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ORIGINAL RESEARCH

Sustained Inflation During Chest Compression: A New Technique of Pediatric Cardiopulmonary Resuscitation That Improves Recovery and Survival in a Pediatric Porcine Model

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BACKGROUND: Chest compression (CC) during sustained inflations (CC+SI) compared with CC with asynchronized ventilation (CCaV) during cardiopulmonary resuscitation in asphyxiated pediatric piglets will reduce time to return of spontaneous circulation (ROSC).

METHODS AND RESULTS: Piglets (20–23 days of age, weighing 6.2–10.2 kg) were anesthetized, intubated, instrumented, and exposed to asphyxia. Cardiac arrest was defined as mean arterial blood pressure <25 mm Hg with bradycardia. After cardiac arrest, piglets were randomized to CC+SI (n=12) or CCaV (n=12) or sham (n=8). Sham-operated animals had no asphyxia. Heart rate, arterial blood pressure, carotid blood flow, cerebral oxygenation, and respiratory parameters were continuously recorded. There were no differences in baseline parameters or the duration and degree of asphyxiation. Median (interquartile range) Time to ROSC was 248 (41–346) seconds compared with 720 (167–720) seconds in the CC+SI group and CCaV group, respectively (*P*=0.0292). There was a 100% higher rate of ROSC in the CC+SI group versus CCaV group, with 10 (83%) versus 5 (42%) achieving ROSC (*P*=0.089), respectively. Piglets in the CC+SI and CCaV groups received intravenous epinephrine boluses to achieve ROSC (8/12 versus 10/12 *P*=0.639). There was a significantly higher minute ventilation in the CC+SI group, which was secondary to a 5-fold increase in the number of inflations per minute and a 1.5-fold increase in tidal volume.

CONCLUSIONS: CC+SI reduced time to ROSC and improved survival compared with using CCaV. CC+SI allowed passive ventilation of the lung while providing chest compressions. This technique warrants further studies to examine the potential to improve outcomes in pediatric patients with cardiac arrest.

REGISTRATION: URL: https://www.preclinicaltrials.eu; Unique identifier: PCTE0000152.

Key Words: animal models of human disease ■ asphyxia ■ cardiopulmonary arrest ■ cardiopulmonary resuscitation and emergency cardiac care ■ chest compression ■ pediatric cardiac arrest ■ sustained inflation

Cardiac arrest in pediatric patients mainly occurs due to respiratory failure rather than ventricular fibrillation, which is the main cause of adult cardiac arrest.[1] Therefore, ventilation during cardiopulmonary resuscitation (CPR) in children is more important than in adults.[1] Children with cardiac arrest of non-cardiac cause (asphyxial arrest) had a higher 30-day survival with more favorable neurological outcomes if they received chest compressions (CC) with rescue breathing compared with CC alone.[2] During pediatric

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CLINICAL PERSPECTIVE

What Is New?

- Using a sustained inflation (or constant distending pressure) during chest compression improved the time to and number of piglets achieving return of spontaneous circulation.
- Chest compression during sustained inflation allowed passive ventilation of the lung, improved lung aeration, minute ventilation, and cardiovascular functions during resuscitation while fewer piglets required intravenous epinephrine administration.

What Are the Clinical Implications?

- Our results are of considerable clinical relevance because improved respiratory and hemodynamic parameters potentially minimize morbidity and mortality in pediatric cardiac arrest patients.
- With chest compression during sustained inflation, fewer piglets required intravenous epinephrine administration, which may be of clinical relevance because epinephrine administration during cardiac arrest causes post-resuscitation myocardial dysfunction, decreased cerebral perfusion, impaired microcirculatory blood flow, and lower rate of survival survival.

Nonstandard Abbreviations and Acronyms

CC	chest compression
CC+SI	chest compression + Sustained Inflation
ROSC	return of spontaneous circulation
SI	sustained inflation

CPR, the Pediatric Resuscitation Task Force within the International Liaison Committee on Resuscitation recommends a 15:2 compression-to-ventilation ratio during bag and mask ventilation and continuous CC with a fixed respiratory rate of 10 to 12 per minute (CCaV) after tracheal intubation.[3]

However, the optimal compression-to-ventilation ratio during CPR in children remains unknown. Several pediatric animal studies compared 15:2 compression-to-ventilation with CCaV,[4] three-sided CPR (2 hands [2 fingers on the sternum and 2 fingers on the chest]), or hemodynamic-directed CPR[5,6] and reported improved time to return of spontaneous circulation (ROSC) and survival. An alternative approach could be superimposing CC with a constant high distending pressure during CPR, which improves hemodynamics and simultaneously allows for passive lung ventilation and thereby adequate oxygen delivery.[7–11] Adult animal studies reported improved hemodynamics when CCs were superimposed with a high distending pressure of 60 to 110 mm Hg.[7,8] Similarly, Hevesi et al superimposed CC with a lower constant distending airway pressure of 15 cmH_2O in asphyxiated adult pigs and observed improved pulmonary artery pressure compared with CPR at 5:1 compression-to-ventilation ratio.[9] Furthermore, applying pressure to the chest of neonates, infants, or children allows for passive lung aeration.[12–17] Tsui et al reported a median tidal volume delivery of 2 to 3.3 mL/kg during chest recoil after gentle pressure was applied to the chest of infants and toddlers.[17] We recently reported that superimposing CC with a sustained inflation (SI) (CC+SI) during CPR significantly improved time to ROSC, systemic and regional hemodynamics, and minute ventilation compared with a 3:1 compression-to-ventilation ratio in asphyxiated neonatal piglets.[12–16] Our approach used a constant distending pressure of 20 to 30 cmH_2O, which resulted in passive ventilation of the lung.[12] This approach was also successfully translated into the delivery room with similar results: significantly shorter mean time to ROSC compared with 3:1 compression-to-ventilation ratio (31 versus 138 seconds)[18] and is currently examined in the SURV1VE-trial, which compares CC+SI with 3:1 compression-to-ventilation during neonatal CPR in the delivery room.[19,20] While the CC+SI technique has been examined in the neonatal subjects,[12–16,18–20] evidence in the pediatric and adult populations is lacking. We aimed to compare the CC+SI technique with CCaV during CPR in asphyxiated pediatric piglets. We hypothesized that asphyxiated pediatric piglets resuscitated with CC+SI would have a reduced time to ROSC compared with CCaV.

METHODS

Thirty-two pediatric mixed breed piglets (20–23 days of age, weighing 6.2–10.2 kg) were obtained on the day of experimentation from the University Swine Research Technology Centre. Pediatric piglets with a current age of 20 to 23 days were included; there were no exclusion criteria. All experiments were conducted after approval of the Animal Care and Use Committee, University of Alberta (AUP00003084) and registered at preclinicaltrials.eu (PCTE0000152) and the protocol is published at protocols.io (http://dx.doi.org/10.17504/protocols.io.bh23j8gn). The study is reported according to the

ARRIVE guidelines[21] and a graphical display of the study protocol is presented in Figure 1. The authors declare that all supporting data are available within the article and materials used to conduct the research are available to any researcher for purposes of reproducing the results or replicating the procedure and data will be shared.

Randomization

Piglets were randomly allocated to control (sham-operated) or intervention: "CC+SI" or "CCaV." Randomization was 1:1 using a computer-generated randomization program (http://www.randomizer.org). A sequential numbered, sealed, brown envelope containing the allocation "sham" or "intervention" was opened after stabilization (step one of randomization). A second sequential numbered, sealed, brown envelope was opened just before the commencement of CPR containing the group allocation "CC+SI" or CCaV" (step two of randomization) (Figure 1).

Sample Size and Power Estimates

Our primary outcome measure was the CPR time to achieve ROSC. Our pilot studies required a mean (SD) of 700 (120) seconds of CPR to achieve ROSC using CCaV. We hypothesized that CC+SI would reduce time to achieve ROSC. A sample size of 24 piglets (12 per group) was sufficient to detect a clinically important (20%) reduction in time to achieve ROSC (ie, 700 versus 560 seconds), with 80% power and a 2-tailed alpha error of 0.05.

Blinding

It was impossible to blind the team to the allocated intervention due to the differences in both interventions. However, the person (G.M.S.) assessing cardiac arrest was blinded to group allocation until after cardiac arrest

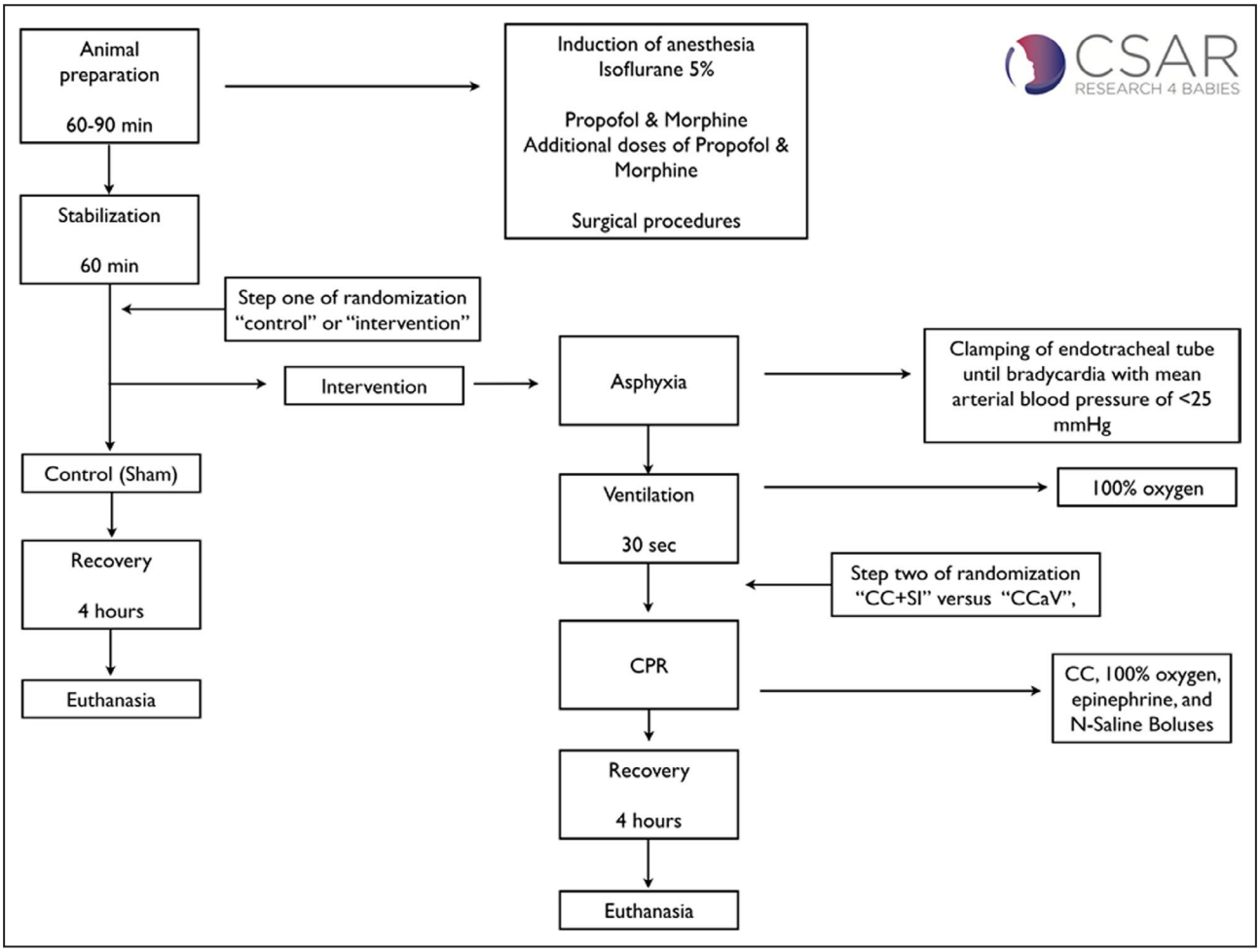

Figure 1. Study flow chart.
CC indicates chest compression; CC+SI, chest compression during sustained inflations; CCaV, chest compression with asynchronized ventilation; and CPR, cardiopulmonary resuscitation.

was confirmed. The statistical analysis was blinded to group allocation and only unblinded after the statistical analysis was completed.

Animal Preparation

Following the induction of anesthesia using isoflurane, piglets were intubated via a tracheostomy, and pressure-controlled ventilation (Sechrist infant ventilator, model IV-100; Sechrist Industries, Anaheim, CA) was commenced at a respiratory rate of 16 to 20 breaths/min and pressure of 20/5 cmH_2O. Oxygen saturation was kept within 90% to 100%. Glucose levels and hydration were maintained with an intravenous infusion of 5% dextrose at 10 mL/kg per hour. During the experiment, anesthesia was maintained with intravenous propofol 5 to 10 mg/kg per hour and morphine 0.1 mg/kg per hour. Additional doses of propofol (1–2 mg/kg) and morphine (0.05–0.1 mg/kg) were also given as needed. The piglet's body temperature was maintained at 38.5 to 39.5°C using an overhead warmer and a heating pad.

Hemodynamic Parameters

A 5-French Argyle (Klein-Baker Medical Inc., San Antonio, TX) double-lumen catheter was inserted via the right femoral vein for administration of fluids and medications. A 5-French Argyle single-lumen catheter was inserted below the right renal artery via the femoral artery for continuous arterial blood pressure monitoring in addition to arterial blood gas measurements. The right common carotid artery was also exposed and encircled with a real-time ultrasonic flow probe (4 mm; Transonic Systems Inc., Ithica, NY) to measure common carotid blood flow.

Piglets were placed in a supine position and allowed to recover from surgical instrumentation until baseline hemodynamic measures were stable (minimum of 1 hour). The ventilator rate was adjusted to keep the partial arterial CO_2 between 35 and 45 mm Hg as determined by periodic arterial blood gas analysis. Mean systemic arterial pressure, systemic systolic arterial pressure, heart rate, and percutaneous oxygen saturation were continuously measured and recorded throughout the experiment with a Hewlett Packard 78833B monitor (Hewlett Packard Co., Palo Alto, CA).

Respiratory Parameters

A respiratory function monitor (NM3, Respironics, Philips, Andover, MA) was used to continuously measure tidal volume, airway pressures, gas flow, and end-tidal CO_2. The combined gas flow and end-tidal CO_2 sensor was placed between the endotracheal tube and the ventilation device.[22,23]

Cerebral Perfusion

Cerebral oxygenation was measured using the Invos™ Cerebral/Somatic Oximeter Monitor (Invos 5100; Somanetics Corp., Troy, MI).[24] The sensors were placed on the right forehead of the piglet and secured with wrap and tape. Light shielding was achieved with a slim cap.

Experimental Protocol

Piglets were randomized into three groups: "CC+SI," "CCaV," or "Sham" using the two-step randomization process as mentioned above to avoid selection bias. The piglets that were randomized to "intervention" were exposed to asphyxia. Asphyxia was achieved by disconnecting the ventilator and clamping the endotracheal tube until mean arterial blood pressure was <25 mm Hg with bradycardia, which was defined as cardiac arrest. Once cardiac arrest was confirmed, a second sequential numbered, sealed brown envelope containing the allocation "CC+SI" or "CCaV" was opened (step two of randomization) (Figure 1). Fifteen seconds after cardiac arrest was diagnosed, positive pressure ventilation was performed for 30 seconds with a Neopuff T-Piece (Fisher & Paykel, Auckland, New Zealand). The default settings for positive pressure ventilation were a peak inflating pressure of 25 cmH_2O,[25,26] a positive end-expiratory pressure of 5 cmH_2O, a gas flow of 8 L/min, and 10 inflations per minute.[3,27] After 30 seconds of positive pressure ventilation, CCs were started according to group allocation. CCs were performed on a resuscitation board using the one-hand chest compression technique[3,27] at a rate of 100/min (guided by a metronome), and operators (G.M.S., S.P., P.Y.C.) were switched every 3 minutes to prevent fatigue.[3,27] CPR was continued for a maximum time of 12 minutes. Epinephrine (0.04 mg/kg per dose) was administered intravenously 2 minutes after the start of positive pressure ventilation, and every minute as needed if no ROSC was observed.[3,27] Bolus Ringer's solution (10 mL/min) was given immediately after each dose of epinephrine up to a total of 10 mL/kg. ROSC was defined as an unassisted heart rate ≥100/min for 15 seconds. After ROSC, piglets recovered and monitored for 4 hours. Sham-operated groups received the same surgical protocol, stabilization, and equivalent experimental periods without asphyxia and resuscitation. At the end of experimentation, piglets were euthanized with an intravenous overdose of sodium pentobarbital (100 mg/kg).

Data Collection and Statistical Analysis

Demographics of study piglets were recorded. Transonic flow probes, heart rate, and pressure

transducer outputs were digitized and recorded with LabChart programming software (ADInstruments, Houston, TX). Airway pressures, gas flow, tidal volume, and end-tidal CO_2 were measured and analyzed using Flow Tool Physiologic Waveform Viewer (Philips Healthcare, Wallingford, CT). For all respiratory parameters, the median value for each piglet was calculated first and then either the mean or median of the median calculated. Hemodynamic data during CPR (ie, mean and diastolic arterial blood pressure, central venous pressure, carotid blood flow) were divided into 4 epochs (0%–25%, 26%–50%, 51%–75%, 76%–100% of CPR time). The data are presented as mean (SD) for normally distributed continuous variables and median (interquartile range, IQR) when the distribution was skewed. The data were tested for normality (Shapiro-Wilk and Kolmogorov-Smirnov test) and compared using Student *t* test for parametric and Mann-Whitney *U* test for nonparametric comparisons of continuous variables, and Fisher's exact test for categorical variables. Differences between groups were also determined by two-way repeated-measures ANOVA, which facilitated investigating interactions between interventions and time points. Post-hoc pairwise comparisons between groups and time points were done using the Tukey method. One-way ANOVA with Tukey post-test was used for the analysis of tissue biochemical markers. Kaplan-Meier survival graphs with Mantel Haenszel log rank test were used to analyze time to ROSC and time of survival. *P* values are 2-sided and $P<0.05$ was considered significant. Statistical analyses were performed with SigmaPlot (Systat Software Inc, San Jose, CA).

Table 1. Characteristics of Newborn Piglets at Baseline, at Commencement of Cardiopulmonary Resuscitation, and Once Return of Spontaneous Circulation Was Restored

Characteristics	Sham (n=8)	CC+SI (n=12)	CCaV (n=12)	*P* Value
Baseline characteristics				
Age, d	22 (21–22)	22 (21–23)	22 (20–22)	0.909
Weight, kg	8.0 (7.4–8.6)	7.6 (7.0–8.2)	8.2 (6.4–8.9)	0.798
Sex (male/female)	2/6	5/7	5/7	0.806
Heart rate, bpm	152 (140–159)	141 (125–170)	178 (143–191)	0.267
Mean arterial pressure, mm Hg	72 (61–83)	76 (70–78)	66 (64–70)	0.078
Common carotid blood flow index, mL/min	77 (74–89)	96 (69–105)	90 (61–116)	0.377
Cerebral oxygenation (%)	50 (44–60)	53 (46–58)	52 (48–53)	0.856
Arterial pH	7.45 (7.41–7.47)	7.42 (7.39–7.43)	7.41 (7.39–7.44)	0.521
Base excess, mmol/L	0.5 (–0.8 to 3.3)	0 (–1.0 to 1.0)	–0.5 (–2.5 to 1.8)	0.514
$paCO_2$, torr	35 (32–40)	37 (35–40)	37 (35–39)	0.581
SpO_2 (%)	99 (97–99)	98 (96–98)	97 (96–99)	0.314
Lactate, mmol/L	2.4 (2.2–2.9)	2.6 (1.7–2.9)	2.8 (2.1–4.1)	0.276
Characteristics at commencement of cardiopulmonary resuscitation				
Heart rate, bpm		67 (52–73)	70 (56–80)	0.601
Common carotid blood flow index, mL		24 (19–26)	17 (15–19)	0.076
Arterial pH		7.03 (7.01–7.11)	6.98 (6.94–7.07)	0.071
$paCO_2$, torr		84 (73–94)	92 (81–105)	0.102
Lactate, mmol/L		7.8 (6.0–9.5)	9.4 (7.6–11.0)	0.099
Base excess, mmol/L		–8 (–9 to –5.5)	–9.5 (–14 to –7)	0.103
Characteristics 1 h after return of spontaneous circulation				
Arterial pH	7.39 (7.36–7.43)	7.32 (7.19–7.37)†,#	7.33 (7.28–7.41)	0.044
$paCO_2$, torr	40 (37–41)	41 (35–55)	36 (30–44)	0.246
Lactate, mmol/L	–1.0 (–2.0 to –0.3)	–7.0 (–8.0 to –1)†,#	–5.0 (–9.5 to –3.5)†,#	0.021
Base excess, mmol/L	2.8 (2.5–3.1)	7.4 (3.6–7.8)†,#	5.8 (3.8–10.8)	0.028

Data are presented as median (interquartile range), and sex as n (%). bpm indicates beats per minute; CC+SI, chest compression during sustained inflations; and CCaV, chest compression with asynchronized ventilation.

†Significantly different from sham group.

#Significantly different from baseline values.

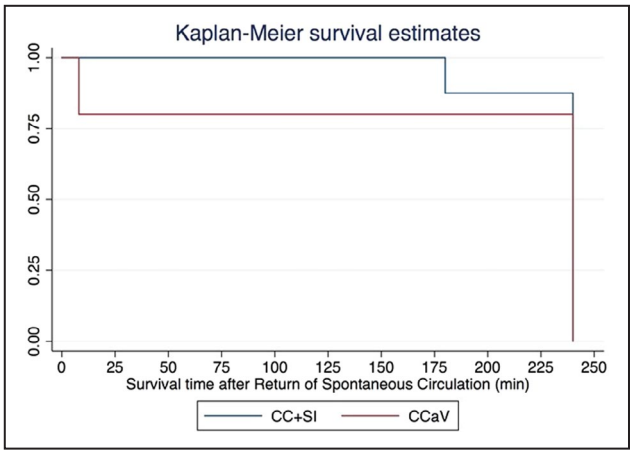

Figure 2. Kaplan-Meier survival graph comparison between chest compression with asynchronized ventilation (CCaV) and chest compression during sustained inflations (CC+SI).

RESULTS

Thirty-two newborn mixed breed piglets 20 to 23 days of age, weighing 7.8 (±1.1) kg were randomly assigned to the CCaV group (n=12), the CC+SI group (n=12), and the sham-operated group (n=8). There were no differences in the baseline parameters between the groups (Table 1). The median (IQR) duration of asphyxia was similar within groups; 330 (310–369) seconds in the CCaV group and 322 (256–340) seconds in the CC+SI group (P=0.355). Table 1 represents values of pH, pCO_2, lactate, and hemoglobin at the start of CPR (end of asphyxia), and the values of pH, pCO_2, and lactate 1 hour after ROSC.

Resuscitation

During CPR, the CC+SI group and the CCaV group had 100 (99–103) and 99 (98–102) CC/min, respectively. Time to ROSC was significantly decreased in the CC+SI group with 248 (41–346) seconds compared with 720 (167–720) seconds in the CCaV group (P=0.0292). There was a 100% higher rate of ROSC in the CC+SI group compared with the CCaV group, with 10 (83%) versus 5 (42%) achieving ROCS (P=0.089), respectively. Overall, 7/10 in the CC+SI group and 4/5 piglets in the CCaV survived to 4 hours after ROSC, (P=0.416) (Figure 2).

During CPR, the differences in the epinephrine administration were not significant between groups. Fewer piglets in the CC+SI group received intravenous epinephrine boluses to achieve ROSC than in the CCaV group (8/12 versus 10/12; P=0.639). Piglets in the CC+SI group received 3.5 (0–5.8) intravenous epinephrine boluses compared with 8.0 (1.8–11) in the CCaV group (P=0.123).

Respiratory Parameters During Chest Compression

During CPR, the CC+SI group had 100 (99–103) inflations/min until ROSC in comparison with 20 (19–22) inflations/min in the CCaV group (P<0.0001). In the CC+SI group, the inspiratory and expiratory tidal volume were 25.0 (19.3–31) and 24.0 (18.8–30.4) mL and in the CCaV group 11.5 (8.9–13.8) and 16.2 (10.6–28.6) mL, respectively (Table 2). There was a significantly higher minute ventilation in the CC+SI group, which was secondary to a 5-fold increase in the number of inflations per minute and a 1.5-fold increase in tidal volume (Table 2, Figure 3). End-tidal CO_2 and positive end-expiratory pressure were also significantly higher in the CC+SI group, while peak inspiratory flow was similar between groups (Table 2). Further analysis revealed that with each cycle of CC+SI, a tidal volume of 1 mL was gained, whereas during CCaV a loss of 6 mL per CCaV cycle was observed (P=0.078) (Figure 4).

Changes in Hemodynamic Parameters

Baseline hemodynamic parameters were similar between groups. During CPR, CC+SI had a significant higher mean and diastolic arterial blood pressure within the 0% to 25% time of CPR epoch (Figure 5). The mean (SD) mean arterial and diastolic arterial blood pressure during CC+SI and CCaV was 35.6 (6.0) versus 23.5 (6.3) mm Hg, and 18.6 (3.6) and 13.2 (2.6) mm Hg, respectively (Figure 5). Furthermore, central venous

Table 2. Respiratory Parameters During the Duration of Chest Compression

Respiratory Parameter	CC+SI (n=12)	CCaV (n=12)	*P* Value
Peak inflation pressure, mm Hg	29 (4)	27 (8)	0.9825
Positive end expiratory pressure, mm Hg	30 (5)	7 (1)	<0.0001
Peak inflation flow, mL/min	7 (1)	6 (0.5)	0.0677
Tidal volume, mL/kg#	24 (19–30)	16 (10–28)	0.1783
Minute ventilation, mL/min#	2508 (1918–3037)	324 (211–571)	0.0001
End-tidal carbon dioxide, mm Hg	64 (16)	39 n	0.0004

Data are presented as mean (SD), unless indicated # median (interquartile range). CC+SI indicates chest compression during sustained inflations; and CCaV, chest compression with asynchronized ventilation.

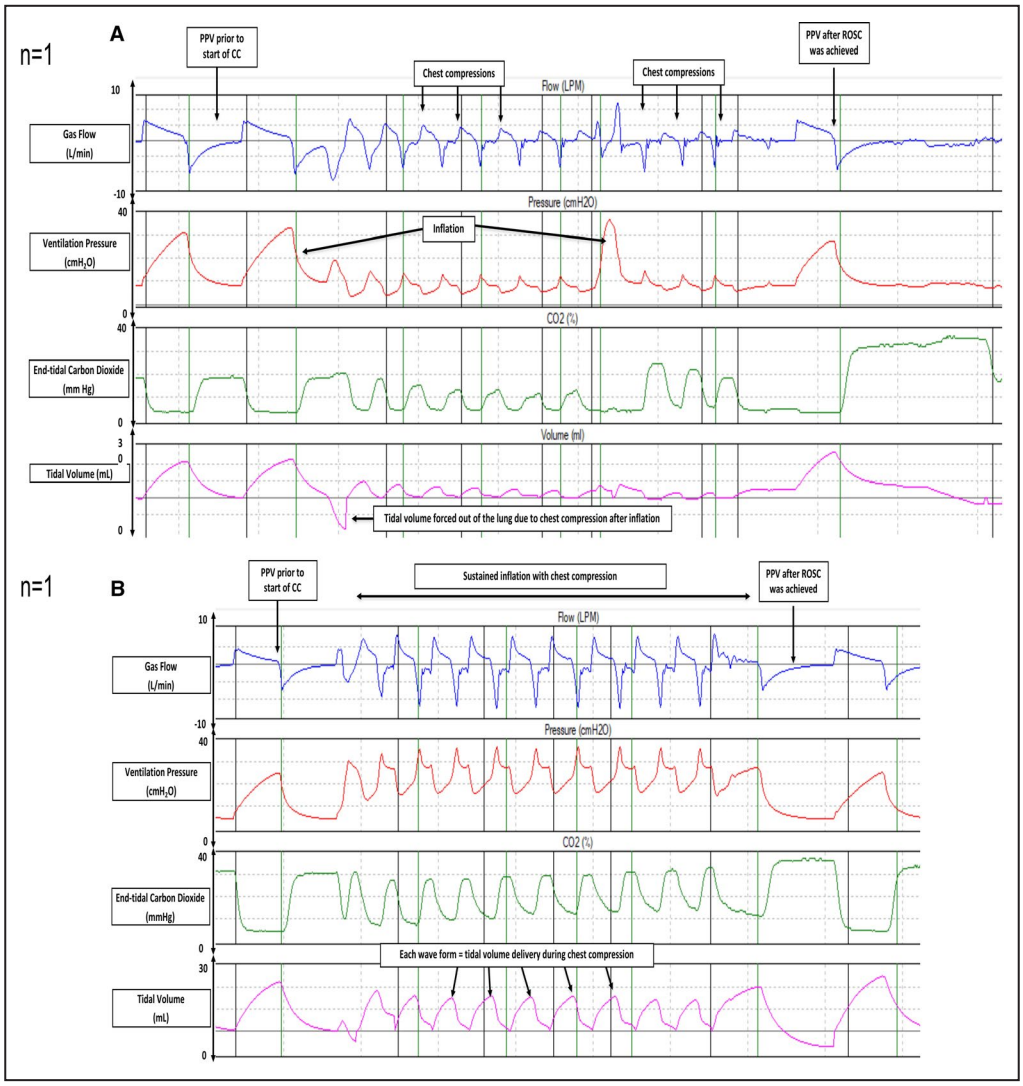

Figure 3. Examples of respiratory waveforms during cardiopulmonary resuscitation in the chest compression with asynchronized ventilation (CCaV) (n=1) (A) and chest compression during sustained inflations (CC+SI) (n=1) groups (B; gas flow, airway pressure, end-tidal CO_2, and tidal volume).

pressure was lower during CC+SI, however, this did not reach statistical significance (Figure 5). During the 4-hour recovery period, the CC+SI group had lower heart rate, higher mean arterial blood pressure, and higher common carotid blood flow and cerebral regional oxygen saturation (Figure 6), which indicated better recovery of piglets following CC+SI compared with those resuscitated by CCaV, however the differences between groups were not statistically different.

DISCUSSION

Current pediatric resuscitation guidelines recommend 15:2 compression-to-ventilation ratio during bag and mask ventilation and CCaV once an advanced airway is secured.[3] Pediatric animal studies comparing 15:2 compression-to-ventilation with CCaV,[4] three-sided CPR, or hemodynamics-directed CPR[5,6] reported improvement in time to ROSC and survival. Neonatal animal studies compared 3:1 compression-to-ventilation with CCaV or CC+SI and reported significantly faster time to ROSC and survival with CC+SI but not with CCaV. Furthermore, human pilot data demonstrated that CC+SI has a faster time to ROSC compared with 3:1 compression-to-ventilation.[12–16,18–20] To our knowledge, our study is the first to compare CC+SI to CCaV in CPR using a pediatric piglet model of asphyxia. The results of our study can be summarized as follows: (1) CC+SI significantly reduced time to ROSC with 100% more piglets achieving ROSC; (2) minute ventilation, and therefore alveolar oxygen delivery was significantly increased in the CC+SI group (Table 2), (3) CCs during CC+SI pushed

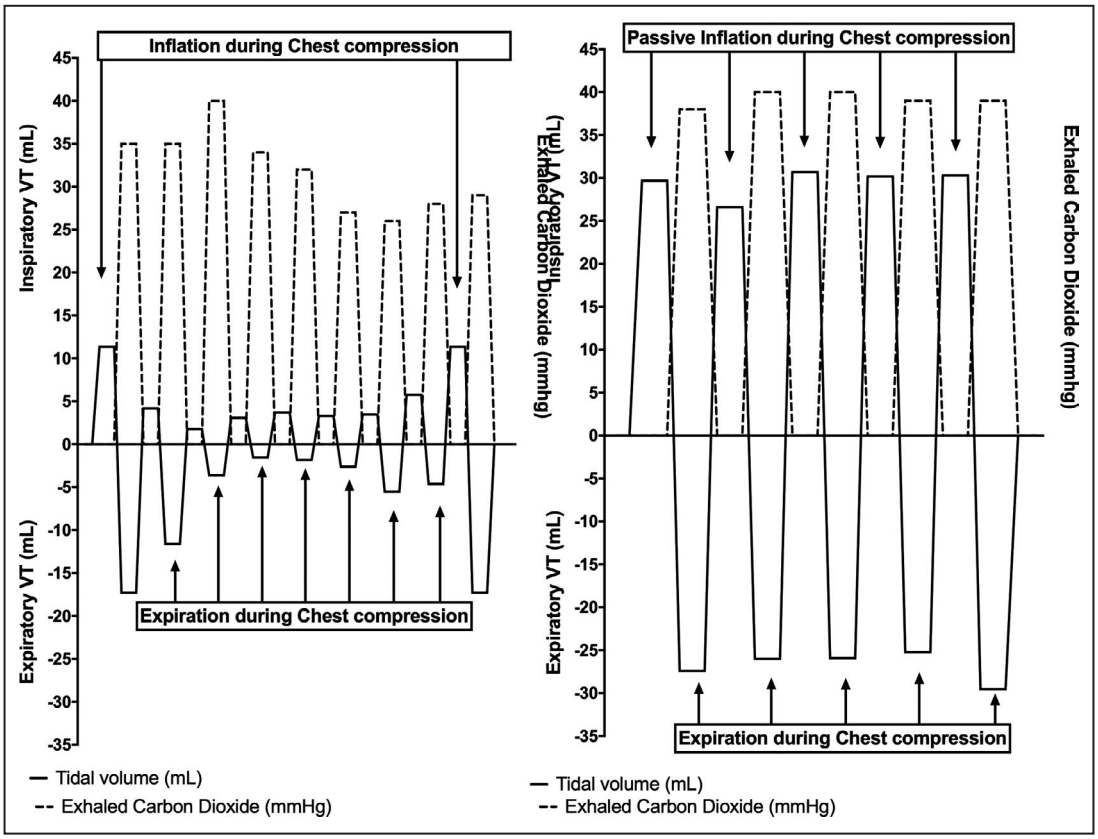

Figure 4. Average changes in inspiratory and expiratory tidal volume and end-tidal carbon dioxide CO_2 during chest compression with asynchronized ventilation (CCaV) (n=12) and chest compression during sustained inflations (CC+SI) (n=12).
Chest compression pushes air out of the chest and during chest recoil air passively enters the lung.

air out of the lung, and during chest recoil air was passively drawn back into the lungs (Figures 3B and 4), and (4) CC+SI improved hemodynamics during recovery. We speculate that improved hemodynamics and increased minute ventilation, and therefore increased alveolar oxygen delivery, may have contributed to the faster time to ROSC in the CC+SI group.

The thorax pump theory states that any maneuver which increases the intrathoracic pressure will result in blood flow during CPR.[28] Chandra et al reported higher carotid blood flow and arterial blood pressure when each CC was superimposed with a distending pressure of 60 to 110 mm Hg.[7,8] Hevesi et al used a distending CPAP pressure of 15 cmH_2O continuously during CPR of asphyxiated adult piglets and observed improved pulmonary artery pressure compared with the 5:1 compression-to-ventilation ratio.[9] Furthermore, a study in newborn lambs showed that using a constant high distending pressure of 40 cmH_2O during ventilation at birth improves carotid and pulmonary blood flow.[29] Similarly, a study by our group observed a higher carotid and pulmonary blood flow during CC+SI of asphyxiated newborn piglets with a distending pressure of 30 cmH_2O.[12] In the current study, we used a distending pressure of 25 cmH_2O during CC+SI and observed a higher mean and diastolic blood pressure compared with CCaV (Figure 6). Furthermore, there are concerns that sustained inflations or a high distending pressure could impair venous return. In our previous study comparing CC+SI with 3:1 C:V in asphyxiated newborn piglets we did not observe impairment of venous return.[12] Similar, providing a single sustained inflation of 30 seconds or CC+SI to asphyxiated near-term lambs did not impede venous return.[30,31] Also, a recent randomized trial in late preterm infants using sustained inflations did not observe impaired venous return.[32] In the current study, the central venous pressure was lower in the CC+SI group compare to CCaV, which suggest that CC+SI at the currently used pressures does not impair venous return.

A mathematical model suggested that the optimal compression-to-ventilation ratio in children depends on body weight, and ventilations should increase with decreasing weight.[33] Interestingly, during CCaV, only a 10:1 to 12:1 compression-to-ventilation ratio is delivered.[3] During CC+SI, the compression-to-ventilation

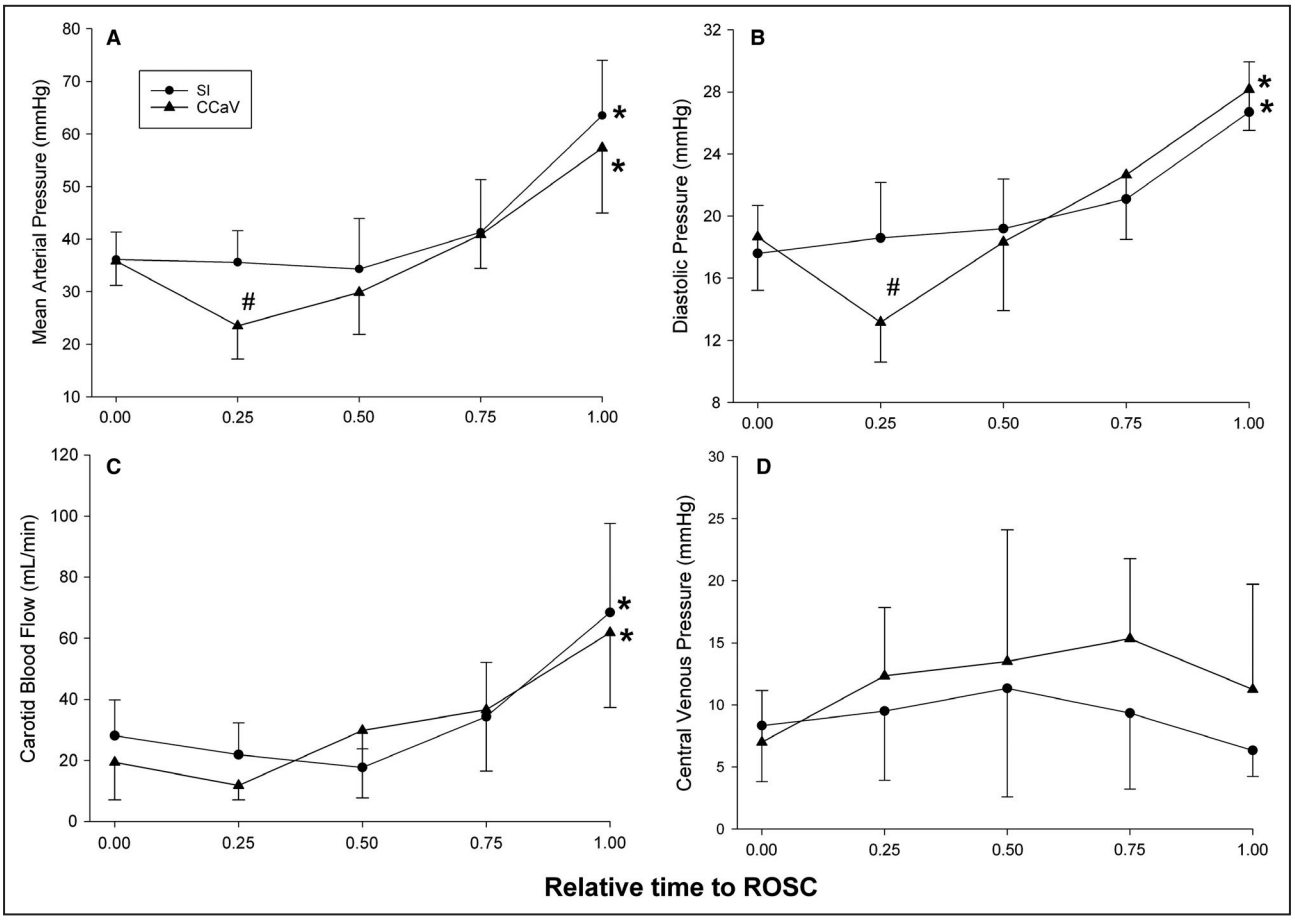

Figure 5. Temporal changes in (A) mean arterial blood pressure, (B) diastolic arterial blood pressure, (C) central venous pressure, (D) carotid blood flow during cardiopulmonary resuscitation of CC+SI (●) and CCaV (▲) groups.
*P<0.05 significantly different from time 0 and #P<0.05 significantly different between CCaV=chest compression with asynchronized ventilation and CC+SI=chest compression during sustained inflations. ROSC indicates return of spontaneous circulation.

ratio was 1:1, which equaled to 100 inflations/min during 100 CC/min, which led to significantly higher minute ventilation. Indeed, during CC+SI tidal volume is passively delivered during CC. Tsui et al reported a median tidal volume delivery of 2 to 3.3 mL/kg during chest recoil when a gentle pressure was applied to the chest of infants and toddlers.[17] Similarly, Hevesi et al used a distending pressure of 15 cmH_2O during CPR and reported minute ventilation of 7.6 L/min compared with standard CPR with 4.7 L/min.[9] The increased minute ventilation led to improved oxygenation and CO_2 elimination during CC.[9] Winkler et al reported a tidal volume between 125 and 309 mL during CC with a distending pressure of 20 or 30 cmH_2O compared with compression-only CPR without distending airway pressure using an adult manikin model.[10] Solevåg et al reported that the optimal distending pressure is 25 cmH_2O to deliver an adequate tidal volume in newborn piglets.[25] In the current study, we also used a distending pressure of 25 cmH_2O and observed a tidal volume of 14 to 34 mL during CC+SI; in CCaV the peak inflation pressure of 25 cmH_2O during inflations resulted in 8 to 52 mL tidal volume delivery.

During CC+SI, a constant high distending pressure is applied during CC, which results in continuous tidal volume delivery, lung recruitment, and lung aeration (Figures 3 and 4).[13,34,35] In comparison, during CCaV the lung is deflated as each CC presses air out of the lung resulting in lung de-recruitment and atelectasis. In a neonatal piglet model, Li et al reported a volume gain of 2.3 mL/kg per CC+SI cycle,[13] while during CCaV a cumulated volume loss of 4.5 mL/kg occurred for each CCaV cycle.[13] In the current study, the volume gain during CC+SI was 1 mL per CC+SI cycle while during CCaV the volume loss was 6 mL per CCaV cycle (P=0.078). This is concerning as a loss in V_T could cause lung de-recruitment and atelectasis leading to impaired oxygenation and delay in ROSC. This is of considerable clinical relevance as improved lung aeration will result in increased pulmonary blood flow, increased oxygenated blood flow to allow

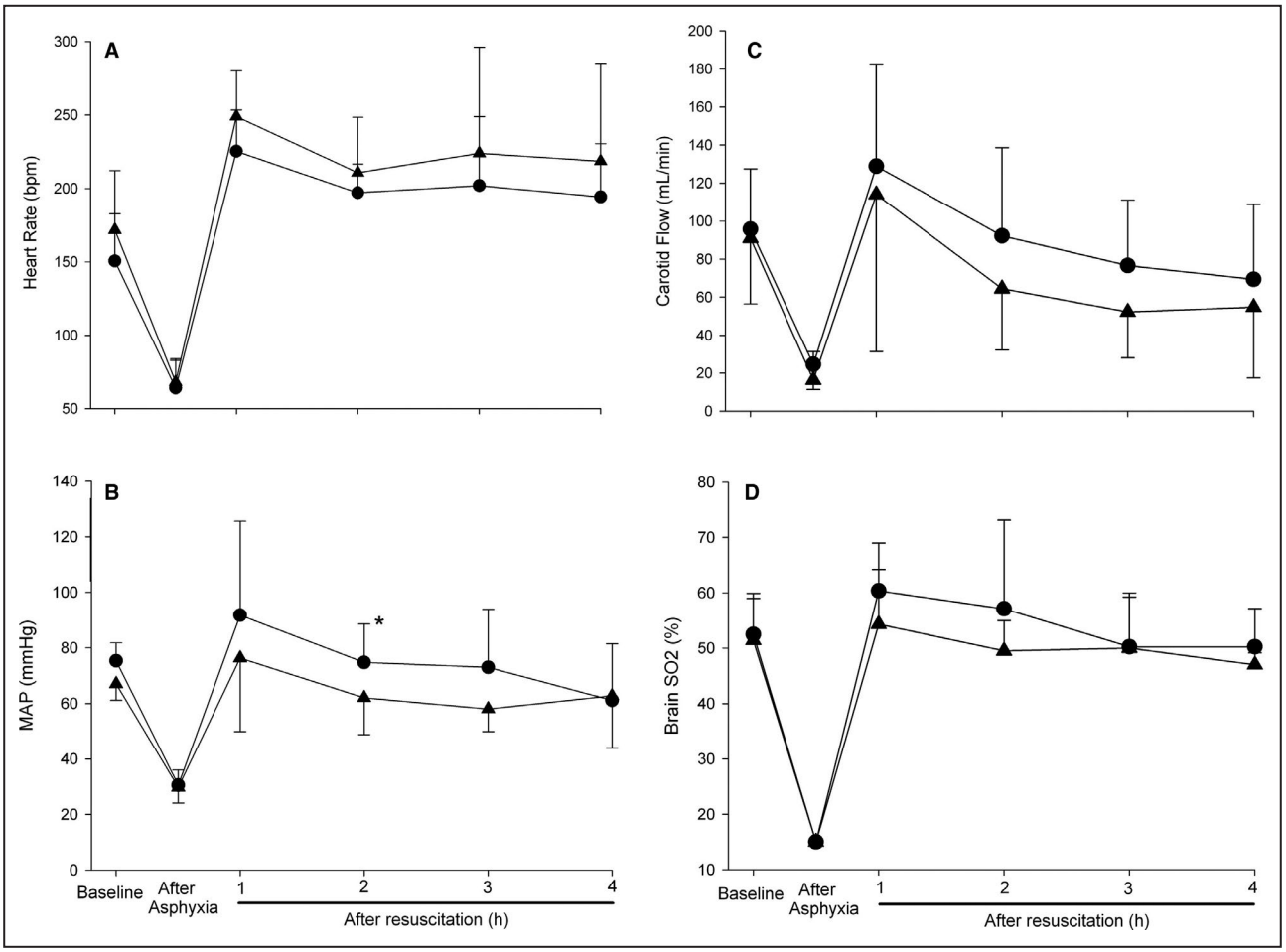

Figure 6. Temporal changes in (A) heart rate, (B) mean arterial blood pressure, (C) carotid blood flow, and (D) brain oxygenation during asphyxia and recovery of CC+SI (•) and CCaV (▲) groups.
All values represent mean (standard error of the mean). *P<0.05 significantly different between chest compression with asynchronized ventilation (CCaV) and chest compression during sustained inflations (CC+SI).

restoring cardiac function, and better tissue oxygen delivery during CPR. In comparison, the volume gain during CC+SI could lead to hyperventilation and hypocarbia during CPR. Unfortunately, we did not obtain an arterial blood gas immediately after ROSC, which is a limitation of the current study. However, our previous studies did not observe hypocarbia immediately after ROSC.[12,14–16]

Limitations

Our use of a piglet asphyxia model closely simulates asphyxia events in children leading to bradycardia and cardiac arrest, in contrast to models of cardiac arrest induced by other means including ventricular fibrillation. However, several limitations should be considered: All piglets were sedated/anesthetized and intubated with a tightly sealed endotracheal tube to prevent any endotracheal tube leak, which may not occur in all pediatric patients. Nevertheless, our findings are still clinically relevant as the distribution of cardiac output during asphyxia episodes are qualitatively similar. Our resuscitation model is slightly different from the currently recommended resuscitation guidelines, as we administered the first dose of epinephrine 90 seconds after CC was initiated and then every 60 seconds, which is different to the current advanced pediatric resuscitation guidelines,[3,27] which may have influenced our results.

CONCLUSIONS

CC+SI reduced time to ROSC and improved survival compared with using CCaV. CC+SI allowed passive ventilation of the lung while providing chest compressions. This technique warrants further studies to examine the potential to improve outcomes in pediatric patients with cardiac arrest.

ARTICLE INFORMATION

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Disclosures

None.

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