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Experimental paper

Evaluation of coronary perfusion pressure and diastolic blood pressure calculation methods in a swine model of pediatric cardiopulmonary resuscitation

Jeremy C. Zuckerberg[a,b,c], Tiffany Ko[c], M. Katie Weeks[c], Nicholas J. Widmann[c], Martha F. Kienzle[a,b,c], Hunter A. Gaudio[c], Luiz Eduardo V. Silva[d], Ron W. Reeder[e], Robert M. Sutton[a,b,c], Robert A. Berg[a,b,c], Todd J. Kilbaugh[a,b,c,1], Ryan W. Morgan[a,b,c,1,*]

Abstract

Introduction: Measurement of coronary perfusion pressure (CoPP) and diastolic blood pressure (DBP) during cardiopulmonary resuscitation (CPR) is important for titration of physiologic-directed CPR. However, agreement between different calculation methods and their relative performance as outcome discriminators are not well established.

Methods: Four calculation methods, differentiated by sampling technique, were retrospectively applied to pressure waveforms from piglet CPR: late diastole ($CoPP_{65}$, DBP_{65}), mid-diastole ($CoPP_{50}$, DBP_{50}), diastolic minimum ($CoPP_{min}$, DBP_{min}), and diastolic mean ($CoPP_{mean}$, DBP_{mean}). Inter-method agreement was assessed by Bland-Altman analysis and Cohen's kappa statistic. Logistic regression was used to evaluate performance in discriminating return of spontaneous circulation (ROSC) and to identify optimal thresholds.

Results: Relative to $CoPP_{65}$, measurements by $CoPP_{50}$, $CoPP_{min}$, and $CoPP_{mean}$ were within 5 mmHg limits of agreement (LOA) in 97%, 64%, and 99% of instances with kappa 0.88, 0.76, and 0.91, respectively. Relative to DBP_{65}, measurements by DBP_{50}, DBP_{min}, and DBP_{mean} were within 5 mmHg LOA in 98%, 71%, and 99% of instances with kappa 0.90, 0.80, and 0.91, respectively. The areas under the ROC curves (AUC) for $CoPP_{65}$, $CoPP_{50}$, $CoPP_{min}$, and $CoPP_{mean}$ were 0.777, 0.792, 0.787, and 0.788, and optimal thresholds to discriminate ROSC were 15.3, 15.8, 12.3, and 14.7 mmHg, respectively. The AUCs for DBP_{65}, DBP_{50}, DBP_{min}, and DBP_{mean} were 0.813, 0.827, 0.833, and 0.826, and optimal thresholds to discriminate ROSC were 28.6, 27.3, 26.2, and 29.7 mmHg, respectively.

Conclusions: During piglet CPR, measurements by late diastole, mid-diastole, and diastolic mean strongly agreed, whereas those at diastolic minimum were more discrepant. All methods performed similarly in discrimination of ROSC.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Coronary perfusion pressure, Diastolic blood pressure, Pediatrics

Introduction

Cardiopulmonary resuscitation (CPR) is performed for more than 15,000 children suffering in-hospital cardiac arrest annually in the United States.[1,2] Survival to hospital discharge with favorable neurologic outcome is achieved in less than half of these children.[1] Effective CPR is dependent on attaining adequate myocardial perfusion, the magnitude of which is determined by the coronary perfusion pressure (CoPP).[3–5] During CPR, CoPP is defined as the difference between aortic (AoP) and right atrial (RAP) pressures during the decompression phase of a chest compression, referred to as "diastole" for simplicity.[6,7] Prior studies have demonstrated the importance of CoPP as a major determinant in achieving return of

* Corresponding author at: The Children's Hospital of Philadelphia, 3400 Civic Center Boulevard, 9NW59, Philadelphia, PA 19104, USA.
E-mail address: morganr1@chop.edu (R.W. Morgan).

[1] These co-authors contributed equally to this manuscript.

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spontaneous circulation (ROSC) and survival to hospital discharge.[8,9] As such, recent resuscitation guidelines endorse physiologic monitoring of metrics including CoPP and its driving force, diastolic blood pressure (DBP), to assess and guide CPR quality.[10,11] In prospective studies of animal models of cardiac arrest, CPR titrated to CoPP and DBP improves both short term survival and neurologic outcomes compared with standard CPR.[3,12–14]

Titrating resuscitation efforts to CoPP or DBP requires continual and accurate identification and calculation of these parameters. Given that myocardial perfusion during CPR varies throughout the duration of diastole, the measurement of these metrics may vary depending on the moment of sampling during diastole.[7,15,16] Consequently, there are several different calculation methods for DBP and CoPP.[17] The degree of agreement between these calculation methods and their respective performance during CPR as predictors of ROSC are not well established. To address these knowledge gaps, this study was designed to evaluate the intermethod agreement between existing CoPP and DBP calculation methods and to assess the performance of these metrics in discriminating between subjects with versus without ROSC in an animal model of pediatric in-hospital cardiac arrest.

Methods

Study design and data sources

This was a retrospective analytic study of data from laboratory experiments utilizing porcine models of pediatric in-hospital cardiac arrest undergoing manual CPR. To assure a pediatric model, analysis was narrowed to experiments with 1–2-month-old (∼10 kg) swine. Comprehensive laboratory records were reviewed and hemodynamic recordings from all animals were examined for completeness.

Experimental protocols and data collection

The Children's Hospital of Philadelphia Institutional Animal Care and Use Committee approved all experimental protocols, which were conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Comprehensive descriptions of animal preparation and anesthetic and surgical methods are available in previous publications.[13,14,18,19] In brief, healthy swine were anesthetized and mechanically ventilated with a mixture of room air, oxygen, and isoflurane. High-fidelity, solid-state, micromanometer-tipped catheters (MPC0500, Millar Instruments) were advanced such that the aortic and central venous transducers terminated in the descending thoracic aorta and right atrium, respectively. Prior to and during the experimental protocol, the electrocardiograph, AoP, RAP, pulse oximetry, and end-tidal carbon dioxide ($ETCO_2$) waveforms were displayed and recorded at 1000 Hz (PowerLab, ADInstruments, Inc.). For subsequent analysis, data streams were downsampled to 100 Hz by block averaging.

Pre-experimental normal saline was administered to replace overnight fasting fluid deficits and normalize central venous pressure. In all protocols, a seven-minute period of asphyxia was induced by clamping the endotracheal tube prior to induction of ventricular fibrillation.

After the asphyxial period and induction of ventricular fibrillation, one of three types of resuscitation were performed, namely standard CPR with guideline-based chest compression depths and epinephrine dosing (depth-guided CPR; DG- CPR), hemodynamic directed CPR (HD-CPR), and noninvasive optical neuromonitoring CPR (NOM-CPR). In all animals, chest compressions and vasopressor therapy were initiated according to one of the three resuscitation protocols, described below:

1. DG-CPR: The target chest compression depth was 1/3 of the anterior-posterior chest diameter, consistent with current guidelines.[10] This target depth was determined based on the pre-experimental chest diameter prior to chest molding. Chest compression depth was visualized and guided in real time using a CPR quality monitoring defibrillator (Zoll R-Series, Zoll Medical, Chelmsford, MA). Epinephrine was dosed every four minutes beginning two minutes into CPR.
2. HD-CPR: Chest compression depth was titrated to meet systolic blood pressure (SBP) targets (80 – 100 mmHg depending on study protocol) and vasopressors were titrated to maintain at least a minimum CoPP or DBP threshold target (CoPP 20 mmHg or DBP 30 or 40 mmHg, depending on study protocol). Vasopressors were dosed as frequently as every one minute in a rotation of epinephrine, epinephrine, and vasopressin to maintain or exceed the threshold CoPP or DBP.
3. NOM-CPR: Cerebral tissue oxyhemoglobin concentration, [HbO_2], was continuously monitored using a noninvasive frequency-domain diffuse optical spectroscopy sensor. Depth of chest compressions and administration of epinephrine starting at two minutes of CPR were titrated to achieve a goal of at least a 1.3 μmol/L increase in [HbO_2] from the value measured at one minute of CPR.[18]

In all protocols, epinephrine dosing was 0.02 mg/kg and, when used, vasopressin dosing was 0.4 U/kg. The first defibrillation attempt was performed either 10 or 15 min into CPR. In addition to guidance from the CPR quality monitoring defibrillator or physiologic waveforms, chest compression rate was guided with a metronome set to a rate of 100 per minute. Further descriptions of these protocols are available in previous publications.[13,14,18,19]

Inclusion criteria, exclusion criteria, and definition of ROSC

All experiments within a seven-year period using an asphyxial cardiac arrest model in 1–2-month-old swine undergoing manual CPR were considered. Any subjects without complete hemodynamic recordings or anesthetic records from the resuscitation period were excluded. Moreover, subjects with artifactual AoP or RAP waveforms reported in laboratory records were excluded. The primary outcome of ROSC was defined as return of an organized electrocardiographic rhythm generating a SBP > 50 mmHg sustained for more than 60 s following the first defibrillation attempt. Physiologic data beginning two minutes into CPR through the first defibrillation attempt were included, and the first two minutes were excluded to avoid including the initial period of chest molding. The outcome of the first defibrillation attempt alone was evaluated for each animal to mitigate the confounding effects of multiple outcomes within a single subject.

Calculation methods

Four previously described calculation methods for DBP and CoPP were evaluated.[17] Although other calculation methods have been described, because anterograde coronary blood flow occurs predominantly during the relaxation phase of chest compressions, the methods included in this study were limited to those considering diastole alone, omitting calculation methods that included systole.[7,15,16] All methods are described below with visual depictions shown in

Fig. 1. In all methods, CoPP was calculated as the difference between AoP and RAP whereas DBP was the correlate considering AoP alone without the contribution of RAP. While the term "diastole" implies an organized myocardial cycle, the methods herein retain this nomenclature for simplicity and for consistency with the majority of resuscitation science literature and CPR guidelines.[4,5,10]

1. Mid-diastole (DBP_{50}, $CoPP_{50}$): Mid-diastole was defined as the moment 50% between adjacent systolic peaks. Given the rapid sampling frequency of the pressure transducers used in these experiments, the average of a 10% time range was taken to avoid overvaluing a singular data point. Thus, DBP_{50} was the average AoP and, similarly, $CoPP_{50}$ was the average difference between AoP and RAP of all data points measured 45–55% between systolic peaks.
2. Late diastole (DBP_{65}, $CoPP_{65}$): Late diastole was defined as the moment 65% between adjacent systolic peaks. Similar to mid-diastole above, an average of a 10% time range was taken between 60–70% to define DBP_{65} and $CoPP_{65}$.[5,20,21] Some authorities have described measuring CoPP at the end of the relaxation phase, prior to the onset of the next systolic upstroke.[17] We chose to define late diastole 65% between systolic peaks for methodologic standardization in the definition of the moment of sampling, to avoid inadvertently capturing the subsequent systolic upstroke, and to remain consistent with other studies.[5,20,21]
3. Diastolic minimum (DBP_{min}, $CoPP_{min}$): DBP_{min} was defined as the minimum AoP during the peak-to-peak compression cycle. The difference between DBP_{min} and the time-coincident RAP was defined as $CoPP_{min}$.
4. Diastolic mean (DBP_{mean}, $CoPP_{mean}$): To calculate the average pressures throughout diastole, the period of diastole itself required definition. To do so, an *a priori* threshold was set as 20% of the pulse pressure, calculated as the difference between the preceding SBP and mid-diastolic pressure. This threshold was recalculated for each compression. Diastole was defined as the period during which the aortic pressure fell below this threshold. The AoP and difference between AoP and RAP were averaged during this interval to arrive at DBP_{mean} and $CoPP_{mean}$, respectively.

Each chest compression was individually assessed according to each method. The entire CPR period prior to the first defibrillation

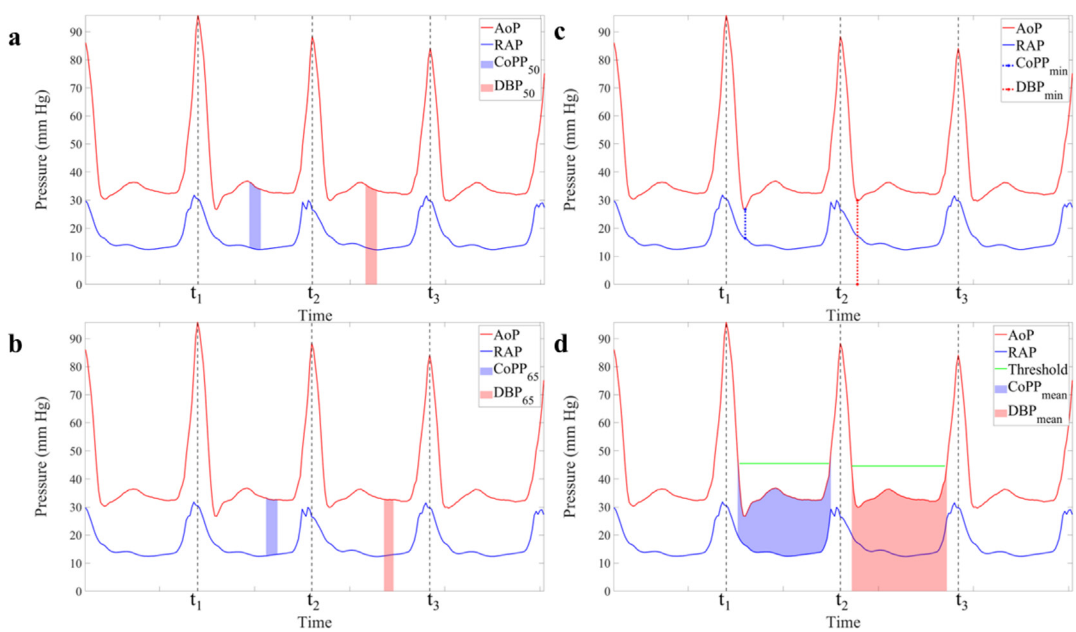

Fig. 1 – Calculation methods. As shown in these sample waveforms, each chest compression was defined by the peak AoP occurring at times t_1, t_2, t_3. Each calculation was performed as follows: a. Mid-diastole: $CoPP_{50}$, shown in blue shading, is the average difference between AoP and RAP during the interval between $t_i + 0.45\ (t_{i+1} - t_i)$ and $t_i + 0.55\ (t_{i+1} - t_i)$. DBP_{50}, shown in red shading, is the average AoP during the same interval. b. Late diastole: $CoPP_{65}$, shown in blue shading, is the average difference between AoP and RAP during the interval between $t_i + 0.6\ (t_{i+1} - t_i)$ and $t_i + 0.7\ (t_{i+1} - t_i)$. DBP_{65}, shown in red shading, is the average AoP during the same interval. c. Diastolic minimum: $CoPP_{min}$, shown as the blue vertical line, is the difference between AoP and RAP at the point of minimum AoP during a given compression cycle. DBP_{min}, shown as the red vertical line, is the minimum AoP during a given compression cycle. d. Diastolic mean: To define the diastolic period, an *a priori* threshold was set as 20% of the pulse pressure calculated as the difference between the preceding SBP and mid-diastolic pressure. The green line shows this threshold recalculated for each compression. Diastole was defined as the period during which the aortic pressure fell below this threshold. Shown in blue shading, $CoPP_{mean}$ is the average difference between AoP and RAP during this diastolic period. Shown in red shading, DBP_{mean} is the average AoP during this same interval. *Definition of abbreviations:* AoP – aortic pressure; RAP – right atrial pressure; CoPP – coronary perfusion pressure; DBP – diastolic blood pressure. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

attempt was used for physiologic calculations regardless of vasopressor timing. Intermethod agreement was evaluated by averaging metrics in 15-second epochs whereas performance in discriminating the outcome of ROSC was assessed by averaging methods over the entire CPR period.

Statistical analysis

Intermethod agreement

To assess the intermethod agreement between the four calculation methods, Bland-Altman plots were constructed, depicting the difference as a function of the mean of two corresponding measurements.[22,23] Each of mid-diastole, diastolic minimum, and diastolic mean were compared against late diastole. Late diastole was used as the reference method, consistent with prior publications.[5,20,21] This analysis was performed using 15-second epoch-level average data. *A priori* limits of agreement (LOA) were set as ± 5 mmHg, within which measurement differences were considered unlikely to be clinically significant. These LOA are consistent with prior publications of minimum clinically important differences in blood pressure readings because they are likely clinically relevant and reasonably discernable for bedside clinicians during CPR.[4,20,24,25] The degree of agreement was assessed with the proportion of measurement differences within these LOA.[22,23] In a *post hoc* evaluation, this Bland-Altman analysis was repeated in each of the three resuscitation protocols individually.

The above approach evaluates paired measurements for interchangeability within LOA. To assess the agreement upon nominal classifications of CPR performance, Cohen's Kappa statistic was calculated.[26] Here, each measurement was dichotomized according to current clinical threshold targets of CoPP $\geq$ 20 mmHg or DBP $\geq$ 30 mmHg.[4,5,10,11] The kappa statistics of agreement of CPR classification were calculated according to late diastole compared to each of mid-diastole, diastolic minimum, and diastolic mean to determine the degree to which methods agreed regarding whether CoPP and DBP met clinical thresholds.

Logistic regression

To evaluate each calculation method as a predictor of ROSC, logistic regression models were constructed. Each of the four measurement approaches was used as a predictor variable to discriminate the binary outcome of ROSC. The areas under the receiver operator characteristics (ROC) curves (AUC) were compared by the DeLong test to evaluate for statistical significance. Optimal statistical operating thresholds for each method were determined on the ROC curves by minimized Euclidean distance from sensitivity and specificity of 100%.

Results

Study cohort

Of the 227 subjects that met initial inclusion criteria, 23 were excluded, yielding a final study cohort of 204 subjects from 11 experimental protocols over a five-year period as shown in Fig. 2. As shown in Table 1, the cohort consisted of 67% females, aged 48.2 ± 7.0 days, weighing 10.4 ± 0.9 kg, and 50.7 ± 5.5 cm in length. In total, 198,960 chest compressions were analyzed, and ROSC was achieved in 68.1% of animals. The distribution of resuscitation types was as follows: 36 DG-CPR, 153 HD-CPR, and 15 NOM-CPR. Table 2 shows the CPR characteristics, including the compression depth and rate, number of epinephrine and vasopressin doses received, and CoPP and DBP values by each of the calculation methods.

Intermethod agreement

Fig. 3 demonstrates the Bland-Altman plots comparing each of mid-diastole, diastolic minimum, and diastolic mean to the reference method of late diastole for both CoPP and DBP. Relative to $CoPP_{65}$, measurements by $CoPP_{50}$, $CoPP_{min}$, and $CoPP_{mean}$ were within 5 mmHg LOA in 97%, 64%, and 99% of instances, respectively. When CPR performance was dichotomized by the threshold target CoPP $\geq$ 20 mmHg, the kappa statistics of agreement for $CoPP_{65}$ compared to each of $CoPP_{50}$, $CoPP_{min}$, and $CoPP_{mean}$ were 0.88, 0.76, and 0.91, respectively. Relative to DBP_{65}, measurements by DBP_{50}, DBP_{min}, and DBP_{mean} were within 5 mmHg LOA in 98%, 71%, and 99% of instances, respectively. When CPR performance was dichotomized by the threshold target DBP $\geq$ 30 mmHg, the kappa statistics of agreement for DBP_{65} compared to each of DBP_{50}, DBP_{min}, and DBP_{mean} were 0.90, 0.80, and 0.91, respectively. In the *post hoc* Bland-Altman analysis of each of the three resuscitation protocols individually, measurements by $CoPP_{50}$, $CoPP_{min}$, and $CoPP_{mean}$ were within 5 mmHg LOA of those by $CoPP_{65}$ in 94–98%, 61–65%, and 98–99% of instances, respectively. Similarly, measurements by DBP_{50}, DBP_{min}, and DBP_{mean}

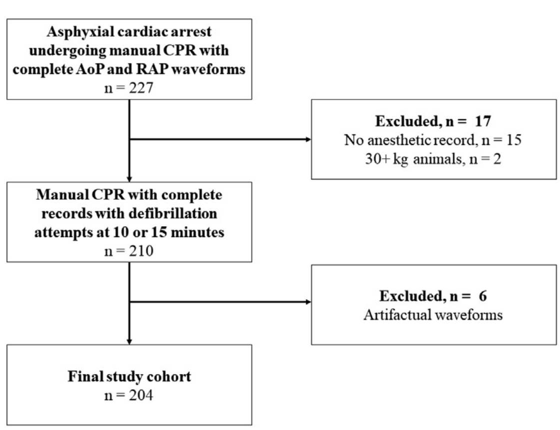

Fig. 2 – Study population enrollment. *Definitions of abbreviations:* CPR – cardiopulmonary resuscitation; AoP – aortic pressure; RAP – right atrial pressure.

Table 1 – Cohort characteristics.

Parameter	Value
Subjects (N)	204
Compressions (N)	198,960
ROSC (%)	68.1
Sex (% F)	67.2
Age (d)	48.2 ± 7.0
Weight (kg)	10.4 ± 0.9
Length (cm)	50.7 ± 5.5
CPR type (N)	
DG-CPR	36
HD-CPR	153
NOM-CPR	15

Definitions of abbreviations: ROSC – return of spontaneous circulation; CPR – cardiopulmonary resuscitation; DG-CPR – depth-guided CPR; HD-CPR – hemodynamic directed CPR; NOM-CPR – noninvasive optical neuromonitoring CPR.

Table 2 – CPR characteristics. Data are presented as median [interquartile range]. Data are derived from the full CPR period prior to the first defibrillation attempt, which occurred at 10 or 15 min of CPR, depending on study protocol.

Parameter	Value
Compression	
Depth (cm)	37.4 [33.7, 42.5]
Rate (per min)	99.8 [99.4, 100.4]
Vasoactive Doses	
Epinephrine	4 [2, 6]
Vasopressin	1 [0, 2]
CoPP (mmHg)	
$CoPP_{50}$	20.2 [13.3, 25.4]
$CoPP_{65}$	19.3 [13.2, 24.0]
$CoPP_{min}$	15.1 [8.0, 20.6]
$CoPP_{mean}$	19.4 [12.3, 24.4]
DBP (mmHg)	
DBP_{50}	32.3 [26.5, 37.6]
DBP_{65}	31.9 [26.2, 36.8]
DBP_{min}	28.5 [20.5, 34.2]
DBP_{mean}	32.9 [26.8, 38.2]

Definitions of abbreviations: CoPP – coronary perfusion pressure; DBP – diastolic blood pressure.

were within 5 mmHg LOA of those by DBP_{65} in 97–98%, 66–73%, and 97–99% of instances, respectively.

ROSC discrimination

Table 3 displays the AUC for the ROC corresponding to each predictor variable along with the ideal statistical discriminator thresholds determined by the Euclidean distance method with the associated sensitivity and specificity. Comparing CoPP and DBP methods, the AUC of DBP_{min} exceeded that of $CoPP_{min}$ ($p < 0.05$). Within CoPP methods, the AUCs of $CoPP_{50}$ and $CoPP_{mean}$ exceeded that of $CoPP_{65}$ ($p < 0.05$ for both). Within DBP methods, the AUCs of DBP_{50} and DBP_{mean} exceeded that of DBP_{65} ($p < 0.05$ for both). Optimal operating thresholds for CoPP and DBP methods ranged from 12.3 to 15.8 and 26.2 to 29.7 mmHg, respectively. This represents a relative range of 28% and 13% for CoPP and DBP, respectively.

Discussion

This retrospective analytic study of CPR waveforms in a swine model of pediatric asphyxia-associated cardiac arrest is, to the authors' knowledge, the first large-scale analysis of DBP and CoPP measurements by established calculation methods. We identified strong agreement between measurements obtained at mid-diastole, late diastole, and diastolic mean within *a priori* 5 mmHg LOA, but characterized considerable heterogeneity of measurements obtained at diastolic minimum. Further, we demonstrated that all methods performed similarly as discriminators of ROSC. However, the optimal operating threshold of the diastolic minimum approach varied substantially from the remaining methods. Moreover, these translational laboratory data suggest the more commonly clinically available DBP measurements discriminated ROSC at least as strongly as the CoPP values.

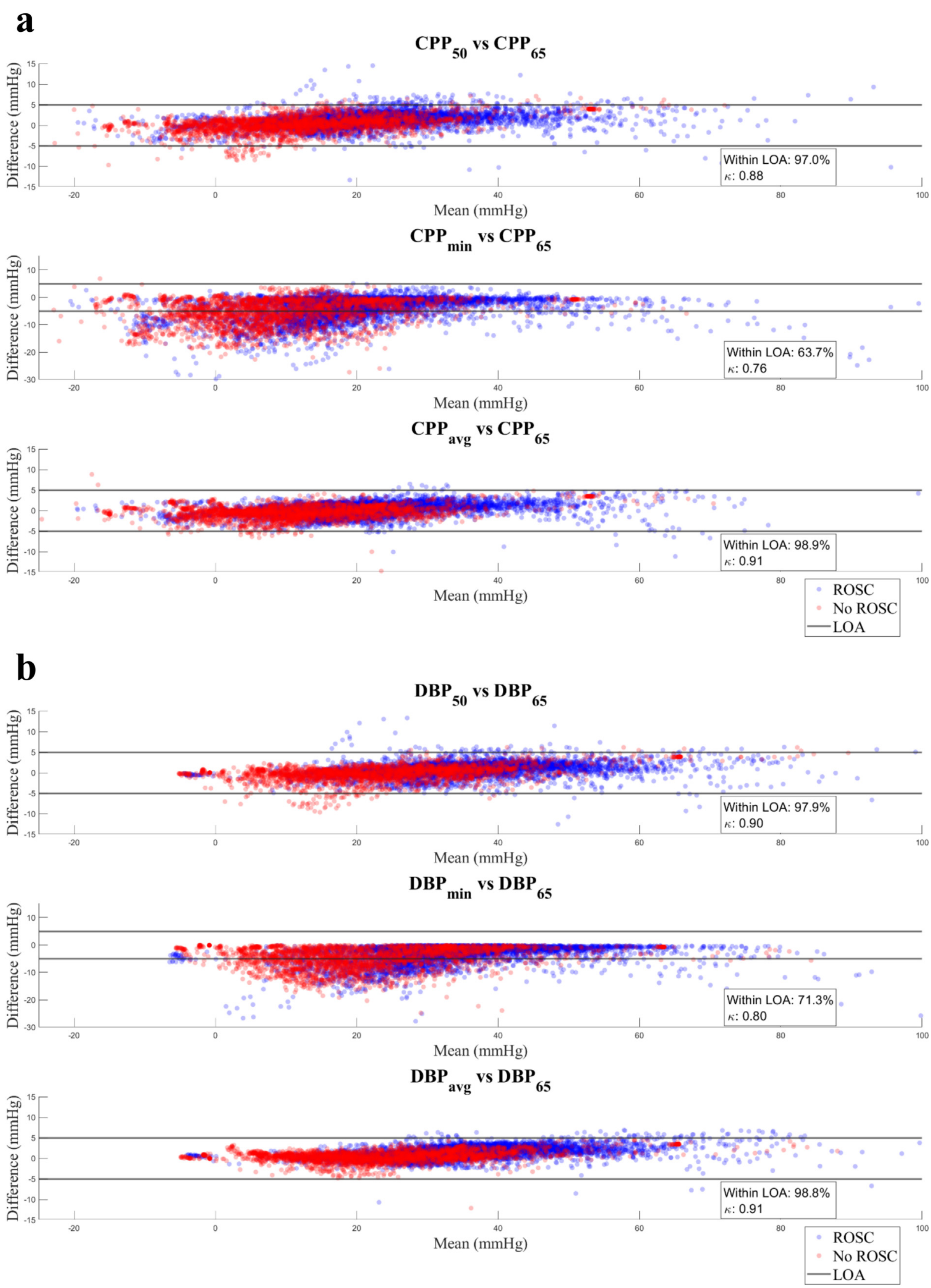
a
CPP50 vs CPP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 97.0%
κ: 0.88
CPPmin vs CPP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 63.7%
κ: 0.76
CPPavg vs CPP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 98.9%
κ: 0.91
ROSC
No ROSC
LOA
b
DBP50 vs DBP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 97.9%
κ: 0.90
DBPmin vs DBP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 71.3%
κ: 0.80
DBPavg vs DBP65
Difference (mmHg)
Mean (mmHg)
Within LOA: 98.8%
κ: 0.91
ROSC
No ROSC
LOA

Table 3 – Receiver operator characteristics curve properties for classification of subjects with versus without ROSC. * denotes methods with AUC greater than that of late diastole in its respective category by the DeLong Test ($p < 0.05$). Thresholds in units of mmHg with their associated sensitivity and specificity for the primary outcome of ROSC were determined by optimized Euclidean distance from sensitivity and specificity of 100%.

	AUC	Threshold (mmHg)	Sensitivity (%)	Specificity (%)	p
CoPP Methods					
$CoPP_{65}$	0.777	15.3	82	72	–
$CoPP_{50}$	0.792	15.8	82	72	0.01*
$CoPP_{min}$	0.787	12.3	77	72	0.48
$CoPP_{mean}$	0.788	14.7	83	71	0.04*
DBP Methods					
DBP_{65}	0.813	28.6	86	69	–
DBP_{50}	0.827	27.3	90	68	0.01*
DBP_{min}	0.833	26.2	78	77	0.07
DBP_{mean}	0.826	29.7	86	71	< 0.01*

Definitions of abbreviations: AUC – area under the curve; CoPP – coronary perfusion pressure; DBP – diastolic blood pressure; ROSC – return of spontaneous circulation.

Multiple factors influence AoP waveform characteristics, including systemic vascular resistance, arterial compliance, and ventriculoarterial coupling. As a result, the aortic pressure waveform is inherently dynamic, reflecting the interaction between these variables. Furthermore, in the context of manual CPR, stroke volume is not fixed as it varies with chest compression depth, rate, and recoil. The product of the systemic vascular resistance and arterial compliance is the resistance-compliance time constant, which dictates the exponential decay of the arterial pressure during diastole.[27] As a result, AoP is not constant through diastole; rather, it is a function of time. Therefore, the measurements of DBP and CoPP depend on the moment of sampling within the diastolic period. Our data demonstrate the strong concordance amongst values obtained at mid-diastole, at late diastole, and by diastolic mean with greater than 97% of paired measurements agreeing within 5 mmHg LOA. Furthermore, the kappa statistics between these methods when dichotomizing CPR performance by current clinical threshold targets approached 0.9. As such, these calculation methods can be considered nearly physiologically equivalent. Nevertheless, measurements at diastolic minimum displayed significant variability from the remaining methods with approximately 30% of measurements outlying the LOA, as shown by the broad Bland-Altman distribution in Fig. 3. As a result of this degree of variability, the kappa statistics weakened to less than 0.8 when comparing the diastolic minimum to the remaining methods.

All CoPP and DBP calculation methods performed similarly as statistical discriminators ROSC. There were, however, notable nuances. The AUCs of late diastole underperformed the remainder, though the magnitudes of the AUC differences were nominally small and were unlikely physiologically or clinically relevant. Interestingly, DBP measurements discriminated ROSC better than did CoPP measurements, though the differences did not consistently achieve statistical significance. We initially hypothesized that CoPP would better discriminate ROSC than DBP alone, as CoPP accounts for both the driving and opposing pressures to myocardial perfusion. However, our data suggest DBP performs at least as well as CoPP as a predictor of ROSC. Further studies are needed to elucidate the mathematical and clinical significance of the possible superiority of using DBP during CPR compared with CoPP.

None of these existing calculation methods account for the contribution of diastolic time to coronary perfusion. Whereas existing CoPP and DBP calculation methods provide instantaneous measurements, coronary blood flow occurs throughout the entire duration of diastole.[7,15,16] We speculate that the duration of diastole impacts myocardial perfusion and the ability to achieve ROSC in addition to the driving pressures of CoPP and DBP. Further work

Fig. 3 – Bland-Altman plots. Each calculation method was compared to late diastole. Each data point represents a 15-second epoch of averaged measures by both methods, plotted as the mean versus the difference of the paired measurements. Blue data points are epochs corresponding to animals that achieved ROSC, whereas red data points are epochs corresponding to animals that did not achieve ROSC. Solid black lines are the limits of agreement (LOA) of ± 5 mmHg. a. CoPP methods compared to $CoPP_{65}$ (top to bottom): $CoPP_{50}$ – within LOA: 97.0%, kappa (j): 0.88. $CoPP_{min}$ – within LOA: 63.7%, j: 0.76. $CoPP_{mean}$ – within LOA: 98.9%, j – 0.91. b. DBP methods compared to DBP_{65} (top to bottom): DBP_{50} – within LOA: 97.9%, j – 0.90. DBP_{min} – within LOA: 71.3%, j – 0.80. DBP_{mean} – within LOA: 98.8%, j – 0.91. *Definitions of abbreviations:* CoPP – coronary perfusion pressure; DBP – diastolic blood pressure; LOA – limits of agreement; ROSC – return of spontaneous circulation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

is necessary to evaluate the effects of diastolic time during CPR on outcomes.

As a result of the measurement discrepancies between methods, the optimal discriminator thresholds derived from the logistic regression models produced varying results. Whereas the optimal operating threshold by $CoPP_{min}$ was 12.3 mmHg, that of $CoPP_{50}$ was 15.8 mmHg, a 3.5 mmHg absolute difference and 28% relative difference. Similarly, the DBP_{min} threshold differed by as much as 13% from the other methods. This illustrates the challenges of comparing values reported across research studies without specifying the calculation approach, as the method itself may account for some of the differences. Moreover, the proprietary algorithms employed by commercially available bedside monitoring devices to determine and display DBP remain unpublished. This limits the ability to translate target thresholds derived from research studies to clinical care. The measurement incongruencies between methods, particularly considering the minimum method, may affect interpretation of CPR performance quality relative to published clinical targets and may, in turn, impact decision-making during resuscitation efforts at the bedside.[10,11] With ongoing efforts to optimize CPR quality at the bedside using these physiologic parameters, authors and bedside monitoring companies should precisely document their specific calculation methods. When informed by future robust translational and clinical studies, the resuscitation science community should prioritize standardization of CoPP and DBP calculation methods, as well as other common data elements.

Limitations

This study has notable limitations to its generalizability. This study is a *post hoc* analysis of previously performed laboratory-based studies, and as such *a priori* sample size calculations were not performed. Most of the experiments included in this study used variable, physiology-directed vasoactive dosing and real-time chest compression depth titration. As a result, this analysis did not evaluate the complexities of the vasoactive pharmacokinetics and pharmacodynamics that may affect the behavior of aortic and right atrial pressures during the decompression phase of CPR. Furthermore, the pressure transduction systems used clinically are more susceptible to noise than the high-fidelity manometers used in the laboratory experiments included in this study. Thus, clinically derived values may have more intermethod disparities and, as a result, may perform differently as predictors of ROSC than in this study.

Conclusions

In this retrospective analytic study of CPR waveforms in a swine model of pediatric asphyxia-associated cardiac arrest, CoPP and DBP calculations at mid-diastole, late diastole, and by diastolic mean produced physiologically similar measurements. Conversely, the measurements and classification of CPR performance by the diastolic minimum approach differed somewhat from the remaining techniques. Despite these measurement discrepancies, all performed similarly as predictors of ROSC. These data establish the intermethod agreement between four existing CoPP and DBP calculation methods and the performance of these metrics in discriminating between animals with versus without ROSC.

Author contributions

JCZ, TK, MWK, NJW, MFK, HAG, LEVS, RWR, RMS, RAB, TJK, and RWM contributed to study conception and design. JCZ, MWK, NJW, and RWM contributed to the acquisition of data. All authors contributed to the analysis and/or interpretation of data. JCZ drafted the manuscript. All authors critically revised the manuscript. All authors have approved the final version of the manuscript for publication.

Credit authorship contribution statement

Jeremy C. Zuckerberg: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Tiffany Ko:** Writing – review & editing, Methodology, Conceptualization. **M. Katie Weeks:** Writing – review & editing, Methodology, Conceptualization. **Nicholas J. Widmann:** Writing – review & editing, Methodology, Conceptualization. **Martha F. Kienzle:** Writing – review & editing, Methodology, Conceptualization. **Hunter A. Gaudio:** Writing – review & editing, Methodology. **Luiz Eduardo V. Silva:** Writing – review & editing, Methodology, Conceptualization. **Ron W. Reeder:** Writing – review & editing, Methodology, Conceptualization. **Robert M. Sutton:** Writing – review & editing, Methodology, Conceptualization. **Robert A. Berg:** Writing – review & editing, Methodology, Conceptualization. **Todd J. Kilbaugh:** Writing – review & editing, Methodology, Conceptualization. **Ryan W. Morgan:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author details

[a]Department of Anesthesiology and Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, PA, USA [b]Department of Anesthesiology and Critical Care Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA [c]Resuscitation Science Center, Children's Hospital of Philadelphia, Philadelphia, PA, USA [d]Department of Biomedical and Health Informatics, Children's Hospital of Philadelphia, Philadelphia, PA, USA [e]Division of Pediatric Critical Care Medicine, Department of Pediatrics, University of Utah, Salt Lake City, UT, USA

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