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Continuous Chest Compressions with Asynchronous Ventilations Increase Carotid Blood Flow in the Perinatal Asphyxiated Lamb Model

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Abstract

Background: The neonatal resuscitation program (NRP) recommends interrupted chest compressions (CC) with ventilation in the severely bradycardic neonate. The conventional 3:1 compression-to-ventilation (C:V) resuscitation provides 90 CC/min, significantly lower than the intrinsic newborn heart rate (120–160 beats/min). Continuous CC with asynchronous ventilation (CCCaV) may improve success of return of spontaneous circulation (ROSC).

Methods: Twenty-two near-term fetal lambs were randomized to interrupted 3:1 C:V (90 CC + 30 breaths/min) or CCCaV (120 CC + 30 breaths/min). Asphyxiation was induced by cord occlusion. After five min of asystole, resuscitation began following NRP guidelines. The first dose of epinephrine was given at 6 minutes. Invasive arterial blood pressure and left carotid blood flow were continuously measured. Serial arterial blood gases were collected.

Results: Baseline characteristics between groups were similar. Rate of and time to ROSC was similar between groups. CCCaV was associated with a higher PaO_2 (22±5.3 vs. 15±3.5 mmHg, $p<0.01$), greater left carotid blood flow (7.5±3.1 vs. 4.3±2.6 ml/kg/min, $p<0.01$) and oxygen delivery (0.40±0.15 vs. 0.13±0.07 mL O_2/kg/min, $p<0.01$) compared to 3:1 C:V.

Conclusion: In a perinatal asphyxiated cardiac arrest lamb model, CCCaV showed greater carotid blood flow and cerebral oxygen delivery compared to 3:1 C:V resuscitation.

INTRODUCTION

Perinatal asphyxia occurs in approximately 1 per 1,000 term births in the United States and is responsible for almost 25% of the greater than 4 million neonatal deaths worldwide (1, 2). Newborn infants requiring chest compressions (CC) and/or epinephrine are at high risk for hypoxic-ischemic encephalopathy (HIE) leading to neurological morbidity or death. Early

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return of spontaneous circulation (ROSC) may decrease mortality and improve outcome among survivors of HIE.

The current pediatric and adult basic life support guidelines emphasize priority in initiating early CC and to minimize interruptions (3, 4). Adult animal models with ventricular fibrillation-induced cardiac arrest that received uninterrupted CC have shown improved hemodynamics and neurologic outcomes (5–8). A few clinical studies have reported on improved survival when providing uninterrupted CC (9–11). However, a large randomized clinical trial did not demonstrate higher rates of survival or favorable neurologic outcomes in individuals with out-of-hospital cardiac arrest who were randomized to continuous CC (12). The applicability of these findings to the neonatal population is limited, as the presence of the ductus arteriosus might prevent build-up of diastolic pressure and coronary perfusion pressure with continuous CC in newly born infants in the DR. (13)

In contrast to adults, where sudden cardiac arrest leads to an abrupt cessation in cardiac output in the setting of well-oxygenated blood, neonatal cardiac arrest arises from profound bradycardia as a result of oxygen depletion, carbon dioxide accumulation and increasing lactic acidosis secondary to asphyxia. Severe metabolic acidosis and substrate depletion can lead to profound vasodilation in the asphyxiated state as opposed to sudden cardiac arrest, which can influence the effect of chest compressions on hemodynamic parameters in the asphyxiated newborn. In the asphyxiated neonate with cardiac arrest due to severe hypoxemia and hypercarbia, ventilation remains critical in establishing ROSC and resuscitation with exclusive CC in asphyxiated piglet models has not shown to be effective in achieving ROSC (14, 15). Ventilation of the lungs is, therefore, a critical component of neonatal resuscitation. Furthermore, in the presence of extreme bradycardia or cardiac arrest, pulmonary blood flow cannot be sustained and gas exchange does not occur with ventilation alone. The optimal ventilation strategy immediately after birth has not been determined and different compression-to-ventilation (C:V) ratios have not shown improved outcomes or higher quality compressions in pre-clinical and neonatal manikin models, respectively (16–20). In addition, the pediatric and adult CC rate in individuals with a secure airway is 100 CC/min, which is higher than the intrinsic baseline heart rate at rest (≈70–90 beats per minute -bpm). Interestingly, the current recommendation of 90 CC/min in neonatal resuscitation is considerably lower than the normal newborn resting heart rate (≈120–160 bpm).

Our understanding and knowledge of resuscitative medicine in newborns is limited to postnatal animal and simulation manikin models that do not adequately depict the transitioning fetal circulation, fluid-filled alveoli, patent ductus arteriosus and ductus venosus inherent to newborn infants (21–23). Taking into consideration that adult patients in cardiac arrest who receive uninterrupted CC may have improved survival, that the evidence behind the current recommended C:V ratio in newborn resuscitation is weak and that heart rate is the predominant factor in determining cardiac output in neonates, we hypothesize that uninterrupted,continuous CC with asynchronous ventilations (CCCaV) in a perinatal asphyxiated cardiac arrest newborn lamb model with transitioning circulation leads to quicker ROSC and better hemodynamic variables compared to the 3:1 C:V ratio recommended by the neonatal resuscitation program (NRP).

METHODOLOGY

Animal Preparation

The study protocol has been approved by the Institutional Animal Care and Use Committee (IACUC, protocol #20734) at the University of California Davis. All experiments were performed according to animal ethical guidelines, in compliance with the ARRIVE guidelines (24). Time-dated near-term (139–141 day gestation; term is 145 days) pregnant ewes (Dorper-cross) were procured by Van Laningham Farm, Arbuckle, CA. Following an overnight fast, the ewe was medicated with intravenous diazepam and ketamine. The ewe was intubated with a 10.0-mm cuffed endotracheal tube (ETT) and general anesthesia was provided by 2–3% inhaled isoflurane. The ewe was continuously monitored with a pulse oximeter and an end-tidal CO_2 ($ETCO_2$) monitor. Following a cesarean section, the fetal lamb was partially exteriorized and intubated with a 4.5-mm cuffed ETT. The fetal lung fluid in the ETT was partially drained passively by gravity by tilting the head to the side and, thereafter, the ETT was occluded to prevent gas exchange. A catheter was placed in the right carotid artery to measure blood pressures and collect blood samples. The right jugular vein was catheterized for fluid and medication administration. A left carotid flow probe (2-mm) was placed to measure blood flow. A pulse oximeter was placed on the right forelimb for continuous capillary oxyhemoglobin saturation monitoring. Following instrumentation, the umbilical cord was tied and cut. In the rare event that a lamb would have a complication related to the instrumentation and needed to be euthanized prior to the experiment, the lamb would not count toward the total number.

Experimental Protocol

After the cord was cut, the lamb was delivered onto a radiant warmer. During the asphyxial period, an umbilical arterial catheter was placed for blood collection (invasive blood pressure monitoring continued to be obtained by transducing the right carotid artery catheter to avoid interruptions in data during blood draws). A three-lead EKG was applied to the lamb. Asystole was defined by the absence of carotid blood flow, flat tracing in the arterial blood pressure waveform and absent heart rate (assessed by auscultation). Resuscitation was started five minutes from the time of asystole. The initiation of resuscitation was defined by the onset of positive pressure ventilation (PPV) with 21% oxygen by means of a T-piece resuscitator (25). After 30 seconds of effective PPV through the ETT, CC were initiated and inspired oxygen was increased to 100% (26). The first dose of epinephrine (0.03 mg/kg) was administered intravenously at six minutes from the onset of resuscitation if ROSC had not been achieved. This time point is chosen to approximate the time taken to administer intravenous epinephrine in clinical scenarios (27, 28). Subsequent epinephrine administration at the same dose was given every three minutes until ROSC or for a total of four doses. ROSC was defined by a sustained heart rate >100 bpm and a mean arterial blood pressure > 40 mm Hg. Arterial blood gases (ABG) were collected approximately every 1–2 minutes during active resuscitation and at the time of ROSC, 5, 10 and 15 minutes post ROSC. Content of arterial oxygen (CaO_2) was calculated using the equation: (1.34 * Hgb [g/dL] * SaO_2 %/100 %) + (PaO_2 [mm Hg] * 0.0031). Oxygen delivery to the brain was estimated by multiplying CaO_2 and left carotid blood flow.

Lambs have a keel-shaped chest that is different from humans, which could hamper chest compressions in the anterio-posterior direction. Chest compressions were, therefore, given manually in the medio-lateral direction. Chest compressions were provided by one individual (PV) for all experiments. An adaptor was attached between the ETT and T-piece resuscitator and connected to a respiratory function monitor (NM3, Respironics, Philips, Andover, MA) that would display the respiratory rate and which was visible to the individual who was providing PPV. The individuals participating in the code were unable to see the hemodynamic parameters displayed on the laptop screen by the acquisition software. As per the NRP guidelines, the resuscitators chanted “One and two and three and breathe” during resuscitation. We only gave PPV during the “breathe” phase in the 3:1 C:V arm. For lambs randomized to CCCaV, the individual tasked to give PPV provided a breath every 2 seconds and the one giving CC, compressed the chest twice every second. However, a dedicated scribe who could monitor the calculated CC rate from the arterial blood pressure tracing would provide feedback to the resuscitator on the CC rate.

Lambs were randomized into two groups using opaque sealed envelopes and we did not control for confounders.

3:1 C:V (control) group: 3:1 C:V (control) group: at the onset of resuscitation, PPV with set pressures of 35/5 cm H_2O with 21% oxygen were provided by a T-piece resuscitator (25, 29). After 30 seconds of PPV, CC were initiated at a C:V ratio of 3:1 to achieve 90 compressions and 30 breaths per minute, and inspired oxygen was increased to 100%. The breath was administered during a pause in compressions as recommended by NRP.

CCCaV group: CCCaV group: at the onset of resuscitation, PPV with set pressures of 35/5 cm H_2O with 21% oxygen was provided by a T-piece resuscitator. After 30 seconds, continuous CC were given at a rate of 120 compressions/min and PPV was continued at 30 breaths/min and inspired oxygen was increased to 100%. Chest compressions were not paused during breaths and were administered asynchronously with breaths.

Given the nature of experiments, the investigators could not be blinded. A dedicated scribe who could monitor the calculated heart rate from the arterial blood pressure tracing on the data acquisition software would provide feedback to the resuscitator on the CC rate.

Sample Size Calculation

Data from previous experiments from 6 lambs with cardiac arrest induced by umbilical cord occlusion resuscitated by 3:1 C:V demonstrated a mean time to ROSC of 5.9 minutes (standard deviation 2.2 minutes). One experiment with CCCaV resulted in ROSC at 3.1 minutes (difference in time to ROSC of 2.8 minutes). We planned a study of a continuous response variable (time to ROSC) from independent control (3:1 C:V) and experimental lambs (CCCaV) with 1 control per experimental subject. In our previous studies, the time to ROSC with 3:1 C:V resuscitation was normally distributed with a standard deviation of 2.2 minutes. If the true difference in the experimental and control means is 2.8 minutes, we will need to study 11 experimental lambs and 11 control lambs (for a total of 22 lambs) to be able to reject the null hypothesis that the population means of the experimental and control

groups are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

This sample size of 22 lambs will have adequate power (0.8) to evaluate a 2.5 ml/kg/min difference in carotid blood flow during chest compressions based on a standard deviation of 2 ml/kg/min from previous studies. However, given the high incidence of ROSC in this model (approximately 80%), we may not have adequate power to show a difference in incidence of ROSC.

Data Analysis

Hemodynamic variables were continuously recorded using a computer with acquisition and analysis software (BIOPAC systems, Goleta, CA). Hemodynamic data was acquired using BIOPAC AcqKnowledge software, which has an acquisition sample rate of 2000 Hz. Data was extracted by 10s increments and averaged over one minute. Continuous variables are expressed as mean and standard deviation (SD). Categorical variables are analyzed using χ^2 test with Fisher's exact test as required. Continuous variables are analyzed by 1-way ANOVA between groups with Fisher's post hoc test within groups. Cox proportional hazards model was used to analyze time variables. SPSS 24 (IBM, Armonk, NY) was used for statistical analysis. Statistical significance was defined as $P<0.05$. All lambs were included in the analysis.

RESULTS

A total of 22 lambs were studied with 11 lambs in each group (3:1 C:V vs. CCCaV). Characteristics of the lambs, including baseline hemodynamic parameters, weight, sex distribution and ABG analysis were similar between the groups (Table 1). Cord occlusion caused severe metabolic and respiratory acidosis in all lambs and time to cardiac arrest (asystole) was not significantly different between the groups.

Success of ROSC and Epinephrine

The incidence of ROSC was similar at 91% (10/11 lambs in each group) as was the median (interquartile range [IQR]) time to achieve ROSC at 6.1 (2.9 – 7.1) min in the 3:1 C:V group compared to 6.2 (4.2 – 6.9) min in the CCCaV group (p= 0.84; Table 2). Successful resuscitation without the need for epinephrine was the same with 4/11 lambs (36%) in each group achieving ROSC prior to epinephrine administration. All lambs that achieved ROSC after epinephrine did so after a single dose.

Hemodynamic Parameters

The average (SD) chest compression rate was 88 (7) CC/min in the 3:1 C:V group and 122 (6) CC/min in the CCCaV group. There was no difference in the systolic, diastolic and mean blood pressures during CC between the groups (Table 3). The mean left carotid blood flow (SD) was significantly higher during CC in the lambs that received CCCaV at 7.5 (3.1) ml/kg/min compared to 4.2 (2.6) ml/kg/min in the 3:1 C:V group (p <0.01).

Arterial Blood Gas Analysis

The partial oxygen tension (PaO_2) in the blood during CC was significantly greater in the CCCaV vs. the 3:1 C:V group at 22 (5.3) vs. 15 (3.5) mm Hg ($p < 0.01$; Table 3). CaO_2 was also significantly higher in the CCCaV group at 5.3 (2.1) ml O_2/dL vs. 3.0 (1.4) ml O_2/dL in the 3:1 C:V group ($p = 0.03$). Fetal baseline left carotid oxygen delivery (C-DO_2, calculated by multiplying the oxygen content in blood by the left carotid blood flow) was similar between the groups at 2.4 (1.7) ml O_2/kg/min and 2.6 (1.5) ml O_2/kg/min in the CCCaV and 3:1 C:V group, respectively (Table 1). The C-DO_2 was improved with continuous uninterrupted chest compressions at 0.4 (0.15) ml O_2/kg/min compared to 0.13 (0.07) ml O_2/kg/min in the 3:1 C:V group (Figure 1).

ROSC vs. non-ROSC

The two lambs that did not achieve ROSC had similar systolic, diastolic and mean blood pressures during chest compressions [26 (3.8), 9 (2.1) and 16 (3.2) mm Hg, respectively, with CCCaV vs. 24 (2.3), 6 (1.6) and 13 (1.9) mm Hg, respectively, with 3:1 C:V]. Thus, the blood pressures in the two lambs that did not achieve ROSC were similar to the blood pressures observed in the lambs that were successfully resuscitated. The mean left carotid blood flow was also similar between the two lambs that did not achieve ROSC at 1.6 (0.4) vs. 1.9 (0.4) ml/kg/min in the 3:1 C:V and CCCaV groups, respectively.

There was no difference in the hemodynamic variables at the time of ROSC and for the following hour post ROSC (Figure 2). The oxygen delivery to the brain at the time of ROSC was similar between groups (approximately 2.4 ml O_2/kg/min) and comparable to the baseline values (Tables 1 and 2).

DISCUSSION

In the severely asphyxiated newborn not responding to ventilation, optimal cardiovascular support with CC+PPV is vital to improve survival without neurological morbidity. The optimal C:V ratio that efficiently delivers oxygen to the brain and heart and hastens ROSC, however, remains unknown. In adult cardiopulmonary resuscitation, coronary perfusion pressure (estimated by subtracting diastolic aortic pressure from right atrial pressure) > 20 mm Hg has been shown to be a strong predictor of achieving ROSC (30). Experiments on adult pigs with cardiac arrest induced by ventricular fibrillation have demonstrated a stepwise increase in diastolic blood pressure with each successive CC and an abrupt drop in blood pressure following interruption of CC (8). In the resuscitation of the newly born in the delivery room with a patent ductus arteriosus, it is not clear if this relationship is maintained. In fact, we have demonstrated in the current experiments that newborn lambs with a transitioning circulation and a patent ductus arteriosus were successfully resuscitated despite maintaining mean diastolic blood pressures at approximately 7 to 10 mm Hg (Figure 2B). The relatively low diastolic aortic pressures must be sufficient to adequately perfuse the coronary arteries of the newborn heart and an attempt to maintain higher diastolic blood pressures may not be necessary (13).

Optimizing oxygen delivery to the brain during resuscitation may potentially be associated with better neurological outcomes. An important finding in the current study highlights that the left carotid blood flow is significantly greater when providing continuous uninterrupted chest compressions with asynchronous ventilation compared to 3:1 compression-to-ventilation resuscitation in spite of attaining comparable systolic, diastolic and mean aortic blood pressures during compressions. This is possibly secondary to higher CC rate in lambs from the CCCaV group. The carotid flows in the two lambs that did not achieve ROSC (1.6 ml/kg/min with 3:1 C:V vs. 1.9 ml/kg/min with CCCaV) were considerably lower than what was observed in the lambs that achieved ROSC (4.2 ml/kg/min in 3:1 C:V vs. 7.5 ml/kg/min with CCCaV). No conclusions can be drawn from such a small number, but we speculate that greater coronary blood flow would be observed with greater left carotid blood flow, which may explain ROSC success. Furthermore, serial ABG analyses during CC demonstrated that CCCaV achieved a greater PaO_2 (22 ±5.3 mm Hg) compared to 3:1 C:V (15 ±3.5 mm Hg), which implies improved pulmonary blood flow during CCCaV. With fetal hemoglobin with a P50 of 19 mmHg, these values fall along the steep portion of the hemoglobin-oxygen dissociation curve resulting in significant differences in SaO_2 and oxygen content between the two groups. Severe acidosis results in a rightward shift in the hemoglobin-oxygen dissociation curve and explains how a PaO_2 of 22 mm Hg has a SaO_2 of 33% (Figure 3) (31).

In a newborn piglet asphyxia model with cleared lung fluid and a closed ductus arteriosus comparing CCCaV to 3:1 C:V, 29% of CC overlapped with ventilation in the CCCaV group as opposed to 25% in the 3:1 C:V group with no effect on hemodynamic parameters (20). There is no evidence, therefore, to suggest that overlapping CC and ventilation adversely affect hemodynamics or ventilation. The aforementioned study showed a similar incidence of ROSC and hemodynamics. However, notable differences exist between the piglet study and the current study: (1) the mode of asphyxia was by hypoxic ventilation and tracheal tube occlusion, (2) the degree of asphyxia did not lead to cardiac arrest and (3) IV epinephrine was administered one minute after CC were commenced and hence the duration of CC was relatively short.

In the current study, improved left carotid blood flow and a greater PaO_2 resulted in more oxygen delivery (DO_2) to the brain with CCCaV. When assessing cerebral DO_2 (C-DO_2) compared to fetal baseline values, lambs that received CCCaV maintained a considerably greater C-DO_2 at 17% (0.4/2.4 ml O_2/kg/min) compared to 5% (0.13/2.6 ml O_2/kg/min) in the 3:1 C:V group. The neonatal heart is structurally and functionally very different from the pediatric and adult heart. The neonatal heart is less compliant and cardiac output is predominantly influenced by the frequency of contractions (heart rate) rather than by the volume of blood in the ventricles (preload/stroke volume). A study using a mathematical model of the human cardiopulmonary system has demonstrated that the most effective CC frequency depends upon body size and weight with higher CC frequency conferring optimal perfusion in newborns (32). Achieving a higher CC rate (i.e. continuous CC at 120 CC/min with asynchronous ventilation at 30 breaths/min) is likely to increase blood flow to essential organs compared to the traditional 90 CC/min and 30 breaths/min during resuscitation.

Fetuses and new-born animals of many species have been shown to survive for much longer periods in the absence of oxygen compared to adults of the same species (33). The median time to asystole in this study is comparable to asystole times (median 12 – 18 min) in previous publications by our group (25, 34). The relative length of time required to induce severe bradycardia and cardiac arrest in the newly born explains why the majority of severely asphyxiated newborns have a heart rate. We acknowledge several limitations in the current study. Neurologic outcomes were not assessed. Pulmonary arterial blood flow was not measured because an incomplete seal following a thoracotomy may have impacted adequacy of chest compressions and ventilation. The current model is of asystolic cardiac arrest and the response to chest compressions in severe bradycardia were not explored. In spite of the prolonged asphyxial period and time in asystole, an extended period of cardiac arrest may have decreased ROSC success and revealed a difference between the resuscitation techniques. The hemodynamic parameters observed in this study may not directly translate to the human newborn owing the interspecies differences in chest anatomy and chest compression method. Nonetheless, such fundamental questions as the hemodynamic effects of CC in the context of fetal shunts and fluid-filled lungs and the optimal compression-to-ventilation ratio in newborns underscore the large knowledge gap in neonatal resuscitation. The asphyxiated newborn lamb with transitioning physiology closely mimics the newborn in the delivery room and is the ideal model to study newborn physiology. This study provides accurate real time measurement of invasive physiologic parameters and frequent ABG analysis; valuable information that cannot be obtained from clinical studies.

CONCLUSION

In a perinatal asphyxial cardiac arrest lamb model, CCCaV showed higher PaO_2, greater carotid blood flow and oxygen delivery to the brain compared to the conventional 3:1 C:V resuscitation. No difference between groups was observed in the time to ROSC, the rate of ROSC or the number of epinephrine doses administered. Experimental studies surviving animals up to 24h to assess short-term neurologic outcomes and assessment of brain injury by immunohistochemistry are necessary before conducting clinical trials.

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Impact Statement:

- In a perinatal asphyxiated cardiac arrest lamb model, continuous chest compressions with asynchronous ventilation improved carotid blood flow and oxygen delivery to the brain compared to the conventional 3:1 compression-to-ventilation resuscitation.
- Pre-clinical studies assessing neurodevelopmental outcomes and tissue injury comparing continuous uninterrupted chest compressions to the current recommended 3:1 compression-to-ventilation during newborn resuscitation are warranted prior to clinical trials.

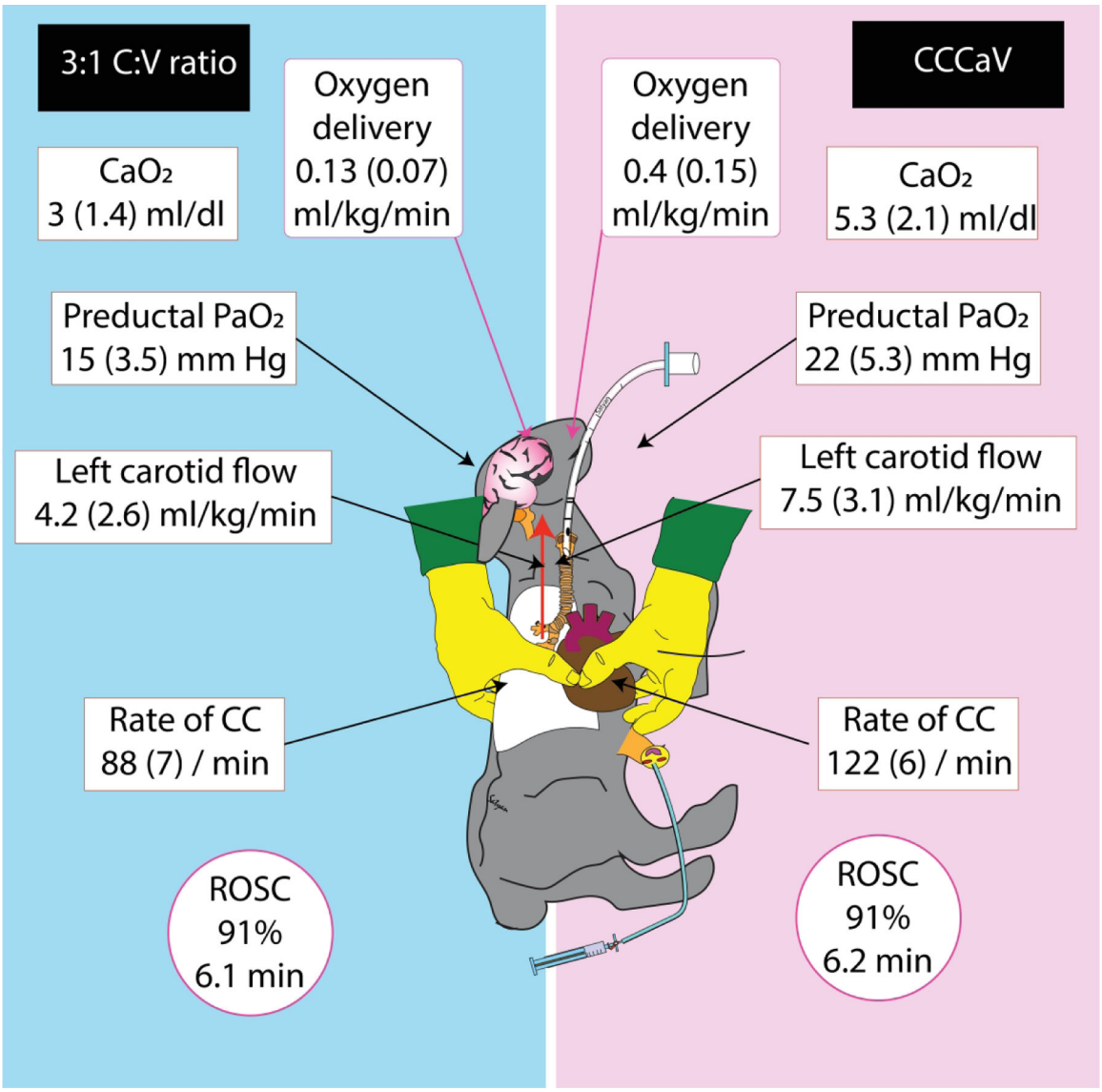

Figure 1:

Graphical abstract illustrating the differences in hemodynamic parameters and arterial blood gas analysis between the two study groups. C:V = compression-to-ventilation; CCCaV = continuous chest compressions with asynchronous ventilation; PaO_2 = partial arterial oxygen tension; ROSC = return of spontaneous circulation. Copyright Satyan Lakshminrusimha.

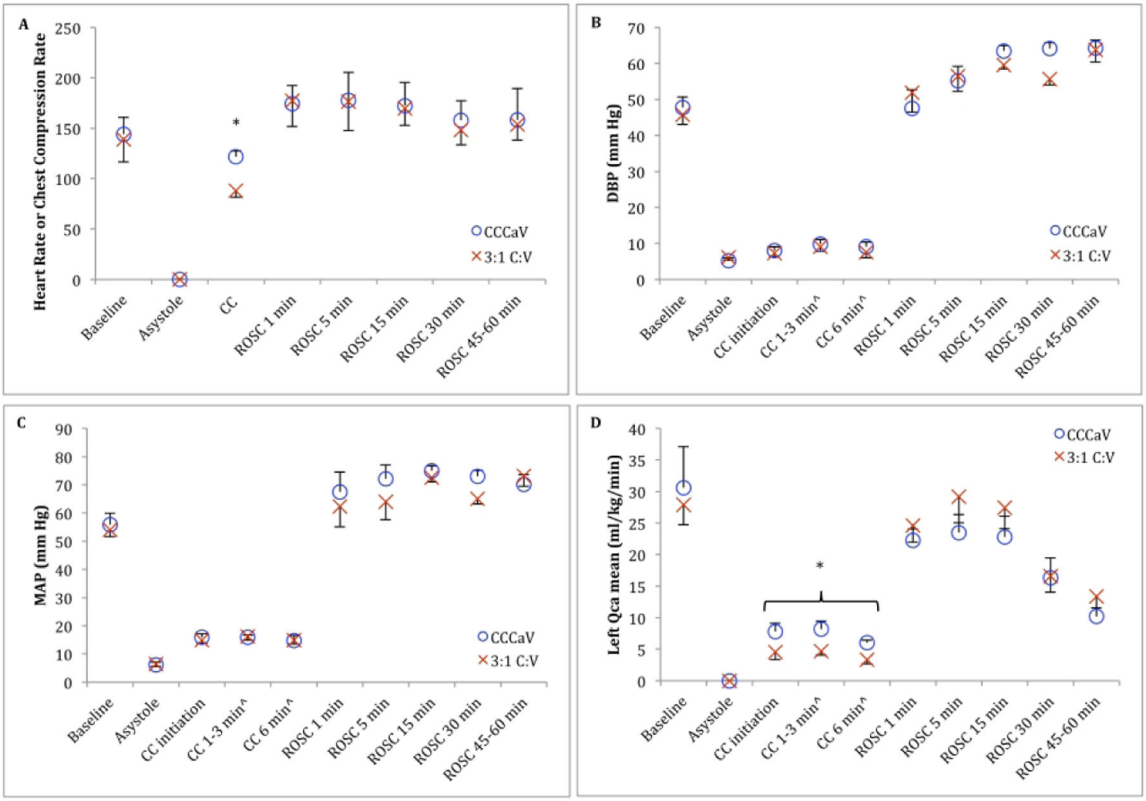

Figure 2:

Hemodynamics differences between 3:1 C:V and CCCaV. (A) There was no difference in heart rate during the study period. By study design, chest compression rates were significantly different between groups. (B) There was no difference in diastolic blood pressure between the two groups during the study period. Diastolic blood pressure range between 7 to 10 mm Hg during chest compressions. (C) There was no difference in mean blood pressure between the two groups during the study period. (D) Mean left carotid blood flow was significantly higher with CCCaV compared to 3:1 C:V. DBP = diastolic blood pressure; C:V = compression-to-ventilation; CCCaV = continuous chest compressions with asynchronous ventilation; MBP = mean blood pressure; Qca = carotid blood flow. * p value < 0.05. ^ at 1–3 min, n = 9 lambs in the CCCaV group and at 6 min, n = 7 lambs in the 3:1 C:V and CCCaV groups.

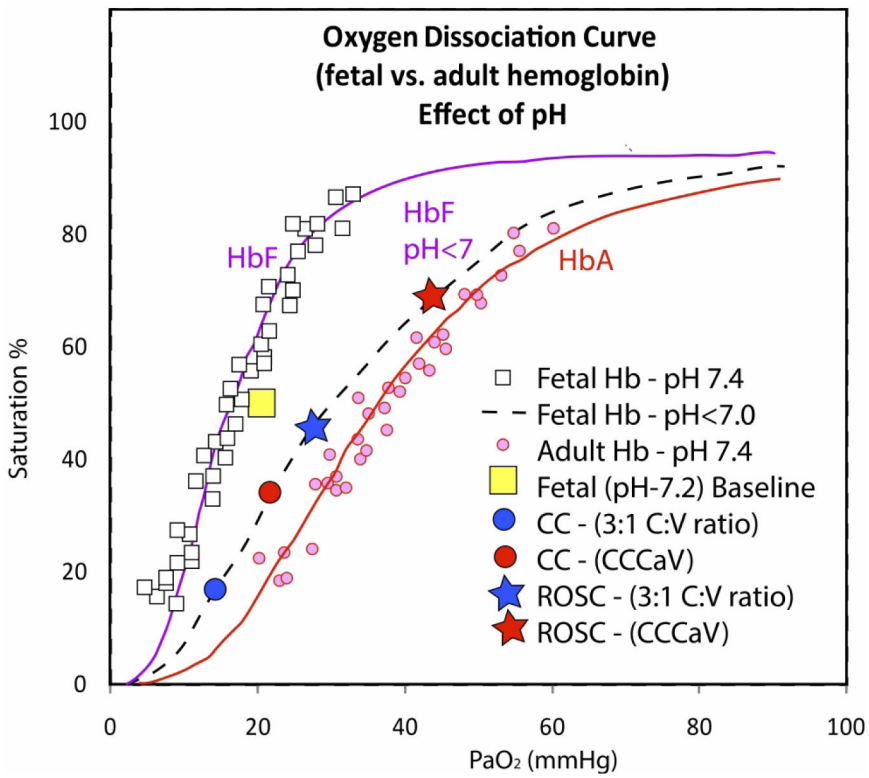

Figure 3:

Effect of pH on oxygen hemoglobin dissociation curve in fetal lambs and adult sheep (modified from Moraga F et al, Fetal and maternal blood oxygen affinity: A comparative study in llamas and sheep, Comp Biochem Physiol A Physiol 115: 111–115, 1996). Fetal hemoglobin (open squares) has a higher affinity for oxygen compared to adult hemoglobin (small pink circles). Acidosis causes a rightward shift in the oxygen hemoglobin dissociation curve (dashed line). During resuscitation and at the time of return of spontaneous circulation (ROSC), the range of PaO_2 is on the steep part of the curve and a small change in PaO_2 results in a greater change in SaO_2 and CaO_2. CaO_2 = content of arterial oxygen; C:V = compression-to-ventilation; CCCaV = continuous chest compressions with asynchronous ventilation; PaO_2 = partial tension of arterial oxygen; SaO_2 = saturation of arterial oxygen.

Table 1:

Characteristics of lambs in 3:1 compression-to-ventilation (C:V) and continuous chest compressions with asynchronous ventilation (CCCaV) groups

Groups	3:1 C:V (n=11)	CCCaV (n=11)	P value
Weight (kg)	3.9 (1.0)	3.8 (0.8)	0.85
Sex M:F	6:5	5:6	1
Time to asystole (min) [#]	15 (14–19)	13 (12–16)	0.21
Baseline Hemodynamics			
Heart rate (bpm)	139 (22)	144 (17)	0.59
Systolic BP (mm Hg)	66 (8.2)	64 (15)	0.8
Diastolic BP (mm Hg)	46 (8.4)	48 (8.2)	0.63
Mean BP (mm Hg)	54 (7.8)	56 (11)	0.73
Left mean QCa (ml O_2/kg/min)	28 (9.9)	31 (18)	0.71
CaO_2 (ml O_2/dL)	8.1 (3.7)	7.7 (2.7)	0.75
C-DO_2 (mL O_2/kg/min)	2.6 (1.5)	2.4 (1.7)	0.82
Baseline ABG			
PH	7.2 (0.1)	7.2 (0.11)	0.97
$PaCO_2$ (mm Hg)	71 (9.7)	75 (21)	0.61
PaO_2 (mm Hg)	21 (8.5)	21 (5.9)	0.99
SaO_2(%)	49 (23)	51 (19)	0.82
Hemoglobin (g/dL)	12.8 (1.7)	11.6 (1.8)	0.14
Lactate (mmol/L)	2.8 (1.4)	3.7 (3.1)	0.48
Asphyxia ABG			
PH	6.9 (0.1)	6.8 (0.1)	0.33
$PaCO_2$ (mm Hg)	132 (7.8)	131 (20)	0.9
PaO_2 (mm Hg)	2.1 (1.4)	2.8 (1.8)	0.49
SaO_2(%)	1.9 (0.7)	2.4 (1.2)	0.28
Hemoglobin (g/dL)	13.4 (1.2)	11.9 (1.7)	0.06
Lactate (mmol/L)	7.6 (1.3)	8.7 (3.3)	0.36

Continuous variables are reported as mean (SD).

[#]data are median (interquartile range ABG: arterial blood gas; BP: blood pressure; bpm: beats per minute; CaO_2: content of arterial oxygen; C-DO_2: cerebral oxygen delivery; $PaCO_2/O_2$: partial tension of carbon dioxide/oxygen; QCa: carotid blood flow ROSC: return of spontaneous circulation; SaO_2: saturation arterial oxygen

Table 2:

Return of Spontaneous Circulation

Groups	3:1 C:V (n=11)	CCCaV (n=11)	P value
ROSC	10/11 (91%)	10/11 (91%)	1
Time to ROSC (min) #	6.1 (2.9–7.1)	6.2 (4.2–6.9)	0.84
ROSC without Epi	4/11 (36%)	4/11 (36%)	1
At Time of ROSC			
Systolic BP (mm Hg)	86 (28)	85 (18)	0.91
Diastolic BP (mm Hg)	52 (17)	47 (14)	0.59
Mean BP (mm Hg)	62 (23)	68 (19)	0.61
Heart Rate	177 (25)	174 (18)	0.78
Left Qca (ml/kg/min)	25 (8.8)	22 (4.8)	0.48
DO_2 (ml O_2/kg/min)	2.3 (1.4)	2.4 (1.4)	0.89
ABG			
pH	6.8 (0.05)	6.8 (0.1)	0.87
$PaCO_2$ (mm Hg)	120 (15)	112 (23)	0.40
PaO_2 (mm Hg)	27 (11)	44 (21)	0.05
SaO_2(%)	46 (24)	67 (26)	0.09
Hemoglobin (g/dL)	12.9 (1.6)	11.6 (1.5)	0.09
Lactate (mmol/L)	9.6 (1.5)	11.7 (4)	0.17
30-min post ROSC			
ABG			
pH	7.22(0.12)	7.15 (0.15)	0.23
$PaCO_2$ (mm Hg)	42 (16)	47 (14)	0.50
PaO_2 (mm Hg)	95 (29)	74 (18)	0.08
SaO_2(%)	98 (2.5)	95 (2.8)	0.08
Hemoglobin (g/dL)	13.6 (1.1)	12.1 (1.9)	0.06
Lactate (mmol/L)	7.0 (1.0)	9.4 (4.6)	0.20

Values are mean (SD),

data are median (interquartile range). ABG: arterial blood gas; BP: blood pressure; CC: chest compressions; C-DO_2: cerebral oxygen delivery; $PaCO_2/O_2$: partial tension of carbondioxide/oxygen; Qca: carotid blood flow; SaO_2: saturation arterial oxygen

Table 3:

Hemodynamics and Arterial Blood Gas Analysis during Chest Compressions

Groups	3:1 C:V (n=11)	CCCaV (n=11)	P value
CC rate	88 (7)	122 (6)	<0.01
Systolic BP (mm Hg)	31 (11)	28 (9)	0.48
Diastolic BP (mm Hg)	8.1 (3.7)	9.0 (2.6)	0.45
Mean BP (mm Hg)	15 (3.8)	16 (2.4)	0.81
Left Qca (ml/kg/min)	4.2 (2.6)	7.5 (3.1)	<0.01
CaO_2 (ml O_2/dL)	3.0 (1.4)	5.3 (2.1)	0.03
C-DO_2 (mL O_2/kg/min)	0.13 (0.07)	0.40 (0.15)	<0.01
ABG			
pH	6.9 (0.4)	6.8 (0.1)	0.73
$PaCO_2$ (mm Hg)	119 (14)	112 (20)	0.38
PaO_2 (mm Hg)	15 (3.5)	22 (5.3)	<0.01
SaO_2(%)	19 (7.5)	33 (11)	<0.01
Hemoglobin (g/dL)	12.6 (1.0)	11.7 (1.4)	0.20
Lactate (mmol/L)	9.5 (1.3)	11.6 (4.7)	0.27

Values are mean (SD. ABG: arterial blood gas; BP: blood pressure; CC: chest compressions; CaO_2: content of arterial oxygen; C-DO_2: cerebral oxygen delivery; $PaCO_2/O_2$: partial tension of carbon dioxide/oxygen; Qca: carotid blood flow; SaO_2: saturation arterial oxygen