs. 118; Table 3, Supplemental Figure 3B). In the 23-minute asphyxia group, chest compression rate was not associated with survival.

Relaxation (diastolic) arterial pressure (DBP).

Regardless of asphyxia duration, the DBP, an indicator of coronary perfusion during CPR, did not differ between study groups (Table 2, Supplemental Figure 2E and F). However, DBP during BLS and ALS was significantly higher in survivors of both 17-minute and 23-minute asphyxia (Table 3, Supplemental Figure 3C and C1, Supplemental Figure 4C and C1). All survivors exhibited a rapid increase in DBP from 10 mmHg to >20 mmHg with the first administration of epinephrine. In contrast, DBP remained <15 mmHg throughout resuscitation in non-survivors irrespective of asphyxia duration or type of CPR guidance (Supplemental Figure 3C and C1 and Supplemental Figure 4C and C1).

Other hemodynamic parameters.

Among animals that underwent 17-minute asphyxia, the MAP, CVP, SPP, and ICP during BLS were similar for the ETCO₂-guided and standard resuscitation groups, but CPP was higher in the ETCO₂-guided group ($p = 0.05$). During ALS, the MAP ($p = 0.02$), SPP ($p = 0.03$), and CPP ($p = 0.02$) were higher in the ETCO₂-guided piglets (Table 2, Supplemental Figure 2G and I). MAP, SPP, and CPP during both BLS and ALS were associated with survival for this asphyxia duration (Table 3, Supplemental Figure 3D and E). The survivors in both resuscitation groups exhibited an abrupt increase in both SPP and CPP after the first dose of epinephrine (Supplemental Figure 3D1 and E1). In piglets that underwent 23-minute asphyxia, MAP, CVP, SPP, ICP, and CPP did not differ by resuscitation type during BLS. Only ICP was significantly higher in the ETCO₂-guided piglets during ALS after 23 minutes of asphyxia (Table 2, Supplemental Figure 2H and J). As with 17-minute survivors, the 23-minute survivors exhibited significantly higher MAP, SPP, and CPP throughout resuscitation (Table 3, Supplemental Figure 4D and E). Again survivors had a brisk increase in SPP and CPP with the first dose of epinephrine (Supplemental Figure 4D1 and E1).

Postmortem examination.

Autopsy results did not reveal any difference in the occurrence of atelectasis, liver laceration, epicardial hemorrhage, or hemothorax between groups in either the 17-minute or the 23-minute piglets (Table 4).

DISCUSSION

Previously, we showed that the use of ETCO₂ feedback alone to guide chest compression delivery was equivalent to standard CPR that included feedback about chest compression rate, depth, and leaning after 90 seconds of untreated ventricular fibrillation (16). Subsequently, we showed that ETCO₂-guided chest compression delivery resulted in better rates of ROSC and short-term survival (7/14, 50%) than did standard CPR (2/14, 14%; $p=0.04$) after a prolonged (20-minute) asphyxial arrest (17). Our current study compared the benefit from ETCO₂-guided chest compression delivery against the intensity of arrest by using asphyxia durations 3 minutes shorter or longer than our previous study. After 17 minutes of asphyxial arrest the benefit of ETCO₂-guided chest compression delivery over standard CPR was similar to that seen for 20 minutes of asphyxia. Increasing the intensity of asphyxial arrest to 23 minutes negated the benefit of ETCO₂ guidance over standard CPR.

Our 17-minute asphyxia investigation reproduces several findings from our 20-minute study (17). The washout of extreme hypercarbia after asphyxia was again complete by 60 seconds of BLS and ETCO₂ guidance was applicable thereafter. Also, ETCO₂ guidance produced mean ETCO₂ levels during CPR that were 15 torr greater than those produced by standard CPR throughout BLS. The ETCO₂ levels during BLS were consistently greater in survivors than non-survivors (by an average of 17 torr after 90 seconds of BLS). As with our previous study, chest compression rates of 140–150/minute were needed to maximize ETCO₂ levels during CPR. These improvement in ETCO₂ levels and ROSC at asphyxia durations that render standard CPR ineffective suggest that the use of physiologic feedback may be beneficial when experiencing prolonged resuscitation (e.g. difficult-to-reverse etiologies of arrest or when preparing to bridge onto extracorporeal life support).

This study also shows that the hemodynamic and survival benefits of the use of ETCO₂-directed chest compression delivery is limited by asphyxia durations of 23 minutes. The duration of arrest is an established, independent determinant of obtaining ROSC (36–38). We chose longer periods of asphyxia than the commonly used 10–12 minutes because of the potential for physiologic feedback to improve outcomes when CPR is prolonged. Understanding the limits of physiologic feedback to improve outcome may be important when considering the impact of prolonged arrest time on likelihood of successful resuscitation efforts.

The transition in CPR efficacy at 20–23 minutes of asphyxial arrest may not be limited to asphyxia or infant piglets. In models of ventricular fibrillation in infant piglets (39) and 30-kg pigs (40), blood flow deteriorates beyond 20 minutes of arrest, even when CPR starts immediately after arrest and chest deformation is limited by the use of a thoracic vest (41). However, species differences can exist because the deterioration of cerebral and myocardial blood flow can be avoided after fibrillatory arrest in adult dogs with different modalities of CPR and epinephrine administration for 60–90 minutes (42, 43). Thus, the precise timing of when ETCO₂ feedback loses efficacy could differ between piglets and human infants.

Hemodynamic variables are being used in another model of physiologic feedback, hemodynamic-directed CPR (12, 13). The association of ETCO₂ levels during CPR with

other hemodynamics and with survival appears complex. During the first 60 seconds of BLS (the washout period after asphyxia), ETCO₂ levels are high in both survivors and non-survivors and should be ignored. After 90 seconds, ETCO₂ levels become consistently higher in survivors than in non-survivors throughout BLS and ALS. Hemodynamic pressures (arterial relaxation, systemic perfusion, and cerebral perfusion) among survivors peak during BLS (3 minutes), approach non-survivor levels late in BLS (7.5 minutes), and then increase markedly during epinephrine administration at the start of ALS (10 minutes). This hemodynamic pattern in survivors was similar for all three of these hemodynamic variables for both ETCO₂-guided and standard CPR. The paucity of survivors of 23-minute asphyxia make these survival graphs less reliable (Supplemental Figures 4C, 4D, and 4E). These hemodynamic patterns among survivors were also observed in our previous 20-minute asphyxia study (17). Though the hemodynamic patterns are similar for both methods of CPR, the ETCO₂ graph is dependent on the method of CPR. In Supplemental Figure 3A1, survivors of both ETCO₂-guided and standard CPR have ETCO₂ levels > 20 torr. Non-survivors of standard CPR had ETCO₂ levels <15 torr for most of CPR but surprisingly, non-survivors in the ETCO₂-guided CPR group had several ETCO₂ levels > 20 (a finding that we previously observed (17)). Together, these data indicate that prognostication of survival during CPR differs by variable examined and method of CPR. The results suggest that survival is associated with high hemodynamic measurements, non-survival is associated with low ETCO₂ levels, and high ETCO₂ levels may be less helpful when using ETCO₂-guidance. A prospective study of target threshold values for these variables is needed to provide statistical analysis of this apparent association.

We have not determined how ETCO₂-guided chest compression delivery improves survival. The increases in relaxation arterial pressure, SPP, and CPP in survivors at 3 and 10 minutes of CPR could represent responses to endogenous vasopressors during BLS and exogenous epinephrine administration during ALS. It is possible that optimizing chest compression delivery to produce higher ETCO₂ levels reflects improvements in blood flow that enable survivors to respond to vasopressors and meet critical vascular thresholds required for resumption of native circulation. The higher chest compression rates in the ETCO₂-guided group were associated with elevations in ETCO₂ levels and did not negatively impact the generation of necessary perfusion pressures. The high compression rates might also be associated with improved blood flow that helps restore or maintain vascular reactivity to vasopressors. An understanding of how best to titrate compression rate to optimize ETCO₂, perfusion, and ROSC will require further investigation.

Application of our results has several limitations. (1) Severe hypercarbia from asphyxia may confound the use of ETCO₂-guided chest compressions during early resuscitation, but as reported elsewhere, the initial hypercarbia resolved within a minute of resuscitation, and thereafter ETCO₂ level reflected chest compression effectiveness (16, 17, 25, 44). (2) Epinephrine administration may affect pulmonary blood flow and cause transient elevation or decline in ETCO₂ level during CPR (15, 45–51). We did not see fluctuation in ETCO₂ level after administration of epinephrine. The true effect of epinephrine on pulmonary vasculature and ETCO₂ remains controversial and requires further study. (3) Our use of ROSC and 20-minute survival as primary outcomes does not explore long-term outcomes

such as post-arrest neurologic status. Whether high ETCO₂ during resuscitation affects neurologic outcome after prolonged cardiac arrest is not yet known. (4) We were unable to quantify the effect of depth and force alterations on our outcomes. Until a neonatal accelerometer becomes commercially available, we cannot be sure how much compression force contributed to the increased ETCO₂ levels during CPR. The chest compression depth in the standard CPR group was maintained at 1/3 the starting anteroposterior diameter (described in reference (16)). (5) Our piglets were all healthy neonates with no underlying lung disease. The contribution of lung disease to asphyxial arrest may limit the usefulness of ETCO₂-guided resuscitation. (6) Our piglets were mechanically ventilated at a rate of 20 breaths per minute during CPR. Our use of pressure-controlled ventilation at the pre-arrest setting allows us to limit confounding variables but does not conform to current AHA guidelines of 10–12 breaths per minute. This method of ventilation did not result in hyperventilation (Table 4), was the same in both study groups, and has worked well in this model in the past. (7) Our study design precluded true blinding, but our study outcomes were objectively measured and analyzed. (8) The benefit from the increased chest compression rate may be specific to this model and may relate to the compliant neonatal chest wall and the cardiac pump theory of blood flow in resuscitation. (9) The impact of 23 minutes of asphyxia on the effectiveness of the use of ETCO₂-guided chest compression delivery may be specific for this model and may not relate to human application. Additional studies will be needed to determine the safety and efficacy of higher chest compression rates before any recommendation can be made regarding clinical use.

CONCLUSIONS

Physiologic feedback has the potential to augment, continuously and in real-time, current guidelines through the individualization and optimization of resuscitative efforts. Quantitative ETCO₂ guidance has the potential to optimize delivery of chest compressions and improve outcomes from prolonged asphyxial cardiac arrest <23 minutes in duration. Additional studies are necessary to determine how ETCO₂ guidance can be used with other available physiologic data to maximize hemodynamic parameters during pediatric cardiac arrest and to evaluate the impact ETCO₂ guidance on long-term outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of Funding: Research reported in this publication was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development award R21HD072845, by the National Institute of Neurological Disorders and Stroke awards K08NS080984, R01NS060703, R01NS107417, and R21NS095036, by the National Research Service Award for Clinician Scientists in Pediatric Critical Cardiopulmonary Disease T32HL125239, and by the National Center for Research Resources of the National Institutes of Health Roadmap for Medical Research grant UL1RR025005. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Dr. O'Brien's institution received funding from National Institutes of Health (NIH) T32 Institutional Grant (T32HL125239), and she disclosed work for hire. Drs. O'Brien, Lee, Koehler, and Shaffner received support for article research from the NIH. Dr. Lee's institution received funding from the NIH and the American Heart Association, and she received funding from Medtronic (consulting on near infrared spectroscopy technology in

2016). Dr. Koehler's institution received funding from the NIH. Dr. Hunt received funding from the NIH (grant support as a co-investigator), Zoll Medical Corporation (consulting on simulation based medicine education innovation she created called "Rapid Cycle Deliberate Practice" and from medical education technologies that she and her research partners have created that Zoll has a non-exclusive license for, although she has not received any royalties), and National Medical Consultants (for performing expert medical reviews). Dr. Shaffner's institution received funding from the National Institute of Child Health and Human Development, and he received funding from Wolters Kluwer.

Dr. Lee's institution received funding from the NIH; she received support for article research from the NIH; and she received funding from Medtronic. Dr. Koehler received support for article research from the NIH. Dr. Hunt received support for research from the NIH; and she received funding from Zoll Medical Corporation (consulting, patents where Zoll Medical now has a non-exclusive license for two of the devices). Dr. Shaffner's institution received funding from the National Institute of Child Health and Human Development and the National Institute of Neurological Disorders and Stroke; he received funding from Wolters Kluwer; and he received support for article research from the NIH.

REFERENCES

1. Meaney PA, Bobrow BJ, Mancini ME, et al. Cardiopulmonary resuscitation quality: [corrected] improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association. *Circulation* 2013; 128: 417–435 [PubMed: 23801105]
2. Atkins DL, Everson-Stewart S, Sears GK, et al. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. *Circulation* 2009; 119: 1484–1491 [PubMed: 19273724]
3. Berg MD, Schexnayder SM, Chameides L, et al. Part 13: pediatric basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010; 122: S862–875 [PubMed: 20956229]
4. Kleinman ME, Chameides L, Schexnayder SM, et al. Pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Pediatrics* 2010; 126: e1361–1399 [PubMed: 20956434]
5. Girotra S, Spertus JA, Li Y, et al. Survival trends in pediatric in-hospital cardiac arrests: an analysis from Get With the Guidelines-Resuscitation. *Circ Cardiovasc Qual Outcomes* 2013; 6: 42–49 [PubMed: 23250980]
6. Fink EL, Prince DK, Kaltman JR, et al. Unchanged pediatric out-of-hospital cardiac arrest incidence and survival rates with regional variation in North America. *Resuscitation* 2016; 107: 121–128 [PubMed: 27565862]
7. Sheak KR, Wiebe DJ, Leary M, et al. Quantitative relationship between end-tidal carbon dioxide and CPR quality during both in-hospital and out-of-hospital cardiac arrest. *Resuscitation* 2015; 89: 149–154 [PubMed: 25643651]
8. de Caen AR, Maconochie IK, Aickin R, et al. Part 6: Pediatric Basic Life Support and Pediatric Advanced Life Support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2015; 132: S177–203 [PubMed: 26472853]
9. Hartmann SM, Farris RW, Di Gennaro JL, et al. Systematic review and meta-analysis of end-tidal carbon dioxide values associated with return of spontaneous circulation during cardiopulmonary resuscitation. *J Intensive Care Med* 2015; 30: 426–435 [PubMed: 24756307]
10. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: Adult Advanced Cardiovascular Life Support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015; 132: S444–464 [PubMed: 26472995]
11. Manning JE. Feasibility of blind aortic catheter placement in the prehospital environment to guide resuscitation in cardiac arrest. *J Trauma Acute Care Surg* 2013; 75: S173–177 [PubMed: 23883904]
12. Sutton RM, Friess SH, Bhalala U, et al. Hemodynamic directed CPR improves short-term survival from asphyxia-associated cardiac arrest. *Resuscitation* 2013; 84: 696–701 [PubMed: 23142199]
13. Friess SH, Sutton RM, French B, et al. Hemodynamic directed CPR improves cerebral perfusion pressure and brain tissue oxygenation. *Resuscitation* 2014; 85: 1298–1303 [PubMed: 24945902]

14. Naim MY, Sutton RM, Friess SH, et al. Blood pressure- and coronary perfusion pressure-targeted cardiopulmonary resuscitation improves 24-hour survival from ventricular fibrillation cardiac arrest. *Crit Care Med* 2016; 44: e1111–e1117 [PubMed: 27414479]
15. Ryu SJ, Lee SJ, Park CH, et al. Arterial pressure, end-tidal carbon dioxide, and central venous oxygen saturation in reflecting compression depth. *Acta Anaesthesiol Scand* 2016; 60: 1012–1023 [PubMed: 27080141]
16. Hamrick JL, Hamrick JT, Lee JK, et al. Efficacy of chest compressions directed by end-tidal CO₂ feedback in a pediatric resuscitation model of basic life support. *J Am Heart Assoc* 2014; 3: e000450
17. Hamrick JT, Hamrick JL, Bhalala U, et al. End-tidal CO₂-guided chest compression delivery improves survival in a neonatal asphyxial cardiac arrest model. *Pediatr Crit Care Med* 2017; 18: e575–e584 [PubMed: 28817508]
18. Gudipati CV, Weil MH, Bisera J, et al. Expired carbon dioxide: a noninvasive monitor of cardiopulmonary resuscitation. *Circulation* 1988; 77: 234–239 [PubMed: 3121209]
19. Falk JL, Rackow EC, Weil MH. End-tidal carbon dioxide concentration during cardiopulmonary resuscitation. *N Engl J Med* 1988; 318: 607–611 [PubMed: 3125432]
20. Weil MH, Bisera J, Trevino RP, et al. Cardiac output and end-tidal carbon dioxide. *Crit Care Med* 1985; 13: 907–909 [PubMed: 3931979]
21. Kern KB, Sanders AB, Voorhees WD, et al. Changes in expired end-tidal carbon dioxide during cardiopulmonary resuscitation in dogs: a prognostic guide for resuscitation efforts. *J Am Coll Cardiol* 1989; 13: 1184–1189 [PubMed: 2494245]
22. Lindberg L, Liao Q, Steen S. The effects of epinephrine/norepinephrine on end-tidal carbon dioxide concentration, coronary perfusion pressure and pulmonary arterial blood flow during cardiopulmonary resuscitation. *Resuscitation* 2000; 43: 129–140 [PubMed: 10694173]
23. Sanders AB, Kern KB, Otto CW, et al. End-tidal carbon dioxide monitoring during cardiopulmonary resuscitation. A prognostic indicator for survival. *JAMA* 1989; 262: 1347–1351 [PubMed: 2761035]
24. Kolar M, Krizmaric M, Klemen P, et al. Partial pressure of end-tidal carbon dioxide successful predicts cardiopulmonary resuscitation in the field: a prospective observational study. *Crit Care* 2008; 12: R115 [PubMed: 18786260]
25. Grmec S, Lah K, Tusek-Bunc K. Difference in end-tidal CO₂ between asphyxia cardiac arrest and ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest in the prehospital setting. *Crit Care* 2003; 7: R139–144 [PubMed: 14624688]
26. Jin X, Weil MH, Tang W, et al. End-tidal carbon dioxide as a noninvasive indicator of cardiac index during circulatory shock. *Crit Care Med* 2000; 28: 2415–2419 [PubMed: 10921572]
27. Garnett AR, Ornato JP, Gonzalez ER, et al. End-tidal carbon dioxide monitoring during cardiopulmonary resuscitation. *JAMA* 1987; 257: 512–515 [PubMed: 3098993]
28. Gazmuri RJ, Kube E. Capnography during cardiac resuscitation: a clue on mechanisms and a guide to interventions. *Crit Care* 2003; 7: 411–412 [PubMed: 14624676]
29. Idris AH, Staples ED, O'Brien DJ, et al. End-tidal carbon dioxide during extremely low cardiac output. *Ann Emerg Med* 1994; 23: 568–572 [PubMed: 8135436]
30. Sanders AB, Atlas M, Ewy GA, et al. Expired PCO₂ as an index of coronary perfusion pressure. *Am J Emerg Med* 1985; 3: 147–149 [PubMed: 3918548]
31. Gazmuri RJ, von Planta M, Weil MH, et al. Arterial PCO₂ as an indicator of systemic perfusion during cardiopulmonary resuscitation. *Crit Care Med* 1989; 17: 237–240 [PubMed: 2493355]
32. Ornato JP, Levine RL, Young DS, et al. The effect of applied chest compression force on systemic arterial pressure and end-tidal carbon dioxide concentration during CPR in human beings. *Ann Emerg Med* 1989; 18: 732–737 [PubMed: 2500044]
33. Isserles SA, Breen PH. Can changes in end-tidal PCO₂ measure changes in cardiac output? *Anesth Analg* 1991; 73: 808–814 [PubMed: 1952183]
34. Ward KR, Menegazzi JJ, Zelenak RR, et al. A comparison of chest compressions between mechanical and manual CPR by monitoring end-tidal PCO₂ during human cardiac arrest. *Ann Emerg Med* 1993; 22: 669–674 [PubMed: 8457093]

35. Yannopoulos D, Aufderheide TP, McKnite S, et al. Hemodynamic and respiratory effects of negative tracheal pressure during CPR in pigs. *Resuscitation* 2006; 69: 487–494 [PubMed: 16678959]
36. Duggal C, Weil MH, Tang W, et al. Effect of arrest time on the hemodynamic efficacy of precordial compression. *Crit Care Med* 1995; 23: 1233–1236 [PubMed: 7600832]
37. Matos RI, Watson RS, Nadkarni VM, et al. Duration of cardiopulmonary resuscitation and illness category impact survival and neurologic outcomes for in-hospital pediatric cardiac arrests. *Circulation* 2013; 127: 442–451 [PubMed: 23339874]
38. Angelos MG, Butke RL, Panchal AR, et al. Cardiovascular response to epinephrine varies with increasing duration of cardiac arrest. *Resuscitation* 2008; 77: 101–110 [PubMed: 18164797]
39. Schleien CL, Dean JM, Koehler RC, et al. Effect of epinephrine on cerebral and myocardial perfusion in an infant animal preparation of cardiopulmonary resuscitation. *Circulation* 1986; 73: 809–817 [PubMed: 3948377]
40. Lampe JW, Yin T, Bratinov G, Kaufman CL, et al. Effect of compression waveform and resuscitation duration on blood flow and pressure in swine: One waveform does not optimally serve. *Resuscitation* 2018; 131: 55–62 [PubMed: 30092277]
41. Shaffner DH, Schleien CL, Koehler RC, et al. Effect of vest cardiopulmonary resuscitation on cerebral and coronary perfusion in an infant porcine model. *CritCare Med* 1994; 22: 1817–1826
42. Michael JR, Guerci AD, Koehler RC, et al. Mechanisms by which epinephrine augments cerebral and myocardial perfusion during cardiopulmonary resuscitation in dogs. *Circulation* 1984; 69: 822–835 [PubMed: 6697465]
43. Eleff SM, Schleien CL, Koehler RC, et al. Brain bioenergetics during cardiopulmonary resuscitation in dogs. *Anesthesiology* 1992; 76: 77–84 [PubMed: 1729940]
44. Berg RA, Henry C, Otto CW, et al. Initial end-tidal CO₂ is markedly elevated during cardiopulmonary resuscitation after asphyxial cardiac arrest. *Pediatr Emerg Care* 1996; 12: 245–248 [PubMed: 8858644]
45. Gonzalez ER, Ornato JP, Garnett AR, et al. Dose-dependent vasopressor response to epinephrine during CPR in human beings. *Ann Emerg Med* 1989; 18: 920–926 [PubMed: 2504083]
46. Martin GB, Gentile NT, Paradis NA, et al. Effect of epinephrine on end-tidal carbon dioxide monitoring during CPR. *Ann Emerg Med* 1990; 19: 396–398 [PubMed: 2108594]
47. Tang W, Weil MH, Gazmuri RJ, et al. Pulmonary ventilation/perfusion defects induced by epinephrine during cardiopulmonary resuscitation. *Circulation* 1991; 84: 2101–2107 [PubMed: 1657450]
48. Callahan M, Barton C, Matthay M. Effect of epinephrine on the ability of end-tidal carbon dioxide readings to predict initial resuscitation from cardiac arrest. *Crit Care Med* 1992; 20: 337–343 [PubMed: 1541094]
49. Chase PB, Kern KB, Sanders AB, et al. Effects of graded doses of epinephrine on both noninvasive and invasive measures of myocardial perfusion and blood flow during cardiopulmonary resuscitation. *Crit Care Med* 1993; 21: 413–419 [PubMed: 8440112]
50. Cantineau JP, Merckx P, Lambert Y, et al. Effect of epinephrine on end-tidal carbon dioxide pressure during prehospital cardiopulmonary resuscitation. *Am J Emerg Med* 1994; 12: 267–270 [PubMed: 8179728]
51. Rivers EP, Wortsman J, Rady MY, et al. The effect of the total cumulative epinephrine dose administered during human CPR on hemodynamic, oxygen transport, and utilization variables in the postresuscitation period. *Chest* 1994; 106: 1499–1507 [PubMed: 7956410]

Figure 1. Experimental timeline indicating events during asphyxia and resuscitation in minutes. CPR, cardiopulmonary resuscitation; ETCO₂, end-tidal carbon dioxide; ETT, endotracheal tube; BLS, basic life support; ALS, advanced life support; ROSC, return of spontaneous circulation.

Table 1.

Baseline Characteristics of Subjects by Study Group

Variable	17 Minutes Asphyxia			23 Minutes Asphyxia		
	ETCO ₂ Group	Standard Group	<i>p</i>	ETCO ₂ Group	Standard Group	<i>p</i>
Weight (kg)	3.3 ± 0.5	3.3 ± 0.5	0.79	3.51 ± 0.6	3.57 ± 0.5	0.78
ETCO ₂ (torr)	46 ± 2.5	47 ± 1.8	0.50	46 ± 3.3	46 ± 1.6	0.77
HR (beats/min)	230 ± 44	232 ± 36	0.90	206 ± 49	232 ± 51	0.18
DBP (mmHg)	71 ± 14	74 ± 12	0.60	71 ± 14	77 ± 12	0.22
MAP (mmHg)	85 ± 15	88 ± 13	0.55	85 ± 15	89 ± 12	0.44
CVP (mmHg)	7 ± 3	7 ± 3	0.63	7.6 ± 1.7	8.3 ± 1.5	0.30
SPP (mmHg)	78 ± 16	81 ± 13	0.61	77 ± 15	81 ± 12	0.51
ICP (mmHg)	10 ± 4.1	10 ± 1.8	0.99	9.4 ± 1.8	10 ± 2.2	0.27
CPP (mmHg)	75 ± 15	78 ± 12	0.54	76 ± 14	79 ± 12	0.54
pHa	7.41 ± 0.04	7.42 ± 0.04	0.57	7.42 ± 0.04	7.41 ± 0.03	0.44
pHv	7.36 ± 0.06	7.35 ± 0.04	0.57	7.35 ± 0.04	7.34 ± 0.03	0.79
PaCO ₂ (torr)	41 ± 3.0	42 ± 2.4	0.89	42 ± 3.6	42 ± 2.4	0.76
PvCO ₂ (torr)	50 ± 9.1	50 ± 4.4	0.93	51 ± 5.1	50 ± 4.8	0.85
PaO ₂ (torr)	109 ± 32	90 ± 27	0.09	95 ± 20	105 ± 31	0.29
PvO ₂ (torr)	36 ± 6.6	35 ± 7.7	0.99	35 ± 8.2	38 ± 6.4	0.39
BEa	1.3 ± 1.9	1.7 ± 2.7	0.69	2.1 ± 2.6	1.5 ± 2.2	0.55
BEv	2.0 ± 2.7	1.7 ± 2.8	0.75	1.9 ± 3.0	1.5 ± 3.2	0.78
SaO ₂ (%)	97 ± 2.6	95 ± 3.0	0.10	96 ± 4.3	97 ± 4.0	0.65
SvO ₂ (%)	50 ± 11	53 ± 12	0.56	49 ± 15	52 ± 9.3	0.53
Hb (g/dL)	9.8 ± 1.7	10.0 ± 1.4	0.69	9.9 ± 1.6	10.0 ± 1.3	0.91
Temperature (°C)	38.6 ± 0.2	38.6 ± 0.3	0.34	38.8 ± 0.3	38.8 ± 0.2	0.90

Data were collected prior to asphyxia and are shown as mean ± SD.

BEa = base excess arterial; BEv = base excess venous; CPP = cerebral perfusion pressure; CVP = central venous pressure; DBP = diastolic blood pressure; ETCO₂ = end-tidal carbon dioxide; Hb = hemoglobin; HR = heart rate; ICP = intracranial pressure; MAP = mean arterial blood pressure; PaO₂ = arterial oxygen partial pressure; PvO₂ = venous oxygen partial pressure; PaCO₂ = arterial carbon dioxide partial pressure; PvCO₂ = venous carbon dioxide partial pressure; pHa = arterial pH; pHv = venous pH; SaO₂ = arterial oxygen saturation; SvO₂ = venous oxygen saturation; SPP = systemic perfusion pressure.

Table 2.

Hemodynamic Results During Basic and Advanced Life Support by Study Group

Parameter	17 Minutes Asphyxia			23 Minutes Asphyxia		
	ETCO ₂ (n=14)	Standard (n=14)	<i>p</i>	ETCO ₂ (n=14)	Standard (n=14)	<i>p</i>
Basic Life Support (0–10 min of CPR)						
ETCO ₂ (torr)	33 ± 15	18 ± 8	0.004	26 ± 17	20 ± 10	0.21
Comp/min	150 ± 14	101 ± 1	<0.0001	144 ± 9	100 ± 1	<0.0001
DBP (mmHg)	11 ± 7	6 ± 6	0.08	2 ± 4	5 ± 6	0.13
MAP (mmHg)	24 ± 10	18 ± 8	0.13	16 ± 4	17 ± 7	0.42
CVP (mmHg)	16 ± 7	16 ± 5	0.99	20 ± 7	17 ± 5	0.18
SPP (mmHg)	8 ± 14	2 ± 8	0.23	−4 ± 8	1 ± 8	0.11
ICP (mmHg)	14 ± 2	14 ± 4	0.80	16 ± 6	14 ± 4	0.46
CPP (mmHg)	10 ± 9	5 ± 6	0.05	0 ± 7	3 ± 7	0.24
Advanced Life Support (10–20 min of CPR)						
ETCO ₂ (torr)	42 ± 18	19 ± 12	0.0004	25 ± 15	21 ± 11	0.40
Comp/min	158 ± 15	101 ± 2	<0.0001	152 ± 10	100 ± 1	<0.0001
DBP (mmHg)	26 ± 19	14 ± 12	0.06	13 ± 5	14 ± 10	0.80
MAP (mmHg)	45 ± 23	26 ± 15	0.02	31 ± 8	27 ± 11	0.34
CVP (mmHg)	20 ± 10	20 ± 9	0.79	22 ± 8	18 ± 4	0.16
SPP (mmHg)	25 ± 27	7 ± 11	0.03	9 ± 11	9 ± 13	0.98
ICP (mmHg)	16 ± 6	15 ± 5	0.57	20 ± 6	16 ± 3	0.03
CPP (mmHg)	28 ± 21	11 ± 12	0.02	10 ± 10	11 ± 10	0.82

Data represent the cumulative 30-second values during the 10 minutes of basic life support or the 10 minutes of advanced life support and are shown as mean ± SD.

Comp/min = compressions per minute; CPP = cerebral perfusion pressure; CPR = cardiopulmonary resuscitation; CVP = central venous pressure; DBP = diastolic blood pressure; ETCO₂ = end-tidal carbon dioxide; ICP = intracranial pressure; MAP = mean arterial blood pressure; SPP = systemic perfusion pressure.

Table 3.

Hemodynamic Results During Basic and Advanced Life Support by Survival Group

Parameter	17 Minutes Asphyxia			23 Minutes Asphyxia		
	Survivors (n=12)	Non-survivors (n=16)	<i>p</i>	Survivors (n=4)	Non-survivors (n=24)	<i>p</i>
Basic Life Support (0–10 minutes of CPR)						
ETCO ₂ (torr)	36 ± 14	18 ± 9	0.0003	21 ± 5	23 ± 15	0.74
Comp/min	140 ± 27	115 ± 22	0.01	107 ± 14	125 ± 24	0.17
DBP (mmHg)	15 ± 6	4 ± 3	<0.0001	11 ± 6	3 ± 4	0.002
MAP (mmHg)	29 ± 8	16 ± 5	<0.0001	22 ± 5	16 ± 5	0.02
CVP (mmHg)	18 ± 8	15 ± 4	0.13	16 ± 1	19 ± 7	0.54
SPP (mmHg)	10 ± 14	1 ± 8	0.03	6 ± 5	−3 ± 8	0.04
ICP (mmHg)	15 ± 3	13 ± 3	0.03	13 ± 4	15 ± 5	0.32
CPP (mmHg)	14 ± 7	3 ± 4	<0.0001	10 ± 2	0 ± 6	0.007
Advanced Life Support (10–20 minutes of CPR)						
ETCO ₂ (torr)	43 ± 15	21 ± 15	0.0007	30 ± 5	22 ± 14	0.27
Comp/min	143 ± 31	118 ± 27	0.03	111 ± 21	129 ± 28	0.26
DBP (mmHg)	36 ± 14	9 ± 4	<0.0001	27 ± 4	11 ± 6	<0.0001
MAP (mmHg)	56 ± 19	21 ± 5	<0.0001	43 ± 4	27 ± 8	0.0006
CVP (mmHg)	23 ± 12	18 ± 7	0.14	20 ± 2	20 ± 7	0.96
SPP (mmHg)	32 ± 24	4 ± 9	0.0002	23 ± 5	6 ± 11	0.006
ICP (mmHg)	20 ± 4	13 ± 5	0.001	17 ± 2	18 ± 6	0.60
CPP (mmHg)	36 ± 18	8 ± 8	<0.0001	26 ± 4	8 ± 8	0.0001

Data represent the cumulative 30-second values during the 10 minutes of basic life support or the 10 minutes of advanced life support and are shown as mean ± SD.

Comp/min = compressions per minute; CPP = cerebral perfusion pressure; CPR = cardiopulmonary resuscitation; CVP = central venous pressure; DBP = diastolic blood pressure; ETCO₂ = end-tidal carbon dioxide; ICP = intracranial pressure; MAP = mean arterial blood pressure; SPP = systemic perfusion pressure.

Table 4.

Outcomes, Blood Gas Results, and Cardiopulmonary Resuscitation-related Injuries by Study Group

Variable	17 Minutes Asphyxia			23 Minutes Asphyxia		
	ETCO ₂ Group	Standard Group	<i>p</i>	ETCO ₂ Group	Standard Group	<i>p</i>
Outcome results						
ROSC, n (%)	9/14 (64)	3/14 (21)	0.05	1/14 (7)	3/14 (21)	0.60
Time to ROSC (survivors), min	15 ± 4	15 ± 4	0.97	16	19 ± 2	N/A
Successfully defibrillated, n (%)	9/14 (64)	5/14 (36)	0.26	4/14 (29)	5/14 (36)	1.0
Time to defibrillation, min	16 ± 4	14 ± 5	0.31	15 ± 3	14 ± 5	0.80
Defibrillation attempts	3.5 ± 1.6	4.2 ± 1.5	0.23	4.4 ± 1.4	4.5 ± 1.2	0.88
Epinephrine doses	2.3 ± 0.8	2.8 ± 0.6	0.07	2.9 ± 0.3	2.9 ± 0.3	1.0
8-minute CPR arterial blood gas results						
pH	7.05 ± 0.1	7.10 ± 0.15	0.32	7.07 ± 0.2	7.02 ± 0.1	0.34
PaCO ₂ (torr)	60 ± 31	39 ± 26	0.05	46 ± 25	50 ± 21	0.71
PaO ₂ (torr)	126 ± 49	117 ± 90	0.76	164 ± 84	102 ± 52	0.03
BE	-16 ± 2	-17 ± 4	0.31	-18 ± 3	-17 ± 2	0.37
Autopsy results						
Atelectasis, n (%)	10/14 (71)	14/14 (100)	0.10	13/14 (93)	14/14 (100)	1.0
Liver laceration, n (%)	0/14 (0)	1/14 (7)	1.0	0/14 (0)	1/14 (7)	1.0
Epicardial bruises, n (%)	5/14 (36)	5/14 (36)	1.0	5/14 (36)	4/14 (29)	1.0
Hemothorax, n (%)	2/14 (14)	1/14 (7)	1.0	1/14 (7)	0/14 (0)	1.0

Data are shown as mean ± SD unless otherwise specified. Percentages are in parentheses.

BE = base excess; ETCO₂ = end-tidal carbon dioxide; N/A = not applicable; PaCO₂ = arterial partial pressure of carbon dioxide; PaO₂ = arterial partial pressure of oxygen; ROSC = return of spontaneous circulation.