Experimental paper

Chest compression by two-thumb encircling method generates higher carotid artery blood flow in swine infant model of cardiac arrest

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Abstract

Objective: Two-Thumb(TT) technique provides superior quality chest compressions compared with Two-Finger(TF) in an instrumented infant manikin. Whether this translates to differences in blood flow, such as carotid arterial blood flow(CABF), has not been evaluated. We hypothesized that TT-CPR generates higher CABF and Coronary Perfusion Pressure(CPP) compared with TF-CPR in a neonatal swine cardiac arrest model.

Methods: Twelve anesthetized & ventilated piglets were randomized after 3 min of untreated VF to receive either TT-CPR or TF-CPR by PALS certified rescuers delivering a compression rate of 100/min. The primary outcome, CABF, was measured using an ultrasound transonic flow probe placed on the left carotid artery. CPP was calculated and end-tidal CO_2($ETCO_2$) was measured during CPR. Data(mean $\pm$ SD) were analyzed and p-value ≤ 0.05 was considered statistically significant.

Results: Carotid artery blood flow (% of baseline) was higher in TT-CPR (66.2 $\pm$ 35.4%) than in the TF-CPR (27.5 $\pm$ 10.6%) group, p = 0.013. Mean CPP (mm Hg) during three minutes of chest compression for TT-CPR was 12.5 $\pm$ 15.8 vs. 6.5 $\pm$ 6.7 in TF-CPR, p = 0.41 and $ETCO_2$ (mm Hg) was 29.0 $\pm$ 7.4 in TT-CPR vs. 20.7 $\pm$ 5.8 in TF-CPR group, p = 0.055.

Conclusion: TT-CPR achieved more than twice the CABF compared with TF-CPR in a piglet cardiac arrest model. Although CPP and $ETCO_2$ were higher during TT-CPR, these parameters did not reach statistical significance. This study provides direct evidence of increased blood flow in infant swine using TT-CPR and further supports that TT chest compression is the preferred method for CPR in infants.

Keywords: Cardiopulmonary resuscitation, Two-thumb CPR, Two-finger CPR, Swine cardiac arrest, Carotid artery blood flow

Introduction

The current international cardiopulmonary resuscitation (CPR) guidelines emphasize that survival and neurological outcome following cardiopulmonary arrest (CPA) is associated with the quality of CPR.[1,2] The current guideline for neonatal and infant CPA recommended CPR using the two-finger technique (TF) for a single rescuer and the two-thumb encircling technique (TT) for two rescuers. Using an instrumented infant manikin, we previously reported that TT-CPR generates higher compression depth and pressure compared with TF-CPR with equally effective ventilations by lone rescuers.[3,4] Several recently published meta-analyses and reviews of available evidence comparing the two techniques of infant CPR concluded that the TT technique is superior to TF in terms of effectiveness and quality of chest compressions.[5−8]

Most infant studies comparing TT vs TF chest compressions used manikin models and there is a paucity of studies reporting actual blood flow hemodynamics data.[9−13] Although these studies support that TT is a superior technique for chest compression, it is important to note that no studies have reported blood flow dynamics and outcomes such as return of spontaneous circulation (ROSC), survival or neurological disability in infants comparing different chest compression techniques. The ultimate goal of chest compressions during cardiopulmonary arrest is to provide blood flow to vital organs, especially the brain and heart. Measurements of cerebral and cardiac blood flows during CPR are not available in human neonates and infants, hence researches have utilized animal cardiac arrest models to measure blood flows for the comparison of the effectiveness of different CPR techniques. Measurement of carotid artery blood flow (CABF) has been utilized as a surrogate for brain blood flow in multiple previous animal studies of cardiac arrest assessing the effectiveness of CPR.[9]

It is assumed that the improved quality of chest compression by TT technique observed in infant manikin models should result in higher blood flow generation during cardiac arrest, but no previous animal or human studies compared TT vs TF-CPR techniques measuring CABF or cerebral blood flow. To make robust recommendations regarding the preferred method of chest compression in infants, it is important to document that improved chest compression quality with TT-CPR improves blood flow dynamics and outcomes. Thus, the goal of this study was to compare TT-CPR with TF-CPR to determine which technique generates higher CABF. As our previous manikin data suggest that TT-CPR provides better compression depth and pressure,4 we hypothesized that TT-CPR will provide higher CABF compared with TF-CPR in a neonatal piglet cardiac arrest model.

Methods

Design

This prospective, randomized, controlled small animal (swine) study was approved by the University of Florida Health Science Center Institutional Animal Care and Use Committee (IACUC) protocol # 201104898. Qualified individuals supervised by veterinarians managed the animals care in accordance with American Physiological Society guidelines and all facilities meet the standards of the American Association for Accreditation of Laboratory Animal Care. The study's inclusion criteria were defined a priori as the achievement of successful instrumentation and stable baseline hemodynamics before the initiation of the experimental protocol, and the exclusion criteria were unsuccessful instrumentation or inability to achieve baseline hemodynamics after instrumentation due to any complication. This study's protocol or the experimental data have not been registered and submitted to any public registry or website.

Animal preparation

Farm piglets less than 30 days old (weight ∼ 4 kg) of either sexes obtained from the University of Florida Swine Unit were used in this study. Animal preparation was performed as previously described by us.[12] Animals were sedated with ketamine (15 mg/kg) IM followed by administration of anesthesia with 5% isoflurane in 100% oxygen delivered by mask. Endotracheal intubation was then performed, and mechanical ventilation was started (Surgivet Vaporstic Anesthesia Machine, Smiths Medical, USA). Ventilator rate and tidal volume were adjusted to maintain an end-tidal CO_2 of 35−40 mmHg. The lowest concentration of isoflurane that ensured proper anesthesia during surgical instrumentation was used. EKG leads were placed on the limbs for continuous monitoring of heart rate and rhythm. Body temperature was maintained between 37−39 °C using a thermostatically heated mattress throughout the procedure. An ear IV catheter was placed to deliver Saline with 5% Dextrose at a maintenance rate.

Standard cut-down technique was done to expose the left carotid artery, right internal jugular (IJ) vein and right femoral artery. To measure blood flow from the left Carotid artery, a 3 mm transonic flow probe (Animal Blood Flow Meter T206, Transonic Systems Inc, USA) was placed encircling the artery and its position was secured. For invasive continuous blood pressure monitoring, a 4F introducer sheath (Boston Scientific) was placed in the right femoral artery and connected to a fluid-filled catheter transducer. To monitor the right atrial pressure, a 4F 15 cm vascular introducer sheath (Boston Scientific) was introduced in the right IJ vein and advanced to the upper right atrium and connected to a fluid-filled catheter transducer. Following the placement of all vascular catheters, a single dose of Heparin (50 U/kg) was given to each animal.

Experimental protocol

Subsequent to animal instrumentation, cardiopulmonary, hemodynamic and CABF values were collected while the animal rested without any intervention. This was considered as the baseline period. The Right IJ introducer sheath was then used to advance a non-coated guide wire into the right ventricle (RV); correct wire placement in the RV was verified by fluoroscopy. Ventricular fibrillation (VF) was induced by delivering an alternating current to the RV via the non-coated guide wire. The presence of VF was confirmed by the characteristic EKG waveform and the steep fall in aortic pressure. Ventilation was discontinued and the animals were left in untreated VF for 3 min to simulate in-hospital resuscitation. Animals were randomized using a random number generator to one of the two CPR groups: TT-CPR and TF-CPR groups. This allocation was concealed until just before the beginning of chest compressions. The individual performing CPR was then instructed to use chest compression technique as per randomization. The rescuer was blinded to the hemodynamic and ETCO2 data recording during the chest compression. After 3 min of VF, ventilation was resumed with 100% oxygen and chest compressions were given at a rate of at least 100 compressions/min. Chest compressions were delivered for 3 min by the first rescuer. This was followed by 2 min of chest compressions provided by a

Table 1 – Baseline data presented as mean (±SD).

	TT-CPR	TF-CPR	p value
n (males)	6 (5)	6 (5)	
Age (days)	19.3±7.1	16.7±4.7	0.46
Weight	5.9±1.7	4.5±0.4	0.09
Glucose (mg/dL)	176±30	175±43	0.99
Sodium (mM)	135±2.5	135±7.1	0.79
Potassium (mM)	3.6±0.5	4.9±3.7	0.39
Ionized Calcium (mM)	1.3±0.1	1.3±0.2	0.42
pH	7.39±0.06	7.40±0.03	0.84
PCO_2 (mmHg)	35.6±5.9	33.9±9.4	0.71
PO_2 (mmHg)	353±161	358±39	0.94
HCO_3 (mM)	22±3.9	21±4.9	0.66
Base Excess (mM)	−3±4.6	−4±4.5	0.62
Right Atrial venous O_2 saturation (%)	82±4.9	82±3.9	0.80
Heart Rate (BPM)	140±13	138±10	0.74
Systolic BP (mmHg)	79±6	73±3	0.74
Diastolic BP (mmHg)	41±10	34±6	0.23
Mean BP (mmHg)	55±8	47±5	0.14
Right atrial diastolic pressure (mmHg)	4.6±1.6	4.1±0.9	0.65

n, sample size; BP, indicates blood pressure; BPM, beats per minute; mM, millimoles.

second rescuer, after which a quick rhythm check was performed. If the piglet was still in VF, defibrillation was attempted with 20J biphasic shock and CPR was continued for another cycle of 2min per NRP guidelines. At the end of 2min of CPR, the rhythm was checked. If still in VF, another 50J shock was given. Emergency drugs were administered during CPR per NRP guidelines. CPR was continued per NRP guidelines until ROSC or no ROSC within 20min of CPR. ROSC was defined as a perfusing rhythm with a peak aortic systolic pressure of >60mm Hg sustained for 1min. Animals who achieved ROSC remained anesthetized for 30min post-ROSC to simulate intensive care period. CPP was calculated as the difference of each diastolic BP and RAP just before the next chest compression and the mean CPP was averaged over each minute of chest compressions. At the conclusion of the experimental protocol, all animals were humanely euthanized.

Measurements and data acquisition

The primary outcome measures were CABF and CPP. Secondary outcomes are listed and included in Table 2. Hemodynamic data were transferred to a bio-amplifier by ADInstruments Power lab® Systems (Castle Hill, NSW 2154 Australia), which then sent real time continuous data to a laptop computer. Computer software (Chart pro V7.3 by ADInstruments Power lab® Systems; Castle Hill, NSW 2154 Australia) was used to record the data. The sampling rate for data collection was set at 100 data points per second. Venous and arterial blood gas analysis along with plasma concentrations of sodium, potassium, hematocrit, lactate and ionized calcium (iSTAT Blood Gas Analyzer, Windsor, NJ) were performed at baseline and at ROSC in all animals.

Statistical analysis

Data are reported as mean±SD. All data analyses were conducted using PC-Sigma-stat (3.0). Normality and equality of data variances were assessed using the Kolmogorov−Smirnov and Leven test, respectively. For each group, a one-way ANOVA for repeated measures was used (baseline vs. CPR). Student t-test was used to assess differences between groups during the CPR stage. For all analyses, the primary inference was based on the difference between TT-CPR vs. TF-CPR groups. For sample size calculation, the study had over 80% power to detect a difference of 0.37 standard deviations in the raw measures considering a two-tailed p-value ≤0.05 as statistically significant.

Results

Twelve piglets (6 piglets/group) were randomized to either TT-CPR or TF-CPR. All animals met inclusion criteria and had successful ROSC and no animal was excluded from the analysis. Both groups had comparable baseline characteristics, as shown in Table 1. During the resuscitation period, there was no difference in number of epinephrine doses, number of shocks delivered and time to ROSC between groups as shown in Table 2.

Table 2 – Intra-resuscitation parameters and outcomes.

	TT-CPR	TF-CPR	p value
Duration of CPR (min)	8.7±1.4	9±0.6	0.60
Right Atrial Pressure (mmHg)	27.5±8.3	21.4±3.3	0.16
Systolic BP (mmHg)	64.7±14.1	51.1±11.8	0.13
Diastolic BP (mmHg)	23.4±13.3	15.1±6.2	0.23
Mean BP (mmHg)	37.2±13.2	27.1±6.9	0.16
Right atrial pressure during compression (mmHg)	64.4±32.1	50.2±12.7	0.38
Right atrial pressure during relaxation (mmHg)	10.9±3.3	8.5±1.4	0.17
Number of Epinephrine doses	2±1.3	2±0.6	1
Number of Shock delivered	1.6±0.9	1.6±0.5	0.60
Time to ROSC (min)	11.7±1.4	12±0.6	0.60
Coronary perfusion pressure (CPP, mmHg)[a]	12.5±15.8	6.5±6.7	0.41
End tidal CO_2 (ETCO₂, mmHg)[a]	29.0±7.4	20.7±5.8	0.055
Carotid Artery Blood Flow (% of baseline)	66.2±35.4	27.5±10.6	**0.01**

Bold value is statistically significant.
[a] Mean values calculated during the 3min of CPR.

Chest compression rate was significantly higher in the TF-CPR group than in the TT-CPR group during the first three minutes of CPR (151.0 ± 16.86 vs. 178.60 ± 13.59, p=0.011). Even though the aortic systolic, diastolic, and mean blood pressure and right atrial pressure during chest compression and relaxation were $28-55\%$ higher in the TT-CPR group compared with the TF-CPR group, as shown in Table 2, the difference did not reach statistical significance. The mean calculated CPP and measured $ETCO_2$ values for both techniques during the first 3 min of CPR are shown in Table 2. The CPP was almost two-fold higher and $ETCO_2$ was $\sim 40\%$ higher for TT-CPR compared with TF-CPR but the differences were not statistically significant.

Maximum carotid artery blood flow (CABF) for all animals during the first 3 min duration of CPR were obtained by using the peak values with each chest compression which was then used to calculate a mean peak CABF and the changes in CABF is reported as a percentage of the baseline as shown in Table 2. The CABF was more than twice as high for TT-CPR than for TF-CPR for the entire 3 min of CPR. The change in CABF for each minute of CPR is shown in Fig. 1. CABF were significantly higher during the first and second minutes of CPR in the TT-CPR group compared to TF-CPR group. This difference became non-significant at the 3rd minute of CPR. To assess the magnitude of the decline in CABF over time during CPR using the two techniques, the percentage decrease of CABF from minute 1 of CPR to minute 2, and then from minute 2 to minute 3 of CPR is shown in Table 3. Even though the minute 1 CABF was much lower than baseline using TF-CPR compared with TT-CPR, the percentage decrease in CABF during minute 2 was larger in the TF-CPR group.

Discussion

Optimizing blood flow during cardiac arrest by utilizing the most effective chest compression technique is critical during resuscitation. The quality of the delivered chest compressions is a pivotal determinant of successful post arrest outcomes.[11] In neonates and infants, two-thumb encircling and two-finger techniques are recommended in current guidelines,[1,2] largely based on manikin and two animal studies[12,13] reporting blood pressure but not blood flow data. Menegazzi et al. compared TT to TF chest compression in a swine infant model and reported that TT-CPR generated higher systolic and diastolic blood pressures and coronary perfusion pressure (CPP)

compared with the TF technique, but did not measure blood flows.[12] In another study, Houri et al. compared standardized TT vs TF chest compression with and without feedback in a swine asphyxia model of cardiac arrest and reported higher systolic but not diastolic blood pressure.[13] Our study is the first to compare CABF using the two infant CPR techniques in a randomized experiment. We observed that the TT chest compression technique more than doubled the CABF during CPR and provides direct evidence for superior blood flow using the TT technique during resuscitation of an infant swine model of cardiac arrest.

Achieving adequate blood flow during cardiopulmonary resuscitation is important to reduce the risk of the ischemic neurologic injury resulting from cardiopulmonary arrest. Accurate measurement of blood flow to the brain during CPR would provide direct evidence of the superiority of one CPR technique compared with another but measuring brain blood flow remains challenging. Researchers have used several different methods to evaluate brain blood flow including ultrasound based carotid artery blood flow for overall brain blood flow estimates; injection of radioactively labelled microspheres and their measurements in brain tissue or cerebro-cortical laser-doppler flowmetry (LDF) which estimates regional brain blood flow.[14−16] Although the correlation of CABF and cerebral blood flow methods has not been consistent in the literature, researchers demonstrated an equivalent decrease in cerebral blood flow when both methods were used simultaneously in multiple previous CPR studies.[9]

A benefit of measuring CABF by ultrasound compared with microspheres is the ability to continuously measure blood flow, which is of great value during an unstable and highly dynamic situation like CPR. To assess differences in CABF over time related to the chest compression technique, we analyzed the change from BL determined for each animal and then calculate the mean percent change in each group at each minute during the first 3 min of CPR. Our data showed that CABF decreased significantly after 1 min of CPR for both techniques, but the decrease in CABF was significantly higher for TF-CPR as compared to TT-CPR. This result suggests that TT-CPR can help sustain higher CABF for a longer duration of time which may be an important factor in decreasing or delaying neurological injury in infants with cardiopulmonary arrest. During the third minute of CPR, there was no significant difference in the decline in CABF compared with the two minute value between the two groups, suggesting that rescuer fatigue was similar for these different techniques. This has been previously reported by us and others.[17,18]

In our study, the measured aortic blood pressures, $ETCO_2$ and the calculated CPP were higher in the TT-CPR group compared with the TF-CPR group but this trend did not reach statistical significance. Two previous animal studies compared the effects of TT and TF chest compression techniques on blood pressures. Menegazzi et al. reported that TT generated higher systolic and diastolic blood pressures and CPP[12] and Houri et al. reported higher systolic but not diastolic blood pressures generation with TT-CPR.[13] The differences in aortic blood pressures and CPP observed in our study are in agreement with the observations made in these studies; the failure to achieve statistical significance was likely due to the small sample size.

In summary, our finding of significantly higher CABF with the TT encircling technique is relevant to and supports a recommendation that this technique should be the preferred method of chest compression in infants. This result is not unexpected as several recent meta-analyses and reviews concluded that TT-CPR provides superior quality chest compression compared to TF-CPR.[5−8] Further
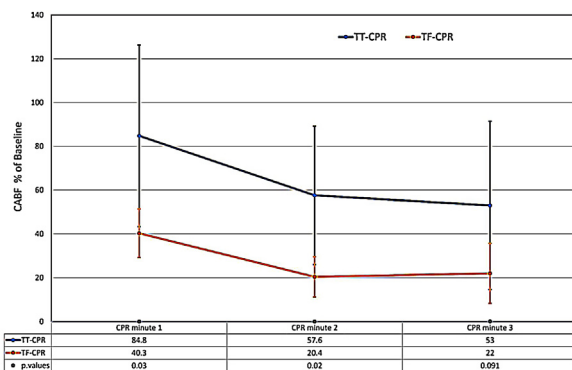
Fig. 1 – Comparison of TT vs. TF mean carotid artery blood flow for each minute during the 3 min of CPR presented as a percentage of pre-arrest baseline flow. Error bars indicate standard deviations (SD).

Table 3 – Comparison of the decrease in the percentage of carotid artery blood flow (CABF) for each technique of chest compression, comparing minute two to minute one and minute three to minute two.

Technique	% decrease in CABF comparing min 1 to min 2	p-value	% decrease in CABF comparing min 2 to min 3	p-value
TT-CPR	33.6 ± 14.3	**0.0022**	11.9 ± 22.0	**0.24**
TF-CPR	51.0 ± 11.8	**0.00013**	-2.50 ± 27	**0.83**

Bold values are statistically significant.

studies that assess neurological outcome and survival are needed to clarify the effects of different techniques and develop robust guidelines for infant CPR.

Limitations

Our study has several limitations. First, due to the nature of the study the investigators could not be completely blinded to the procedures done but were the blinded to the hemodynamic and ETCO2 data during chest compression. Secondly, for various reasons there have always been concerns raised about the relevance of the swine model to human resuscitation; however, many previous findings in swine have been confirmed by other studies in humans.[19,20] Our study observed a higher chest compression rate with the TF technique and we did not compare factors like chest compression depth, recoil and chest relaxation time between the two techniques which potentially can bias the outcome. It is known that the TF chest compression technique usually results in a higher rate if the compression rate is not controlled by the experimental protocol using a metronome feedback device. In our study, we assigned the same individual to perform the first three minutes of CPR and no coaching related to chest compression quality was given to minimize variations in chest compression quality. In addition, the individual performing chest compression was blinded from all hemodynamic monitoring. Even though chest compression rate were higher in TF group, the increased chest compression rate was also observed with the TT group. If increased compression rate potentially resulted in shallower compressions, then this effect would be applicable to both the groups. Lastly, although the CPP and $ETCO_2$ were much higher in the TT group, we failed to show statistically significant differences, which was likely due to the small sample size. We believe that the 92% higher mean CPP with TT-CPR compared with TF-CPR is still important to consider since a previous study observed that the changes in measured CPP underestimates changes in blood flow to the heart; i.e., the magnitude of improved myocardial blood flow seems to be significantly more than the magnitude of CPP increase during CPR.[21]

Conclusion

This study represents the first direct comparison of carotid artery blood flow during TT-CPR vs TF-CPR in a neonatal piglet model of cardiac arrest. TT-CPR achieved significantly higher and longer sustained carotid artery blood flow compared with TF-CPR. Also, although not statistically significant, CPP and $ETCO_2$ trended much higher in TT-CPR as compared with TF-CPR. Further animal studies with survival outcome and neurological assessments are needed to determine if two-thumb encircling chest compression technique can result in better neurologically intact survival in infants.

Conflict of interest statement

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

CRediT authorship contribution statement

Sharda Udassi: Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing. **Ikram U. Haque:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing. **Dalia Lopez-Colon:** Data curation. **Andre Shih:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing. **Dhanya Vasudeva:** Writing - original draft, Writing - review & editing. **Giridhar Kaliki-Venkata:** Investigation. **Michael Weiss:** Conceptualization, Methodology. **Arno L. Zaritsky:** Supervision, Writing - original draft. **Jai P. Udassi:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing.

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