**TITLE:**
The Effect of Chest Compression Location and Occlusion of the Aorta in a Traumatic Arrest Model

**SHORT TITLE:**
Chest Compression Location and REBOA

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**DECLARATIONS:**
The authors report no conflicts of interest in this work.



**AUTHOR CONTIRBUTIONS:**
K.L.A., J.D.M. and V.S.B. conceived and designed the study; M.G.C., S.M.B., K.L.A., J.D.M., and A.A.A. contributed to collecting the data or analyzing and interpreting the data; K.L.A. and V.S.B. contributed to writing the manuscript or providing critical revisions that are important for the intellectual content, and K.L.A, J.D.M., M.G.C., S.M.B., A.A.A., and V.S.B. contributed substantially to approving the final version of the manuscript.

**ABSTRACT**

**Background:** Recent evidence has demonstrated that closed chest compressions directly over the left ventricle (LV) in a traumatic cardiopulmonary arrest (TCA) model improve hemodynamics and return of spontaneous circulation (ROSC) when compared to traditional chest compressions. Resuscitative endovascular balloon occlusion of the aorta (REBOA) is also able to improve hemodynamics as well as control hemorrhage during TCA. We hypothesized that chest compressions located over the LV would result in improved hemodynamics and ROSC when compared to traditional compressions in a swine model of TCA using REBOA.

**Materials and Methods:** Transthoracic echo was used to mark the location of the aortic root (Traditional location) and the center of the LV on animals (n=26) which were randomized to receive chest compressions in one of the two locations. After hemorrhage, ventricular fibrillation (VF) was induced to simulate TCA. After a period of ten minutes of VF, basic life support (BLS) with mechanical CPR was initiated and performed for ten minutes followed by advanced life support (ALS) for an additional ten minutes. REBOA balloons were inflated at minute 6 of BLS. Hemodynamic variables were averaged over the final two minutes of the BLS and ALS periods.

**Results:** There was no significant difference in ROSC between the two groups (p=0.24). In the LV group, ETCO2 was higher during the BLS period (p=0.02).

**Conclusions:** There was no difference in ROSC between LV and Traditional compressions when REBOA was used in this swine model of TCA, however, a larger study may demonstrate that there is a difference.

**Keywords:** Cardiopulmonary resuscitation; Trauma; Balloon Occlusion; Hemodynamics; Survival; Echocardiography

## INTRODUCTION

Resuscitation of traumatic cardiopulmonary arrest (TCA) patients in the pre-hospital setting remains controversial. Survival rates as low as 0% - 3.7% have been reported among TCA victims, thus resuscitation of all TCA patients has been considered by many to be futile and an inappropriate utilization of resources (1-4). More recent reports have described improved survival rates with good neurologic outcomes even when CPR has been performed in a breach of the published guidelines; this includes one report that 24% of military TCA patients survived after receiving CPR in the field (5-10).

Cardiopulmonary resuscitation, including closed chest compressions, has commonly been considered wholly ineffective in TCA partially because the cardiac output generated by closed chest compressions is only about 25% that of open chest compressions and may potentially cause more trauma in a patient that is already suffering from traumatic injuries (11, 12). Fortunately, recent animal studies have demonstrated that chest compressions performed directly over the left ventricle (LV), rather than the traditional 'center of the chest,' improve hemodynamics and return of spontaneous circulation (ROSC) during both non-traumatic cardiac arrest (NTCA) and TCA models – this method may be the closest approximation to open cardiac massage that can be achieved without performing a thoracotomy (13, 14). Additionally, resuscitative endovascular balloon occlusion of the aorta (REBOA) has also been used in both medical arrest and TCA to improve perfusion pressures and survival outcomes in both animal and human studies (15-20). It is possible that improvements in ROSC and hemodynamics are additive when LV chest compressions and REBOA are combined during TCA.

We hypothesized that chest compressions located directly over the LV would increase return of spontaneous circulation (ROSC) when compared to traditional compressions in a swine model of TCA where REBOA is used in the resuscitation of all animals. Secondary analyses included an evaluation of hemodynamic and laboratory variables as well as short-term survival to 60 minutes between the two groups.

## MATERIALS AND METHODS

### Study Design and Setting

We conducted a prospective, randomized comparative investigation approved by our Institutional Animal Care and Use Committee. All procedures involving animals complied with the regulations and guidelines of the Animal Welfare Act, the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and the American Association for Accreditation of Laboratory Animal Care. The housing of animals and the performance of the study took place in the Animal Care Facility at our institution. Reporting adheres to the Animals in Research Reporting In Vivo Experiments (ARRIVE) guidelines (21)

### Animal Preparation

Twenty-six female Yorkshire swine weighing 25-32kg were obtained 2-4 days before experimentation to allow acclimation to the facility. Per the vendor, the animals were free from viral, bacterial and parasitic pathogens.

Animals were housed individually in 4x4 foot cages with rubberized textured flooring in a temperature and humidity-controlled building with a 12-hour light/dark cycle set on a timer. Animals were allowed free access to water and were provided a maintenance diet (PMI Nutrition International, LLC, Brentweed, MO, USA). Within 48 hours of arrival to the facility a physical exam of each animal was performed to evaluate for lesions and to ensure normal heart and lung sounds. A complete blood cell count and blood chemistry analysis were also performed. No pre-treatment with any medications was performed.

All experiments were initiated during the morning hours. Animals were initially sedated with 20mg/kg intramuscular ketamine; general anesthesia was subsequently induced and mechanical ventilation initiated (Fabius GS; Draeger-Siemens, New York, NY) with a mixture of 60% oxygen and isoflurane (1-2.5%) with a tidal volume of 10mL/kg at a respiratory rate of 12 $min^{-1}$. End-tidal CO2

(ETCO2) was monitored by in-line waveform capnography, and the respiratory rate was adjusted to maintain an ETCO2 between 38 and 42 mm Hg prior to induction of cardiac arrest. Continuous cardiac rhythm and heart rate were monitored by electrocardiography (ECG) using standard limb leads. Peripheral capillary pulse oximetry (SpO2) was also monitored continuously. The anesthesia used in this experiment is standard for swine models. All other drugs, routes of administration, and timing of administration are those outlined in CPR guidelines (22, 23). Standard weight based doses were used.

**Interventions**

High fidelity, solid state micromanometer-tipped pressure transducers (Millar MPC-500; Millar Inc., Houston, TX) were advanced through right internal jugular vein and left brachial artery into thoracic locations to measure continuous aortic and right atrial pressures respectively. A 9Fr balloon occlusion catheter was advanced through the left femoral artery to Zone 1 of the descending thoracic aorta, just proximal to the diaphragm (Fogarty, Mountain View, CA). Fluoroscopy was used to position all catheters (Model Siremobile 2U C-arm, Siemens, Inc., Danvers, MA). Unfractionated heparin (100u/kg) was provided to prevent catheter clotting. Near infrared spectroscopy (NIRS) sensors were adhered to the scalp and the right flank to continuously monitor and record cerebral and renal regional oximetry (rSO2) respectively (INOVS 5100C Cerebral/Somatic Oximeter; Covidien, Minneapolis, MN). Once all catheters and sensors were in place, the animals were allowed to acclimate for 10 minutes, and each animal received a bolus of 15 mL/kg of 0.9% saline intravenously to replace overnight fasting fluid deficits.

Animals were placed in a v-shaped trough to eliminate lateral movements during chest compressions. At the onset of the 10-minute acclimatization period inhaled oxygen was decreased to 21%. During the 10-minute acclimatization period, transthoracic echocardiography (TTE) (z.one ultra sp; Zonare Medical Systems, Inc., Mountain View, CA) was used to locate the aortic root (AR) and the center of the LV in two orthogonal planes (the parasternal long axis and parasternal short axis). The animals' skin was marked in the mid-sternum at the level of the AR to represent the Traditional

compression location and at the center of the LV to represent the LV compression location. A multiplane transesophageal (TEE) transducer (P8-3TEE; Zonare Medical Systems, Inc., Mountain View, CA) was used to obtain a mid-esophageal long axis (ME LAX) view of the heart. The TEE transducer was left in place for recording the area of maximal compression (AMC) during compressions.

*Experimental Protocol*

Animals were randomly allocated to LV or Traditional chest compression groups. Allocation was performed using a commonly employed computer-generated randomization program (http://www.randomization.com). Randomization was performed for all animals prior to the beginning of the study and the results for each animal were kept sealed until ventricular fibrillation (VF) had been induced. A graphic display of the general protocol is presented in Figure 1a, and a more detailed outline of the advanced life support (ALS) portion of the protocol is presented in Figure 1b.

During the hemorrhage period, 30% of each animals' blood volume was removed over a 20-minute period, as previously described, at a rate of 1.42 ml/kg/min for the first 7 minutes followed by a rate of 0.76 ml/kg/min over the remaining 13 minutes (14, 24, 25). Blood was removed from the carotid arterial line via aspiration with a 60mL syringe and saved in a blood collection system containing citrate-phosphate-dextrose with Optisol red blood cell preservative solution (Terumo Corp., Tokyo, Japan). The collected blood was then placed in a blood warmer for subsequent experimental transfusion to the same animal.

Ventricular fibrillation (VF) was induced five minutes after the completion of hemorrhage to simulate TCA. VF was induced with a 3second 60Hz 100mA electric current delivered across the thorax (Model 1745A Power Supply; B&K Precision Corporation, Yorba Linda, CA) as previously described (26, 27). VF was confirmed by ECG, the sudden loss of arterial pulsations, and an abrupt reduction of the systolic blood pressure to less than 25mmHg. The induction of cardiac arrest represented time zero during the experiment; mechanical ventilation and anesthesia were simultaneously discontinued at time zero. All animals remained in VF arrest without any intervention for a period of 10 minutes (Non-

intervention period). During the 10-minute Non-intervention period, the allocation to either the Traditional or LV compression groups was unblinded, and the center of the piston on the automatic mechanical compression device (AMCD) (Thumper 407CC; Michigan Instruments, Grand Rapids, MI) was lowered into place over the corresponding skin marking. Defibrillation pads were placed over the right and left lateral chest and connected to a biphasic electronic defibrillator/monitor (Lifepak 20; Physio Control Inc., Redmond, WA).

*Basic Life Support*

After the 10-minute Non-intervention period, Basic Life Support (BLS), was initiated using the AMCD over the allocated position; compressions were delivered at a rate of 100 $min^{-1}$, at a depth of 5cm, with a 50% duty cycle and a compression-ventilation ratio of 30:2. Compressions were briefly interrupted every two minutes to perform a rhythm analysis that lasted 2-5 seconds. During BLS, a 10 second video clip of the ME LAX view was saved for future review. A 10-minute interval of BLS without defibrillation was used as a practical approach because this duration of CPR is necessary to adequately compare CPR techniques (27). At 6 minutes into BLS (16 minutes of cardiac arrest) the REBOA balloon was inflated; this period of time was chosen to simulate the amount of time required to insert and inflate the balloon and to allow adequate time to compare CPR techniques before the other advanced life support interventions were initiated as outlined below.

*Advanced Life Support*

After 10 minutes of BLS, advanced life support was initiated with a 125 Joule (J)(approximately 4J/kg) biphasic waveform defibrillation attempt, resumption of mechanical ventilation with 100% oxygen, continuous compressions at the same rate and depth, and bolus transfusion of 500mL of whole blood (WB) under 250mmHg of pressure (Figure 1b). We elected to transfuse WB since WB is the resuscitation fluid that plasma, packed red blood cells, and platelets in a 1:1:1 ratio attempt to simulate, and fresh WB may be administered in a tactical field care or elsewhere in combat theater when other

blood products are not available or not effective (28, 29). Every two minutes compressions were interrupted for a rhythm analysis that lasted 2-5 seconds. If the rhythm was VF or VT, another 125J defibrillation attempt was provided and compressions were re-initiated. If the animal was in asystole or an organized rhythm, no defibrillation attempt was made and compressions were re-initiated; if an organized rhythm was present at a second consecutive rhythm analysis, compressions were only re-initiated if the animal did not meet criteria for ROSC. At the second and fourth ALS rhythm analyses, epinephrine (0.01mg/kg) followed by a 10mL normal saline flush was administered if the animal had not met criteria for ROSC. During the third and fifth ALS rhythm analyses, amiodarone (5mg/kg) followed by a 10mL normal saline flush was administered if the animal had not met criteria for ROSC and was in a defibrillation-appropriate rhythm (VF or VT).

*Return of Spontaneous Circulation and Post-Resuscitation Care*

Return of spontaneous circulation was defined as an organized rhythm with a sustained aortic systolic blood pressure greater than 60 mm Hg without any intervention for one minute during a scheduled rhythm check. If ROSC was attained, the animals were supported in a simulated intensive care setting until termination of the protocol at minute 60. After ROSC, mechanical ventilation was provided with the initial ventilator settings and 100% oxygen. Respiratory rate was adjusted to maintain an ETCO2 of 38–42 mmHg. Inhales isoflurane was administered as necessary.

An epinephrine infusion was started as needed, at a rate of 0.1mcg/kg/min and titrated by 0.1mcg/kg/min every two minutes to a maximum of 2.0mcg/kg/min, to maintain an aortic systolic blood pressure (SBP) greater than 90mmHg. If the SBP rose above 120mmHg the epinephrine was titrated down by 0.1mcg/kg/min every two minutes. An amiodarone infusion (5mg/kg/hr) was started if the animal had received amiodarone during ALS.

*Termination of the Protocol*

Animals were considered expired if the aortic SBP was less than 60 for 10 minutes after minute 30. Expired animals were euthanized with 100mg/kg sodium pentobarbital, and mechanical ventilation was terminated. Animals that did attain ROSC were supported until minute 60, to ascertain short-term viability; at this time all life support, including medication infusions and mechanical ventilation, were terminated and the remaining animals were euthanized. No post-care was performed as all animals were euthanized at the end of the study.

**Measurements**

Hemodynamic data (aortic systolic (AoS) and diastolic (AoD) blood pressure, right atrial systolic and diastolic blood pressure, SpO2, ETCO2, cerebral and renal regional oximetry) were continuously monitored; the 2-minute intervals at the end of each experimental period (baseline, post-hemorrhage, end of Non-intervention, end of BLS, end of ALS) were averaged and analyzed. Baseline for hemodynamic measurements was defined as the 2-minute interval immediately prior to hemorrhage. Post-hemorrhage was defined as the 2-minute interval immediately prior to time zero. End of non-intervention was defined as the two-minute interval immediately prior to initiation of BLS (systolic and diastolic blood pressures as well as SpO2 were not measurable during the Non-intervention period). Coronary Perfusion Pressure (CPP) was calculated as the difference between the end-diastolic aortic pressure and the simultaneous end-diastolic right atrial pressure.

Arterial blood gas (ABG) specimens were obtained at baseline (immediately prior to hemorrhage), post-hemorrhage (immediately prior to time zero), end of Non-Intervention, end of BLS, and end of ALS during the protocol.

The number of animals that attained ROSC in each group and the number of ROSC animals that survived to 60 minutes was subsequently recorded. The total amount of epinephrine and amiodarone that each animal received were also recorded.

The 10-second TEE video recordings were randomly compiled into a file that was independently assessed at the conclusion of all data collection by an investigator who is certified in TEE and blinded to the remainder of the data. This investigator rated the AMC in each video as being over the LV or AR.

**Outcomes**

The primary outcome was the difference in ROSC between the two experimental groups. Secondary outcomes included the difference in: 1) short-term, 60-minute survival, 2) hemodynamic variables, and 3) ABG variables between the Traditional and LV groups.

**Analysis**

Means and standard deviations were calculated for measured variables of each treatment group across all time intervals. Shapiro-Wilk tests were used to test for normality. The treatment groups were compared on baseline weight and size, as well as the total amount of amiodarone and epinephrine administered using the nonparametric Wilcoxon/Mann-Whitney test. Differences in rates of survival were analyzed using Fisher's exact test. To control for within-subjects variation (due to repeated measures over time) and between-subjects variation (due to different treatment groups), a two-way repeated measures analysis of variance (ANOVA) was performed for the hemodynamic and ABG variables. The Greenhouse-Geisser correction was used to correct for violations of the assumption of sphericity, and the Bonferroni correction was applied for multiple comparisons. Statistical significance was defined as $p<0.05$, and 95% confidence intervals were provided.

Regarding sample size, based on prior data, 43% of animals were expected to attain ROSC (primary outcome) in the LV compressions and 0% in the Traditional group; at the $\alpha = 5\%$ significance level and with 80% power, a total sample size of 26 animals would be required (13 in each arm).

**RESULTS**

There was no difference in the size of the animals or the baseline hemodynamic and laboratory measures between the Traditional and LV groups ($p>0.05$ for all measures) (Table 1). There was 100% agreement between the AMC by TEE review and location of AMCD placement ($\kappa = 1.0$, 95% CI 1.0-1.0).

The mean total dose of epinephrine was similar between the LV (0.45mg ± 0.16mg SD) and Traditional group (0.49 ± 0.16mg SD) ($p=0.55$). The mean total dose of amiodarone was also similar in the Traditional group (175mg ± 151 SD) compared to the LV group (85mg ± 101mg SD) ($p=0.09$).

**Return of Spontaneous Circulation and Short-term survival**

The number of animals that attained ROSC was not significantly higher in the LV group ($p=0.24$) (Table 2). All fourteen animals that attained ROSC did so during the ALS period (Traditional group: two at minute 22 and three at minute 24; LV group: two at minute 22, three at minute 24, and four at minute 26) and all animals that attained ROSC survived to 60 minutes. A post-hoc sample size analysis determined that with the rates of ROSC demonstrated in Table 2, significance level set at $\alpha = 5\%$ and 80% power, an additional 24 animals (12 in each group) would be required to demonstrate a difference in ROSC between the LV and Traditional groups.

**Hemodynamic and Laboratory Variables**

The difference in the hemodynamic variables between the LV and Traditional experimental groups are demonstrated in Table 3. The differences in the mean blood gas analysis variables between the LV and Traditional experimental groups are demonstrated in Table 4. Detailed graphical representation of hemodynamic values across the entire resuscitative period are presented in Appendix A.

**DISCUSSION**

In our study we did not detect a significant difference in ROSC when chest compressions were performed in two different locations in a swine model of traumatic cardiac arrest using REBOA. We did

detect a difference in ETCO2 at the end of BLS between the two groups, but this difference did not persist to the end of the ALS period.

In most instances, performing chest compressions directly over the LV during TCA may be the closest approximation to open chest compressions available in the prehospital setting. In prior work, our group demonstrated that LV compressions improve hemodynamics and ROSC compared to traditional compressions in both NTCA and TCA models without REBOA. In this model, which was identical to our prior TCA model except for the addition of the REBOA catheter, we did not find the difference in ROSC between the two groups to be significant. There was a trend toward improved hemodynamics and ROSC, however, a larger study would be required to verify whether this trend is significant with a larger number of animals (our post-hoc sample size calculation suggests almost twice as many animals would be required). The hemodynamic measures which are the most reliable predictors of survival include ETCO2, AoD and CPP (30-32). In our study there was a significantly higher ETCO2 in the LV group at the end of the BLS period; Appendix A demonstrates that this trend persisted almost the entire resuscitative period. Appendix A also demonstrates a trend toward increased AoD and CPP in the LV group during the ALS period which likely explains the trend toward higher ROSC in the LV group.

It is possible that REBOA provides enough afterload during compressions that the location of compressions becomes less important in general. One possible explanation for the smaller than expected difference in hemodynamics and ROSC between the experimental groups is that the 5 animals which survived in the Traditional group, due to normal anatomic variation, may have had left ventricles that were located closer to the sternum so that the traditional compressions, with the addition of REBOA, were able to provide a similar hemodynamic response as the LV group. Our prior investigations suggest that without the support provided by REBOA those animals would likely not have attained ROSC either (13, 14). In the young healthy swine that were used in this experiment, there was very little anatomic variation (Table 1), so even small anatomic differences could have large clinical implications. In the human model, where the size and anatomic variation of the heart is greater, we would expect that larger movements in chest compression location would be necessary to have similar clinical implications. Nonetheless, the

addition of REBOA, in this TCA model, seems to have improved the performance of Traditional compressions and decreased the importance of chest compression location somewhat.

This study also highlights the impact that REBOA might have on both hemodynamics and survival in TCA. Although we have not yet performed a direct comparison between the animals in this study and the animals in our last TCA study, survival rates in both experimental groups from this work appear to be higher than those in the prior TCA study suggesting that survival may be improved with the use of REBOA regardless of the quality of chest compressions. More work in this field is needed.

**Limitations**

First, this animal model does not precisely replicate the human experience during cardiac arrest. Swine are often used in cardiac arrest studies due to the cardiovascular and metabolic similarities to humans, however, the swine heart is more vertically oriented, there is an extra lobe of lung in the left hemithorax and there are differences in chest wall anatomy which somewhat alter compression mechanics (33-36). In the average human, compression directly over the left ventricle would likely occur even more laterally on the chest that in swine. None of these anatomic differences diminish the importance that different compression locations have on the rate of ROSC and hemodynamic variables during cardiac arrest. Additionally, we analyzed young healthy swine which may which may not be physiologically similar to some TCA patients; however, although trauma is the fourth leading cause of death overall for all ages in humans, trauma is also the leading cause of death for humans ages 1-44 suggesting that a young swine model is likely more reflective of human physiology than an older swine model (5). There is also evidence for sex differences in the magnitude of cardiac and cerebral injury after hemorrhage and ventricular fibrillation, so generalization to male subjects may not be possible (37). Second, in our experiment we induced VF arrest during class III hemorrhage which may not cause TCA in many instances. This was done to limit the number of animals needed to determine if there is a difference in hemodynamics and ROSC after hemorrhage and VF. Further work is being done to determine if these differences persist in class IV hemorrhage. Third, only short-term survival to 60-minutes post-arrest was

evaluated in ROSC animals. Further investigation into long-term survival and neurologic outcomes needs to be performed, however, long-term survival is only possible when short-term survival has been achieved. In this study, if the animals began to demonstrate any movement during the survival period they were sedated, and sedation was not an outcome that we measured. At this time, it is still unclear whether long-term survival and neurologic outcomes can be improved by enhancing hemodynamics with LV compressions. Finally, this study only addressed VF as the initial cardiac rhythm after inducing hemorrhagic shock. Pulseless electrical activity (PEA) is the most common cardiac rhythm in TCA, however, both PEA and VF have higher survival rates from TCA than asystole. It is also possible that the results may vary with PEA or asystole as the initial rhythm, however, we chose to use VF in our model to maintain uniformity between this study and our prior non-traumatic cardiac arrest study (13). Ventricular fibrillation also ensured that our animals were truly in a cardiac arrest state rather than simply in a severe hemorrhagic shock state without palpable pulses which is likely the case with many traumatic PEA models where the most beneficial treatment is the transfusion of blood.

## CONCLUSIONS

Closed chest compressions directed over the LV did not result in a significantly higher rate of ROSC or short-term survival compared to chest compressions in the traditional location when REBOA was used in this swine model of TCA, however, a larger study may demonstrate that there is a difference. There was a significant increase in ETCO2 at the end of the BLS resuscitation period among the LV group.

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## DISCLOSURE

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## FIGURE LEGENDS

**FIGURE 1.** (a) Experimental protocol timeline; (b) Detailed ALS protocol timeline. *=rhythm check, BLS=Basic Life Support, ALS=Advanced Life Support, Post Resusc=Post Resuscitation, t=time, VF=ventricular fibrillation, ROSC=return of spontaneous circulation, J=joules, CPR=cardiopulmonary resuscitation, FiO2=fraction of inspired oxygen, mg-milligram, kg=kilogram, Epi=epinephrine, Amio=amiodarone, prn=as needed, gtt=infusion.

**APPENDIX A.** Hemodynamics.

**Table 1.** Baseline weight and size of animals

| | **Traditional** (n=13) | **LV** (n=13) |
|---|---|---|
| Weight, kg | 29.7 (1.93) | 29.3 (2.02) |
| Vertical distance from sternal notch to aortic root, cm | 7.00 (1.06) | 7.92 (1.37) |
| Vertical distance from sternal notch to mid LV, cm | 11.0 (0.83) | 11.5 (1.07) |
| Lateral distance from sternum to mid LV, cm | 3.36 (0.79) | 3.12 (0.55) |

Values given are mean (SD). No significant differences exist between groups on any of the listed measures at $p<0.05$. LV = left ventricle.

**Table 2**. Rates of survival

| | **Traditional** (n=13) | **LV** (n=13) | **Relative Risk** | **95% CI** | **p-value** |
|---|---|---|---|---|---|
| ROSC | 5 (38%) | 9 (69%) | 0.50 | 0.20-1.3 | 0.24 |
| Survival to 60 minutes | 5 (38%) | 9 (69%) | 0.50 | 0.20-1.3 | 0.24 |

Values given are n (%). ROSC = return of spontaneous circulation, LV = Left Ventricle, CI = Confidence Interval.

Fisher's exact test used to determine p-value.

Table 3

**Table 3.** Results of repeated measures ANOVAs for hemodynamic variables

| | Traditional (n=13) | LV (n=13) | 95% CI of Difference LL | 95% CI of Difference UL | p-value |
|---|---|---|---|---|---|
| **AoS, mmHg** | | | | | |
| Baseline | 96.2 (12.6) | 99.2 (12.0) | -6.95 | 12.9 | 0.540 |
| Post bleed | 66.9 (11.3) | 70.2 (12.6) | -6.46 | 12.9 | 0.498 |
| End of BLS | 86.5 (45.4) | 109 (44.8) | -14.9 | 59.7 | 0.228 |
| End of ALS | 93.8 (55.8) | 109 (58.7) | -32.1 | 62.9 | 0.509 |
| **AoD, mmHg** | | | | | |
| Baseline | 68.4 (11.1) | 70.4 (11.8) | -7.25 | 11.3 | 0.660 |
| Post bleed | 43.9 (9.26) | 45.0 (10.7) | -7.03 | 9.18 | 0.786 |
| End of BLS | 19.3 (11.1) | 25.5 (12.8) | -3.78 | 16.2 | 0.211 |
| End of ALS | 50.7 (49.0) | 72.3 (53.2) | -20.8 | 64.0 | 0.302 |
| **RAS, mmHg** | | | | | |
| Baseline | 8.92 (7.05) | 9.23 (5.97) | -4.98 | 5.60 | 0.905 |
| Post bleed | 7.00 (6.90) | 6.23 (5.79) | -5.93 | 4.39 | 0.761 |
| End of BLS | 64.9 (26.5) | 114 (68.8) | 6.84 | 91.3 | 0.025* |
| End of ALS | 43.5 (21.9) | 59.2 (67.3) | -24.9 | 56.1 | 0.434 |
| **RAD, mmHg** | | | | | |
| Baseline | 2.08 (4.42) | 3.23 (5.38) | -5.15 | 2.84 | 0.556 |
| Post bleed | -0.85 (5.44) | 0.69 (4.92) | -5.74 | 2.66 | 0.457 |
| End of BLS | 2.31 (3.59) | 2.85 (9.35) | -6.27 | 5.20 | 0.848 |
| End of ALS | 6.46 (3.84) | 7.38 (6.42) | -5.21 | 3.36 | 0.661 |
| **CPP, mmHg** | | | | | |
| Baseline | 66.3 (11.9) | 67.2 (13.8) | -9.59 | 11.3 | 0.869 |
| Post bleed | 44.8 (11.0) | 44.3 (12.1) | -9.85 | 8.93 | 0.920 |
| End of BLS | 16.8 (10.5) | 25.8 (14) | -1.99 | 20.2 | 0.103 |
| End of ALS | 44.2 (50.6) | 64.9 (57.4) | -24.2 | 65.7 | 0.349 |
| **SpO2, mmHg** | | | | | |
| Baseline | 99.2 (1.23) | 99.5 (0.97) | -0.59 | 1.21 | 0.486 |
| Post bleed | 97.7 (4.66) | 99.5 (1.13) | -0.97 | 4.51 | 0.196 |
| End of BLS | 59.3 (17.8) | 79.6 (17.8) | -1.60 | 42.1 | 0.066 |
| End of ALS | 81.4 (24.9) | 89.9 (15.5) | -13.2 | 30.1 | 0.416 |
| **ETCO2, mmHg** | | | | | |
| Baseline | 42.8 (2.59) | 41.5 (1.94) | -3.08 | 0.62 | 0.183 |
| Post bleed | 40.3 (3.68) | 40.5 (2.63) | -2.36 | 2.82 | 0.856 |
| End Non-intervention | 12.8 (3.06) | 15.0 (1.67) | -0.01 | 4.37 | 0.051 |
| End of BLS | 24.6 (14.2) | 38.8 (13.0) | -2.61 | -25.8 | 0.019* |
| End of ALS | 22.4 (9.37) | 30.3 (12.1) | -9.37 | 12.1 | 0.074 |
| **Cerebral rSO2, %** | | | | | |
| Baseline | 66.6 (6.98) | 66.8 (5.65) | -4.91 | 5.37 | 0.927 |
| Post bleed | 58.0 (8.15) | 58.3 (8.03) | -6.17 | 6.93 | 0.905 |
| End Non-intervention | 21.8 (10.8) | 24.9 (17.0) | -8.42 | 14.6 | 0.586 |
| End of BLS | 35.6 (14.7) | 39.5 (15.0) | -8.16 | 15.8 | 0.515 |
| End of ALS | 45.2 (18.3) | 51.9 (19.5) | -8.62 | 22.0 | 0.376 |
| **Renal rSO2, %** | | | | | |
| Baseline | 67.7 (2.70) | 67.6 (3.10) | -2.42 | 2.27 | 0.947 |
| Post bleed | 63.2 (2.64) | 63.3 (2.90) | -2.09 | 2.40 | 0.890 |
| End Non-intervention | 50.1 (4.46) | 48.9 (5.41) | -5.17 | 2.86 | 0.559 |
| End of BLS | 49.2 (6.06) | 45.6 (6.95) | -8.89 | 1.66 | 0.170 |
| End of ALS | 50.2 (7.41) | 48.8 (8.88) | -8.07 | 5.43 | 0.689 |

*Significant difference, $p<0.05$; adjusted p-values for repeated-measures ANOVA are reported. Data are reported as mean (SD).

LV = left ventricle, LL = lower limit, UL = upper limit, HR=heart rate, Ao=aortic, RA=right atrial, S=systolic blood pressure, D=diastolic blood pressure, mmHg=millimeters of mercury, SpO2=peripheral capillary oxygen saturation, rSO2=regional oximetry, BLS = basic life support, ALS = advanced life support.

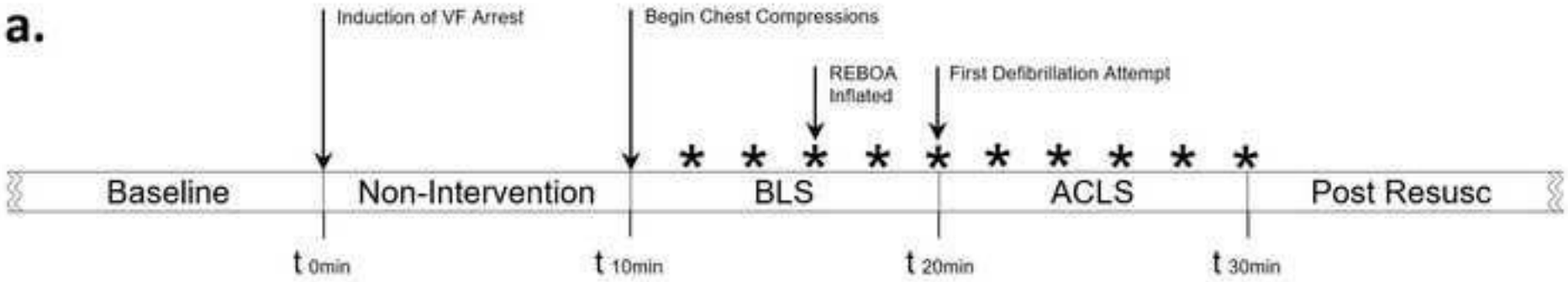
Table 4

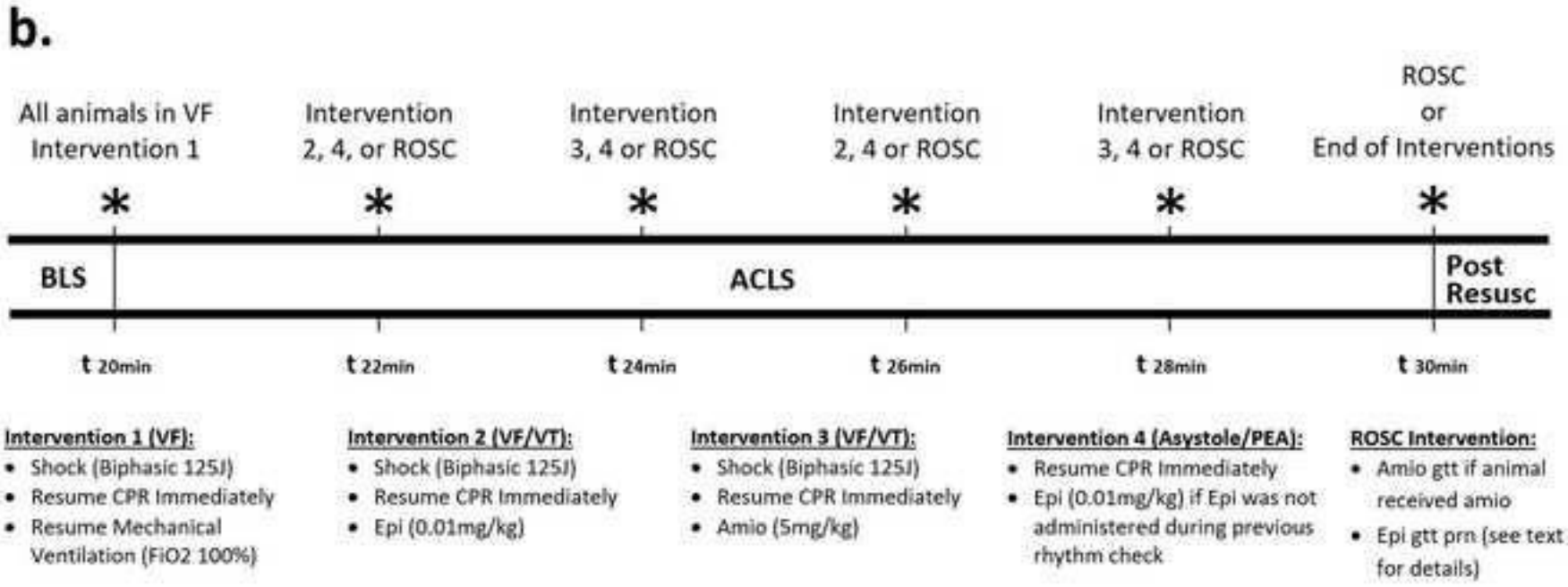
**Table 4.** Results of repeated measures ANOVAs for arterial blood gasses

| | **Traditional** (n=13) | **LV** (n=13) | **95% CI of Difference** LL | UL | **p-value** |
|---|---|---|---|---|---|
| **pH** | | | | | |
| Baseline | 7.47 (0.04) | 7.47 (0.03) | -0.04 | 0.02 | 0.534 |
| Post bleed | 7.47 (0.04) | 7.47 (0.03) | -0.03 | 0.03 | 0.844 |
| End Non-intervention | 7.47 (0.04) | 7.45 (0.03) | -0.04 | 0.01 | 0.256 |
| End of BLS | 7.30 (0.14) | 7.21 (0.14) | -0.01 | 0.05 | 0.103 |
| End of ALS | 7.26 (0.09) | 7.21 (0.13) | -0.03 | 0.14 | 0.207 |
| **pCO2** | | | | | |
| Baseline | 40.9 (4.91) | 39.8 (2.65) | -2.12 | 4.27 | 0.493 |
| Post bleed | 40.7 (3.38) | 39.9 (2.34) | -1.51 | 3.20 | 0.465 |
| End Non-intervention | 39.9 (5.57) | 41.1 (4.59) | -2.89 | 5.37 | 0.542 |
| End of BLS | 43.4 (18.1) | 55.2 (20.2) | -27.4 | 3.70 | 0.129 |
| End of ALS | 37.3 (11.8) | 48.0 (18.2) | -23.1 | 1.72 | 0.088 |
| **pO2** | | | | | |
| Baseline | 189 (20.0) | 183 (24.7) | -11.7 | 24.8 | 0.466 |
| Post bleed | 194 (19.6) | 183 (18.4) | -3.93 | 26.9 | 0.137 |
| End Non-intervention | 107 (52.0) | 82.3 (21.5) | -57.2 | 7.18 | 0.123 |
| End of BLS | 226 (122) | 197 (110) | -122 | -65.7 | 0.539 |
| End of ALS | 203 (101) | 205 (134) | -98.5 | 93.4 | 0.957 |

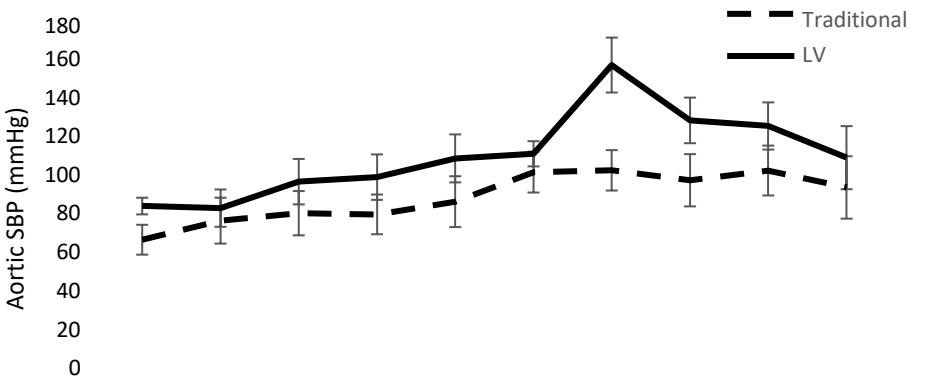
Data are reported as mean (SD). Adjusted p-values for repeated-measures ANOVA are reported.
pCO2 = partial pressure of carbon dioxide, pO2 = partial pressure of oxygen, BLS= basic life support, ALS = advanced life support

Figure 1

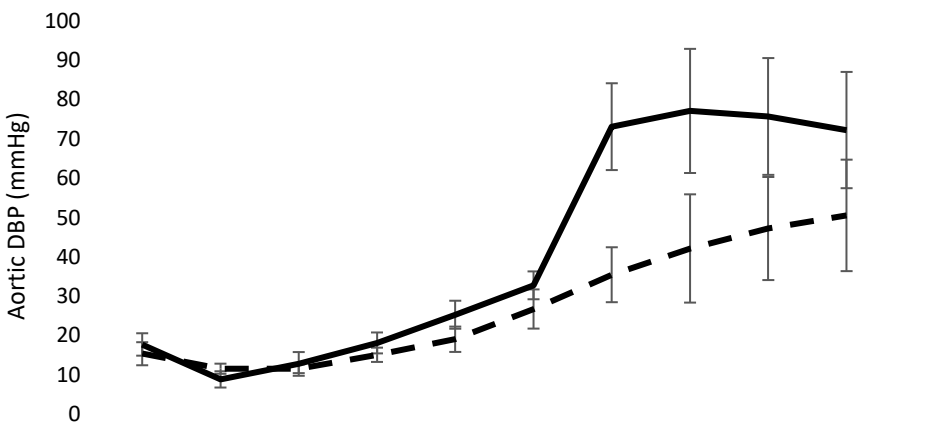

a.
Induction of VF Arrest
Begin Chest Compressions
REBOA Inflated
First Defibrillation Attempt
Baseline
Non-Intervention
BLS
ACLS
Post Resusc
t 0min
t 10min
t 20min
t 30min


b.
All animals in VF Intervention 1
Intervention 2, 4, or ROSC
Intervention 3, 4 or ROSC
Intervention 2, 4 or ROSC
Intervention 3, 4 or ROSC
ROSC or End of Interventions
BLS
ACLS
Post Resusc
t 20min
t 22min
t 24min
t 26min
t 28min
t 30min
Intervention 1 (VF):
• Shock (Biphasic 125J)
• Resume CPR Immediately
• Resume Mechanical Ventilation (FiO2 100%)
Intervention 2 (VF/VT):
• Shock (Biphasic 125J)
• Resume CPR Immediately
• Epi (0.01mg/kg)
Intervention 3 (VF/VT):
• Shock (Biphasic 125J)
• Resume CPR Immediately
• Amio (5mg/kg)
Intervention 4 (Asystole/PEA):
• Resume CPR Immediately
• Epi (0.01mg/kg) if Epi was not administered during previous rhythm check
ROSC Intervention:
• Amio gtt if animal received amio
• Epi gtt prn (see text for details)

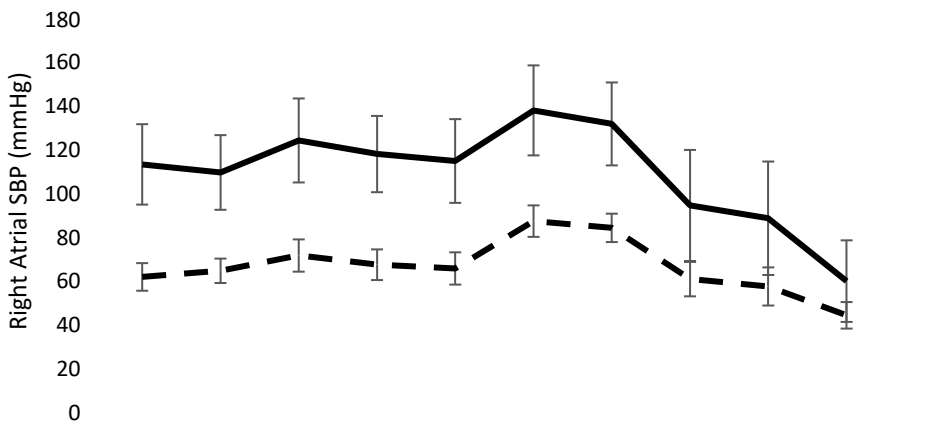
**A. Aortic SBP over time**



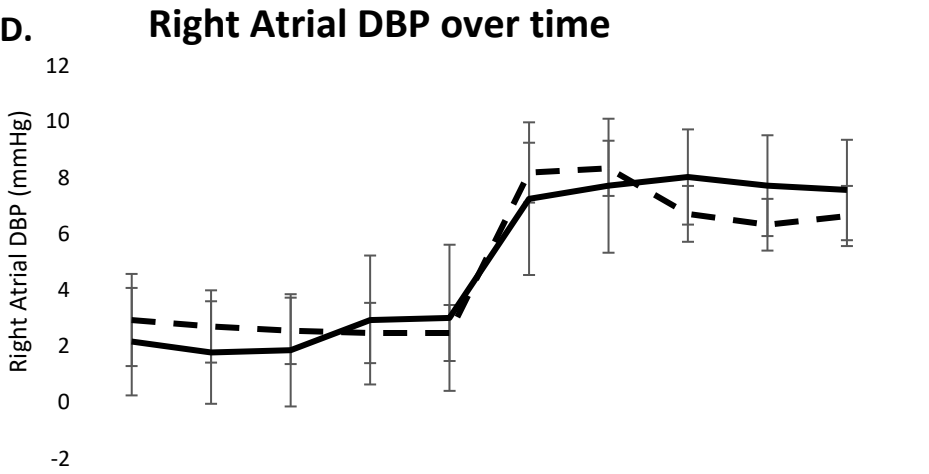

**B. Aortic DBP over time**



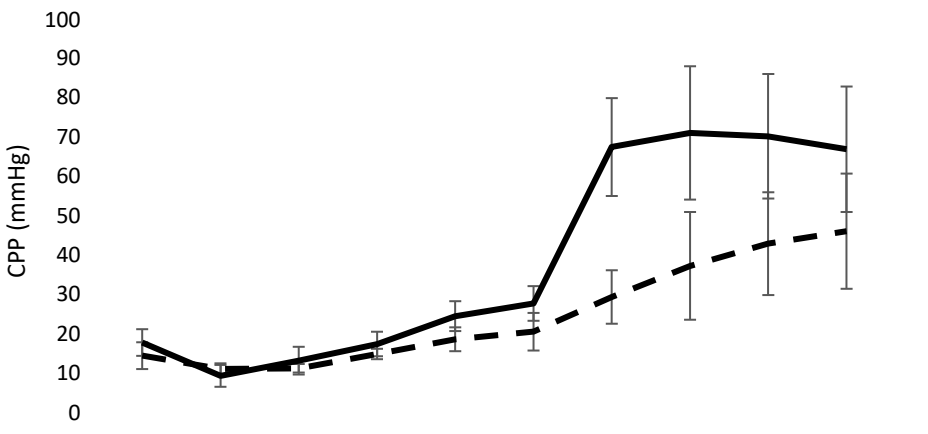

**C. Right Atrial SBP over time**



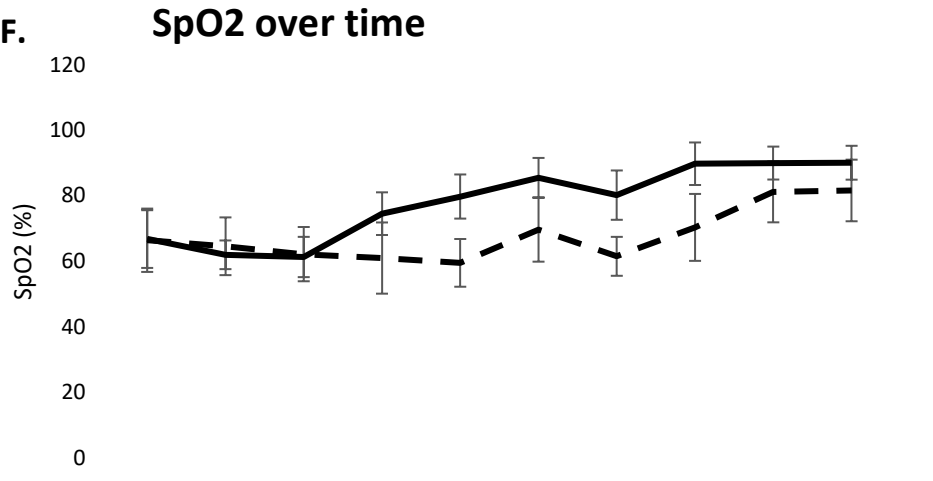

**D. Right Atrial DBP over time**




**E. CPP over time**




**F. SpO2 over time**




**G. ETCO2 over time**