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Continuous Chest Compressions during Sustained Inflations in a Perinatal Asphyxial Cardiac Arrest Lamb Model

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Abstract

Objective—Continuous chest compressions (CCCs) are more effective during resuscitation in adults. Sustained inflation (SI) rapidly establishes functional residual capacity in fluid-filled lungs at birth. We sought to compare the hemodynamics and success in achieving return of spontaneous circulation (ROSC) in an asphyxial cardiac arrest lamb model with transitioning fetal circulation and fluid-filled lungs between subjects receiving CCCs during SI and those receiving conventional 3:1 compression-to-ventilation resuscitation.

Design—Prospective, randomized, animal model study.

Setting—An experimental laboratory.

Subjects—Fourteen newborn term gestation lambs.

Interventions—Lambs were randomized into two groups: 3:1 compression-to-ventilation (control) and CCCs during SI (SI+CCCs). The umbilical cord was occluded to induce asphyxia and asystole. The control group was resuscitated per NRP guidelines. In the SI+CCCs group, SI at 35cm H_2O was provided for 30 seconds with 1-second interruptions before another SI was provided. 120 chest compressions/min started after the initial SI. The first dose of IV epinephrine

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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was given at 6 minutes if ROSC was not achieved, and then every 3 minutes until ROSC or for a total of four doses.

Measurement and Results—All lambs achieved ROSC in a comparable median time (interquartile range) of 390 (225–405) and 345 (204–465) seconds in the SI+CCCs and control groups, respectively. 4/7 (SI+CCCs) and 3/6 (control) lambs required epinephrine to achieve ROSC. Diastolic blood pressures were lower in the SI+CCCs (4 ± 2 mmHg) compared to the control group (7 ± 2 mmHg); $P<0.05$. $PaCO_2$, PaO_2, and lactate were similar between the groups during the study period.

Conclusion—In this perinatal cardiac arrest lamb model with transitioning fetal circulation and fluid-filled lungs, SI+CCC is as effective as 3:1 C:V resuscitation in achieving ROSC. Half the lambs achieved ROSC without epinephrine. CCCs during SI reduced diastolic pressures but did not alter gas exchange or carotid blood flow compared to 3:1 C:V resuscitation.

Keywords

Chest compressions; Epinephrine; Newborn; Resuscitation; Sustained Inflation

Introduction

The need for aggressive neonatal resuscitation requiring chest compressions and epinephrine is rare.[1] However, the majority of newborn survivors who require chest compressions at birth suffer from long-term neurodevelopmental deficits.[2, 3] Scientific evidence guiding the current recommendations for chest compressions during neonatal resuscitation remains limited as it is extrapolated from animal, pediatric, and adult literature, as well as physiologic plausibility and expert opinion. The unique physiology inherent to newborns (fluid-filled alveoli, a patent ductus arteriosus, and high pulmonary vascular resistance with transitioning fetal circulation) limits the application of findings in postnatal models to neonates requiring resuscitation at birth.

The current pediatric and adult basic life support guidelines emphasize priority in initiating chest compressions and to minimize interruptions.[4, 5] Animal studies have shown improved hemodynamics and 24-hour neurologic outcomes in the groups randomized to receive uninterrupted chest compressions, [6, 7] albeit in a recent large randomized clinical trial, individuals who received continuous chest compressions did not have higher rates of survival or favorable neurologic function.[8] Several newborn animal models comparing different chest compressions to ventilation (C:V) ratios did not demonstrate a significant difference in outcomes.[9–11] The current 3:1 C:V ratio recommended by the Neonatal Resuscitation Program (NRP) is an expert consensus, attempting to match the heart and respiratory rates of the newborn.[12]

Although there is insufficient evidence from clinical trials to provide new recommendations, mounting evidence suggests that sustained inflations (SI) may improve physiologic adaption at birth in newborns.[13–17] In a recent study, continuous chest compressions during SI in a postnatal piglet model with bradycardia from tracheal tube occlusion has shown improved success in return of spontaneous circulation (ROSC) with better hemodynamic recovery.[18]

To explore these findings in a perinatal model of severe asphyxia and prolonged cardiac arrest, we hypothesized that continuous chest compressions during SI in a neonatal asphyxiated cardiac arrest lamb model with transitioning fetal circulation and fluid-filled lungs achieves improved hemodynamics, and leads to quicker ROSC compared to the conventional 3:1 C:V resuscitation. In addition, the first dose of intravenous epinephrine was administered at 6 minutes from the onset of resuscitation (to approximate clinical timing) [19] to determine the success of ROSC without giving epinephrine.

Methods

Animal Preparation

This study was approved by the Institutional Animal Care and Use Committee at the State University of New York at Buffalo. Time-dated term (139–141-day gestation) pregnant ewes were obtained from May Family Enterprises (Buffalo Mills, PA). Following an overnight fast, the ewes were induced for anesthesia with intravenous diazepam and ketamine. They were intubated with a 10.0 mm-cuffed endotracheal tube (ETT) and ventilated with 21% oxygen and 2–3% isoflurane at 16 breaths/min. The ewes were continuously monitored with a pulse oximeter and an end-tidal CO_2 ($EtCO_2$) monitor. Following cesarean section, fetal lambs were partially exteriorized and intubated with a 4.5 mm-cuffed ETT. The fetal lung fluid in the ETT was drained passively by gravity by tilting the head to the side and, thereafter, the ETT was occluded to prevent gas exchange during gasping in the asphyxial period. Catheters were inserted into the jugular vein (for fluid and medication administration) and right carotid artery (for blood sampling). A 2 mm flow probe (Transonic Systems Inc, Ithaca NY) was placed around the left carotid artery. A left thoracotomy was performed and a 4 mm flow probe was placed around the left pulmonary artery. The thoracotomy was closed in layers. EKG leads were attached at the right axilla, left axilla and right inguinal area (three-lead EKG). The ECG100C (Biopac Systems, Inc.) was used with Acknowledge Software to record tracings of leads I, II and III. Following instrumentation, the umbilical cord was occluded and then cut, and the lambs were moved from the maternal abdomen to the radiant warmer. During the asphyxial period (prior to resuscitation), an umbilical arterial catheter was inserted to measure continuous invasive blood pressures.

Experimental Protocol

Fourteen lambs were randomized into two groups using opaque sealed envelopes. A five-minute period of asystole was observed prior to initiating resuscitation. Asystole was defined by the absence of carotid blood flow, arterial blood pressure and heart rate. Resuscitation began by removing the ETT occluder and providing ventilation with 21% oxygen by means of a T-piece resuscitator. Upon initiation of chest compressions, inspired oxygen was increased to 100%. The first dose of epinephrine (0.03 mg/kg) was administered into the right atrium through a jugular venous catheter at six minutes from the onset of resuscitation if ROSC had not been achieved. This time point was chosen to approximate the time taken to administer umbilical venous epinephrine in clinical scenarios.[19] 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 heart rate >100 beats/min and mean arterial blood pressure >30 mm Hg. A baseline arterial blood sample was obtained following

instrumentation of the lamb, prior to cord occlusion. Subsequently, an “arrest gas” was obtained one minute prior to resuscitation (four minutes into asystole), and, thereafter, blood sampling was obtained approximately every minute during resuscitation. In lambs that achieved ROSC, a blood gas sample was obtained at the time of ROSC and then every minute until fifteen minutes following ROSC. Arterial blood samples were analyzed using a radiometer blood gas analyzer (ABL 800 FLEX, Denmark).

The lambs were randomized as follows:

3:1 C:V (control) group: at the onset of resuscitation, positive pressure ventilations (PPV) with set pressures of 35/5 cm H_2O at a rate of 40 breaths/min with 21% oxygen were provided with a T-piece resuscitator.[15] After 30 seconds of PPV, chest compressions were initiated at a compression to ventilation ratio of 3:1 to achieve 90 compressions and 30 breaths per minute and inspired oxygen was increased to 100%.

SI group: at the onset of resuscitation, an SI with 35 cm H_2O with 21% oxygen was provided for 30 seconds. SI’s were interrupted for one second (during which time a continuous PEEP of 5 cm H_2O was maintained) before a further 30 seconds of SI was given.[18] Following the first SI, continuous, uninterrupted, chest compressions were initiated at 120 compressions per minute and inspired oxygen was increased to 100%.

Following ROSC, the lambs were placed on a ventilator. The PIP and rate were adjusted gradually based on tidal volumes (goal 8–9 ml/kg) and $PaCO_2$, and the FIO_2 was adjusted to maintain pre-ductal saturations between 85–95%. Lambs were euthanized by administering 100 mg/kg pentobarbital sodium (Fatal-Plus Solution; Vortech Pharmaceuticals, Dearborn MI) approximately 30 minutes into the study.

Data Analysis

Arterial blood flow and pressures were continuously recorded using a computer with AcqKnowledge Acquisition & Analysis Software (BIOPAC systems, Goleta, CA, USA). Continuous variables are expressed as mean and standard deviation. Categorical variables were analyzed using chi square test or Fisher’s exact test as appropriate. Continuous variables were analyzed by one-way ANOVA between groups with Fisher’s post hoc test within groups. Statview 4.0 and SPSS 20 software was used. Statistical significance was defined as $p < 0.05$.

Results

Characteristics of the lambs, including baseline hemodynamics, hemoglobin, gender distribution, birth weight, the amount of lung liquid drained by gravity, and time to asystole, were similar between the study groups (Table 1).

ROSC and Epinephrine

One lamb in the 3:1 C:V group exsanguinated from a liver laceration sustained during chest compressions and was excluded from the analysis. All remaining thirteen lambs were successfully resuscitated. The median time to ROSC was comparable between the SI (390 IQR 225–405 seconds) and control (345 IQR 204–465 seconds) groups (Table 1). Four out

of seven lambs in the SI group and three out of six lambs in the control group required epinephrine to achieve ROSC. One lamb in each group required 2 doses of epinephrine to achieve ROSC. The median time to achieve ROSC following epinephrine administration was 60 (IQR 30–80) seconds in the SI group and 100 (80–130) seconds in the control group (p=0.64). Three lambs in each group achieved ROSC without epinephrine at 210, 210 and 240 seconds in the SI group and 180, 180 and 270 seconds in the control group.

Hemodynamic Parameters

The baseline systolic and diastolic blood pressures, as well as the mean left carotid and left pulmonary artery flows were comparable between the groups (Table 1). The rate of chest compressions (mean ± SEM) in the SI and control group was maintained at 110 ± 5 and 83 ± 3 compressions/min, respectively, approximating the rates defined in the protocol (p <0.01). Upon initiation of chest compressions and throughout the period prior to epinephrine administration, the blood pressures remained constant. The mean systolic blood pressures (± SEM) generated by continuous, uninterrupted, chest compressions (SI group) were similar to the control group (28 ± 1 vs. 30 ± 2 mm Hg, respectively; Figure 1A). However, the mean diastolic pressures generated during chest compressions were significantly lower in the SI group as compared to the control group (4 ± 0.5 mm Hg vs. 7 ± 1 mm Hg, respectively [p <0.05]; Figure 1B). There was no appreciable increase in either the systolic or diastolic blood pressures following epinephrine in either group (Figures 1 and 2). When combining the lambs that required epinephrine to achieve ROSC (n =7), the mean systolic blood pressures (±SEM) prior to epinephrine administration were 28 ± 2, and ≈30 seconds following epinephrine 31 ± 2 mm Hg, which was not significant. Similarly, the mean diastolic blood pressures (±SEM) prior to and following epinephrine administration were 5 ± 1 and 7 ± 1 mm Hg, respectively (not statistically significant). The mean left carotid and pulmonary artery flows were also comparable between the groups throughout the study period (Figure 3).

Arterial Blood Gas Analysis

The ABG analysis at baseline, at arrest, into resuscitation, at ROSC and following ROSC (in the lambs that were successfully resuscitated) are summarized in table 2. There are no significant differences observed between the pH, PaO_2, $PaCO_2$ and serum lactate levels between the two groups throughout the study. Severe metabolic and respiratory acidosis ensued during asphyxia and asystole (pH <6.9, $PaCO_2$ >120 mm Hg and lactate >12 mmol/L). There was a statistically significant decrease in $PaCO_2$ during resuscitation in the SI group from 142 ± 12 at arrest down to 120 ± 10 mm Hg at 3 minutes into resuscitation (p<0.01), and a further decrease to 102 ± 15 at the time of ROSC (p<0.05). In the control group there was a statistically significant drop from 135 ± 21 mm Hg at arrest down to 111 ± 15 mm Hg at 3 minutes into resuscitation (p<0.05). The $PaCO_2$ levels normalized ten to fifteen minutes following ROSC (44 ± 6 and 50 ± 14 mm Hg in the SI and control groups, respectively). The PaO_2 levels remained low (24 ± 6 mm Hg) during resuscitation despite 100% oxygen. However, PaO_2 levels exceeding 250 mm Hg were observed within the first couple of minutes following ROSC that gradually normalized by decreasing the FIO_2 concentration following ROSC.

Discussion

The many physiologic differences (fluid-filled lungs, patent ductus arteriosus, increased pulmonary vascular resistance) in newly born infants compared to older children and adults present an ongoing challenge on how best to resuscitate the severely hemodynamically compromised neonate at birth.

Despite the decline in the incidence of ventricular fibrillation, [20, 21] the nature of sudden cardiac arrest in adults differs greatly to neonatal cardiac arrest. In contrast to adults, where a 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. Oxygen levels remain relatively high in adult cases of sudden cardiac arrest. Adult animal models with ventricular fibrillation induced cardiac arrest that received uninterrupted chest compressions have shown improved hemodynamics and neurologic outcomes.[7, 22, 23] Some clinical studies have reported on improved survival when providing uninterrupted chest compressions, [24–26] although a large randomized clinical trial did not demonstrate higher rates of survival or favorable neurologic outcomes.[8] In the asphyxiated neonate with cardiac arrest due to severe hypoxemia and hypercarbia, ventilation remains critical in establishing ROSC, and resuscitation with exclusive chest compressions in asphyxiated piglet models has not shown to be effective in achieving ROSC.[27, 28]

Ventilation of the lungs is a critical component of neonatal resuscitation. 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, until recently, different C:V ratios have not shown improved outcomes in pre-clinical and neonatal manikin models.[9–11, 29, 30]

Increasing evidence suggests that sustained inflation provided at the onset of resuscitation achieves better lung aeration.[15, 16, 31] In an attempt to optimize ventilation and chest compressions, a novel study by Schmölzer et al. has shown a significant reduction in the time to achieve ROSC and better hemodynamic recovery in asphyxiated newborn piglets that were resuscitated with continuous chest compressions during SI as compared to the conventional 3:1 C:V ratio resuscitation.[18] However, notable differences exist between the aforementioned piglet model and our lamb model: 1) the mode of asphyxia was by hypoxic ventilation and tracheal tube occlusion, 2) the ductus arteriosus was ligated, 3) the degree of asphyxia did not lead to cardiac arrest and hence the duration of resuscitation was relatively short, and 4) intravenous epinephrine was administered after 60 seconds of chest compressions (a time unlikely to be achieved in the delivery room). These differences may explain why our study in a term lamb model of asphyxial cardiac arrest did not show any improved hemodynamics or quicker ROSC when comparing continuous chest compressions during SI to the conventional 3:1 C:V resuscitation. In our study, the success of ROSC, the time to ROSC and the total number of epinephrine doses administered between the two groups were similar. The systolic blood pressures (Figure 1A), and the mean left carotid and pulmonary blood flows (Figure 3) were also comparable between the groups. Interestingly, the diastolic blood pressures were significantly lower in the SI group compared to the

control group (Figure 1B). In the aforementioned study, Schmölzer et al. propose improved hemodynamics when chest compressions are provided during ventilation (SI) following the thoracic pump theory that postulates that increased intrathoracic pressures provide a gradient between the venous and arterial vasculature facilitating antegrade blood flow.[32, 33] However, ROSC was achieved within 23–44 seconds in their SI group and, thus, the duration of chest compressions was very short. Furthermore, the piglets were not asphyxiated to cardiac arrest, and the effects of ventilation may have had a greater impact on hemodynamics and ROSC success rather than the chest compressions. Animal data suggest that SI provided at the onset of resuscitation achieves better lung aeration and improves hemodynamics.[15, 16, 31] A study in preterm rabbits using SI for 20 seconds followed by PPV resulted in a rapid increase in functional residual capacity and uniformly aerated lungs.[16] In preterm lambs, SI facilitates establishment of pulmonary flow and improves cerebral blood flow stability.[31] In addition, a study in near term asphyxiated lambs has shown improved lung compliance and speed of circulatory recovery following a single SI of 35 cm H_2O for 30 seconds immediately after birth.[15]

The lack of improved hemodynamics in our lamb model during an extended period of chest compressions during SI compared to the conventional 3:1 C:V resuscitation suggests that SI may interfere with venous return. The increase in intrathoracic pressure tends to impede venous return from the jugular vein. Diastolic function may be further compromised by the displacement of blood volume from the thoracic pulmonary and systemic arterial compartment to the high capacitance splanchnic venous compartment (Figure 4). Nevertheless, despite very low diastolic blood pressures in the SI (4 ± 2 mm Hg) and the control (7 ± 2 mm Hg) groups (Figure 1B), all the lambs were successfully resuscitated. We speculate that in the severely asphyxiated, inanimate heart, systolic blood pressures generate intermittent myocardial flow during the compression phase of chest compressions that lead to ROSC.

We have also demonstrated that approximately half of the lambs (3/7 in the SI and 3/6 in the control group) were successfully resuscitated without the need for epinephrine. The timing of intravenous epinephrine was based on clinical scenarios where placement of an umbilical venous line and administration of epinephrine required >6 minutes.[19] We chose not to administer endotracheal epinephrine to solely assess the efficacy of intravenous epinephrine. The lambs that required epinephrine at six minutes achieved ROSC in a median (IQR) time of 60 (45–130) seconds from administering the dose(s). These results are similar to findings from another study where we evaluated the optimal timing and route of epinephrine administration.[34] In that study, 10 out of 11 lambs that were randomized to receive RA epinephrine (at a similar dose of 0.03 mg/kg) achieved ROSC in a median (IQR) time of 90 (68–143) seconds following epinephrine administration. These findings confirm the emphasis placed by the NRP guidelines for early intravenous epinephrine administration.

Inferring from the low mean left carotid artery flows (6 ± 2 ml/kg/min) during chest compressions compared to baseline in utero values (25 ± 4 ml/kg/min), cerebral oxygen delivery is likely very low during resuscitation. However, upon ROSC, the mean left carotid flows increase significantly (29 ± 11 ml/kg/min) with better oxygen content (17 mL O_2/dL), thus improving oxygen delivery to the brain. Therefore, establishing ROSC quicker limits

the period of hypoperfusion and subsequent reperfusion injury, and may improve neurologic outcomes.

Finally, when interpreting the arterial blood gases, the very low mean left pulmonary blood flows during resuscitation in both groups (Figure 3B) can explain the persistently elevated $PaCO_2$ and low PaO_2 values. However, despite the elevated $PaCO_2$ values, there was a significant reduction in $PaCO_2$ during resuscitation. The low PaO_2 values despite 100% oxygen inhalation favor high FIO_2 use during resuscitation to optimize the oxygen content in blood. However, due to supraphysiologic PaO_2 values upon ROSC (>250 mm Hg), the FIO_2 needs to be aggressively weaned after ROSC and subsequently adjusted to maintain saturations in the goal range to avoid oxygen free radical damage.[35, 36]

We acknowledge several limitations in our study. We did not measure central venous pressure, right atrial pressure and intrathoracic pressure, limiting our interpretation and understanding of the hemodynamics during SI and chest compressions. An incomplete seal following thoracotomy may have influenced chest compression efficacy. The lambs were euthanized shortly after ROSC and no long-term neurologic outcomes were assessed. Finally, despite the prolonged asphyxial period, time in cardiac arrest, and severely acidotic state, an extended period of cardiac arrest may have decreased success of ROSC, and revealed a difference between the two resuscitation techniques.

Conclusion

In this model of prolonged perinatal cardiac arrest, despite low diastolic blood pressures, approximately half the lambs achieved ROSC without epinephrine. Continuous chest compressions during SI in a neonatal lamb model of perinatal asphyxia and cardiac arrest with transitioning fetal circulation and fluid-filled lungs achieved similar rates of ROSC, hemodynamics and gas exchange when compared to the conventional 3:1 C:V neonatal resuscitation. Further clinical studies evaluating sustained inflation (such as the SAIL trial – NCT 02139800) may provide information on clinical situations where SI is more effective in the delivery room.

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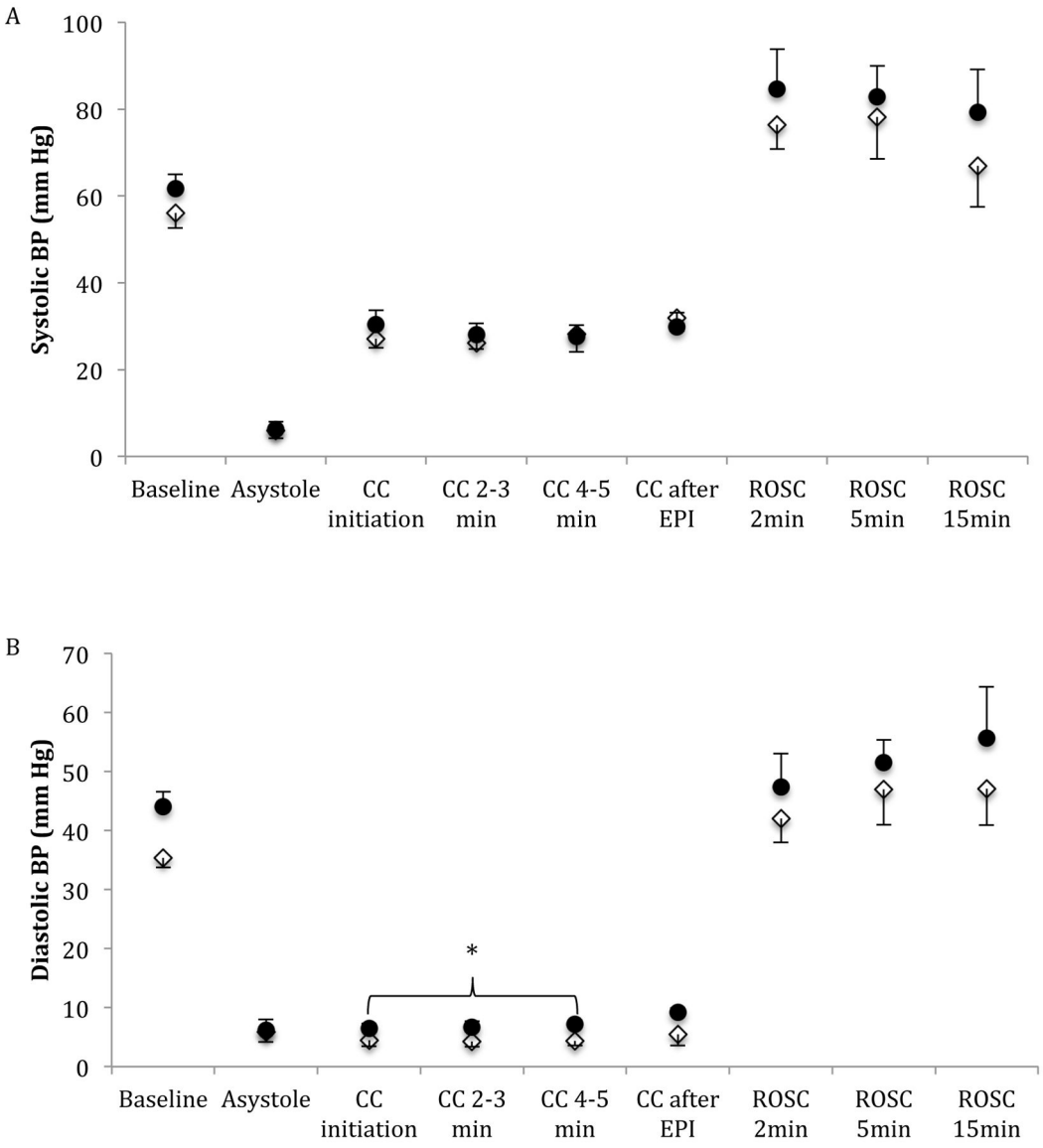

Figure 1. Mean Blood Pressure during Study Period between Groups

There was no difference in systolic blood pressures (A) at any point-in-time during the study period between lambs resuscitated with 3:1 C:V (solid circles) and continuous chest compressions during SI (open diamonds). Diastolic blood pressures (B) were significantly higher in the 3:1 C:V group compared to the SI group during chest compressions (* $P < 0.05$). There was no significant increase in systolic or diastolic blood pressures following epinephrine administration in either group. Data are mean ± SEM bars.

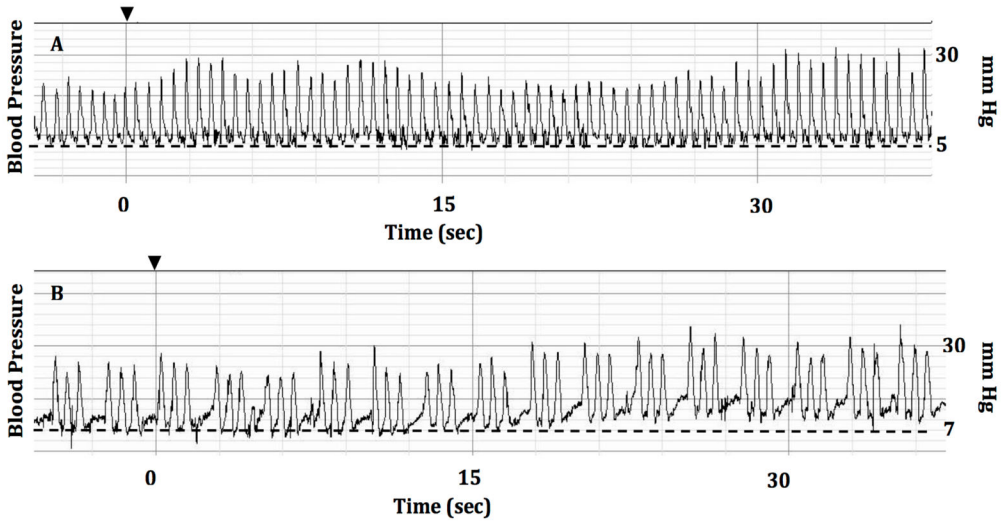

Figure 2. BIOPAC Picture Capturing Invasive Blood Pressure Monitoring

Panel A represents the lambs that received continuous chest compressions during SI. Panel B represents the lambs that received 3:1 C:V resuscitation. The represented lamb in either group received two doses of epinephrine. The arrowhead indicates the first dose of epinephrine administration. The slight increase in diastolic blood pressure is not statistically significant.

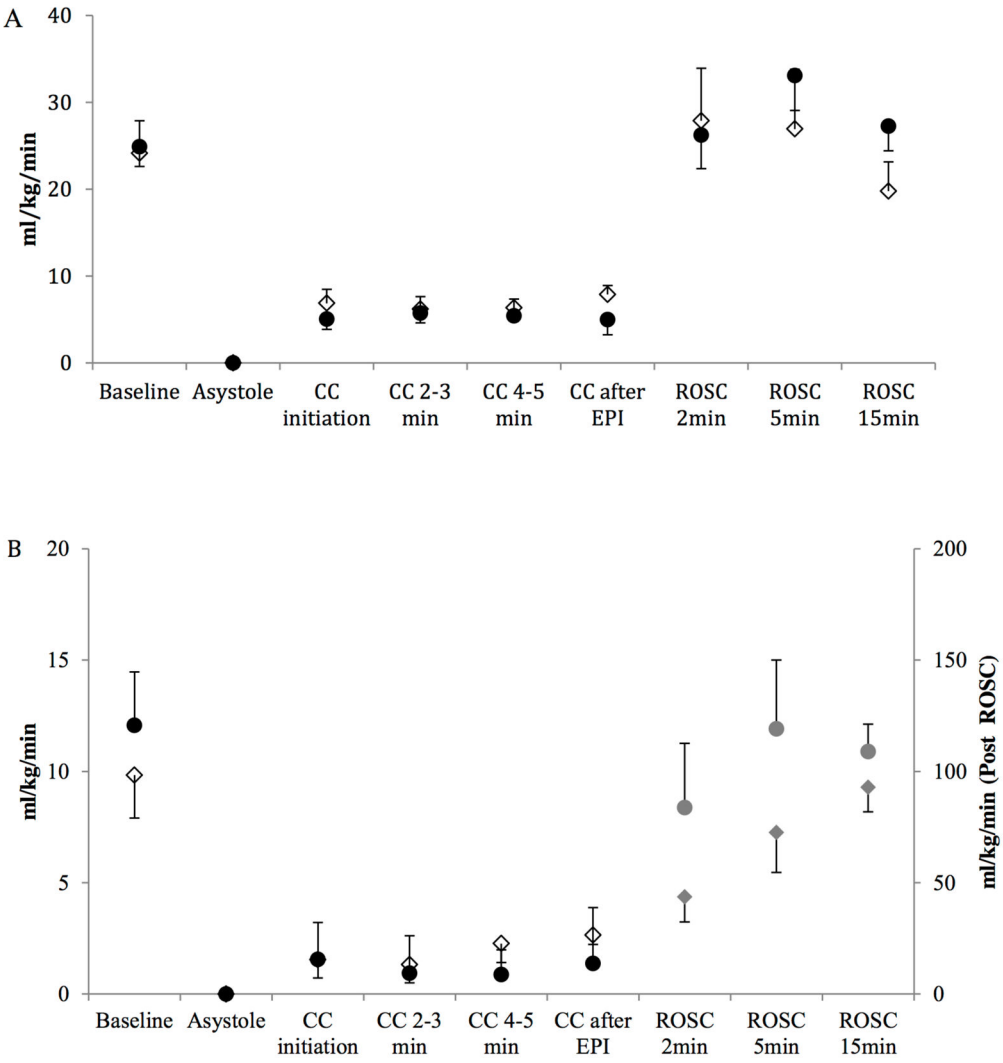

Figure 3. Mean Arterial Blood Flows during Study Period between Groups

Mean left carotid (A) and mean left pulmonary artery (B) blood flows were similar between lambs resuscitated with 3:1 C:V (solid black circles) and continuous chest compressions during SI (open diamonds). The secondary vertical axis in figure 'B' represents the mean left pulmonary artery blood flow following ROSC in the lambs resuscitated with 3:1 C:V (solid grey circles) and continuous chest compressions during SI (solid grey diamonds). Data are mean ± SEM bars.

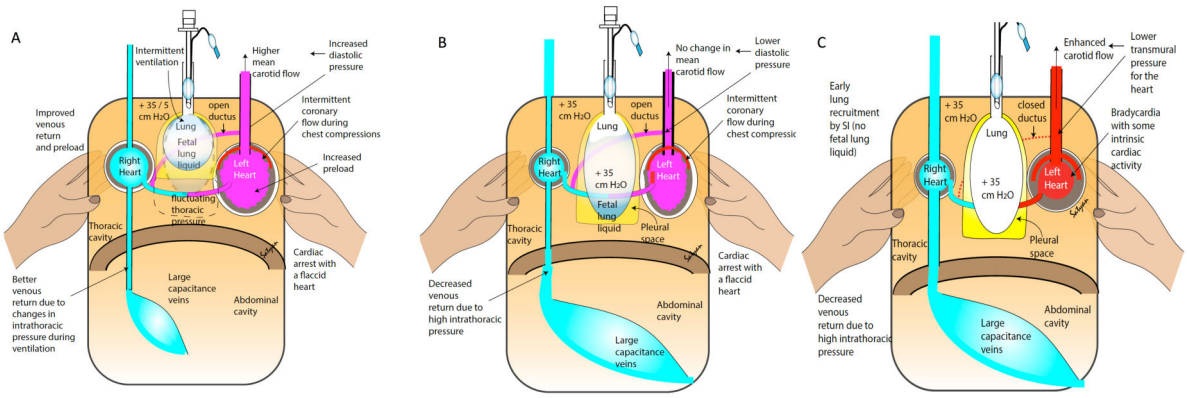

Figure 4. Differences in Hemodynamics during Ventilation and Chest Compressions

During intermittent ventilation, fluctuations in intrathoracic pressures improves venous return and, hence, cardiac output during chest compressions (A). SI may displace blood volume from the intrathoracic system into the high capacitance splanchnic venous compartment. In a neonatal model in asystole (B), chest compressions on a flaccid heart, blood diverting through the patent ductus arteriosus, and increased intrathoracic pressure delivered by SI impeding venous return to the right heart compromise cardiac output. In a post-natal model with bradycardia (C), chest compressions superimposed on intrinsic cardiac activity (and a closed ductus arteriosus), as well as improved lung aeration (owing to resorption of fetal lung fluid) with resultant increase in venous return to the left heart, enhance cardiac output.

Table 1

Lamb Characteristics between Groups

Characteristics	SI Group (n=7)	Control Group (n=6)[#]
Weight (Kg)	4.0 ± 0.5	3.8 ± 0.7
Sex (M:F)	3:4	3:3
Total lung fluid drained (ml/kg)	14 ± 3	16 ± 6
Hemoglobin (g/dL)	14.5 ± 0.7	13.7 ± 0.7
Time to pulselessness (min)	16 (12–19)	17 (16–21)
Time to ROSC (min)	6.5 (3.8–6.8)	5.8 (3.4–7.8)
Total EPI doses	5	4
ROSC without EPI	3/7	3/6
Baseline HD		
Heart Rate (bpm)	150 ± 31	145 ± 12
SBP mean (mm Hg)	56 ± 9	60 ± 8
DBP mean (mm Hg)	35 ± 4	41 ± 7
Mean left Ca flow (ml/kg/min)	24 ± 9	25 ± 6
Mean left PA flow (ml/kg/min)	10 ± 4	12 ± 6

[#]One lamb exsanguinated due to a complication from instrumentation and was excluded from analysis.

IQR: interquartile range; PA: pulmonary artery; ROSC: return of spontaneous circulation; SD: standard deviation.

Table 2

Arterial Blood Gases during Study Period between Groups

Arterial Blood Gas	SI Group	Control Group
Baseline		
pH	7.27 ± 0.04	7.26 ± 0.2
$PaCO_2$ (mmHg)	61 ± 6	60 ± 6
PaO_2 (mmHg)	19 ± 3	17 ± 3
Lactate (mmol/L)	3.5 ± 1	3.8 ± 1
Arrest Gas		
pH	6.86 ± 0.06	6.83 ± 0.06
$PaCO_2$ (mmHg)	142 ± 12	135 ± 21
PaO_2 (mmHg)	3 ± 2	5 ± 2
Lactate (mmol/L)	12 ± 3	14 ± 4
3 min into Resuscitation		
pH	6.84 ± 0.05	6.84 ± 0.03
$PaCO_2$ (mmHg)	120 ± 10	111 ± 15
PaO_2 (mmHg)	25 ± 8	23 ± 2
Lactate (mmol/L)	13 ± 4	15 ± 4
At ROSC		
pH	6.84 ± 0.03	6.81 ± 0.05
$PaCO_2$ (mm Hg)	103 ± 15	110 ± 20
PaO_2 (mm Hg)	161 ± 162	153 ± 132
Lactate (mmol/L)	14 ± 4	15 ± 4
15 min after ROSC		
pH	7.15 ± 0.06	7.10 ± 0.09
$PaCO_2$ (mm Hg)	44 ± 6	50 ± 14
PaO_2 (mm Hg)	66 ± 16	112 ± 38
Lactate (mmol/L)	15 ± 2	14 ± 3

[#]One lamb exsanguinated due to a complication from instrumentation and was excluded from analysis. ± SD are shown.

ROSC: return of spontaneous circulation.