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Clinical paper

Chest compression rates and pediatric in-hospital cardiac arrest survival outcomes☆

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A B S T R A C T

Aim: The primary aim of this study was to evaluate the association between chest compression rates and 1) arterial blood pressure and 2) survival outcomes during pediatric in-hospital cardiopulmonary resuscitation (CPR).

Methods: Prospective observational study of children ≥37 weeks gestation and < 19 years old who received CPR in an intensive care unit (ICU) as part of the Pediatric Intensive Care Unit Quality of CPR Study (PICqCPR) of the Collaborative Pediatric Critical Care Research Network (CPCCRN). Arterial blood pressure and compression rate were determined from manually extracted arterial line waveform data during the first 10 min of CPR. The primary outcome was survival to hospital discharge. Modified Poisson regression models assessed the association between rate categories (80– < 100, 100–120 [Guidelines], > 120–140, > 140) and outcomes.

Results: Compression rate data were available for 164 patients. More than half (98/164; 60%) were < 1 year old. Return of circulation was achieved in 148/164 (90%); survival to hospital discharge in 77/164 (47%). Percentage of events with average rate within Guidelines was 32.9%. Compared to Guidelines, higher rate categories were associated with lower systolic blood pressures (> 120–140, p = 0.010; > 140, p = 0.077), but not survival. A rate between 80- < 100 per minute was associated with a higher rate of survival to hospital discharge (aRR 1.92, CI95 1.13, 3.29, p = 0.017) and survival with favorable neurological outcome (aRR 2.12, CI95 1.09, 4.13, p = 0.027) compared to Guidelines.

Conclusion: Non-compliance with compression rate Guidelines was common in this multicenter cohort. Among ICU patients, slightly lower rates were associated with improved outcomes compared to Guidelines.

Introduction

Thousands of hospitalized children are treated with cardiopulmonary resuscitation (CPR) for a cardiac arrest each year in the United States [1]. Although survival rates have been improving over the last 20 years, still more than half of these children do not live to hospital discharge [2]. Of those who survive, neurological morbidity is common [1].

CPR quality has been implicated as a modifiable risk factor to improve survival from cardiac arrest [3–8]. Several large adult studies have demonstrated that achieving evidence-based targets for chest compression rate [4] and depth [8], release velocity (i.e., recoil between compressions) [9], and chest compression fraction [5,6] (i.e., percentage of time that compressions are provided during arrest) improves survival. Unfortunately, most of the corresponding pediatric data has been collected from out-of-hospital resuscitations [10] or from single center studies [3,11–14], and may not be generalizable. Thus, larger prospective pediatric studies that can evaluate the association between CPR quality metrics and outcomes are necessary.

To that end, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) [15] Pediatric Intensive Care Unit Quality of CPR (PICqCPR) [16] study provides a unique opportunity to evaluate chest compression rates across several pediatric institutions. This study prospectively collected data on pediatric cardiac arrests that occurred in the network ICUs over a three-year period. Using this dataset, the objectives of this investigation were to 1) quantitatively describe compression rates during pediatric cardiac arrest in a multi-institutional collaborative, 2) describe variability in compression rates across the institutions, and 3) associate compression rate with both arterial blood pressure and survival outcomes.

Methods

Setting and design

CPCCRN is a network of pediatric institutions that conducts investigations related to pediatric critical care practice in their pediatric and pediatric cardiac ICUs [15]. The clinical sites and the data coordinating center (DCC) supporting the Network have been funded by the National Institute of Child Health and Human Development since 2004. Further details on the Network can be found at https://www.cpccrn.org.

Between July 2013 and June 2016, CPCCRN conducted the PICqCPR Study to evaluate the association between invasively monitored arterial blood pressures during pediatric CPR and cardiac arrest survival outcomes [16]. This study represents a secondary observational analysis of this multi-center cohort study.

PICqCPR was approved with waiver of informed consent by the Institutional Review Board at each clinical site and the DCC. Data collected on subjects included Utstein-style standardized cardiac arrest and CPR data [17], with assessments of neurological outcomes (pediatric cerebral performance category (PCPC) [18] and functional status scale (FSS) [19,20]) for pre-admission status and at hospital discharge. Because the primary objective of PICqCPR was to associate arterial blood pressure with outcomes, all patients had an arterial line in place at the time of the arrest. Blood pressures were extracted from arterial waveform printouts by manual digitization (PlotDigitizer; Version 2.0; Department of Physics, University of South Alabama). Please see previous publication for more details regarding the methods of the CPCCRN PICqCPR study [16].

Patient population

All children ≥37 weeks gestation and < 19 years old who received external chest compressions for at least 1 min and who had invasive arterial blood pressure monitoring prior to and during CPR in a CPCCRN ICU were eligible for inclusion. Subjects were excluded if the first compression was not captured on the waveform data or compression rate was unable to be determined (e.g., lack of arterial waveform due to line interruption for blood draw, flushing, pressure zeroing).

Measurements

The first 10 min of CPR data were collected for each event. For each one minute epoch, the following data points were extracted from the waveform data: 1) the number of compressions given; 2) the time (s) that compressions were not being performed (pause time); 3) total time (s) that rate could not be determined (e.g., missing data due to arterial line interruption); and 4) mean SBP and DBP (mmHg). Chest compression rate was defined as the "instantaneous" rate between adjacent compressions during periods of uninterrupted compression delivery by the following equation: 60/time between compressions (sec). Chest compression fraction (CCF; proportion of time compressions are performed during arrest) was defined as: 1 – (pause time/(60 – missing data time)). For each minute of CPR, an average of compression rate, CCF, systolic blood pressure, and diastolic blood pressure was calculated (minute-level average), and then for each event, the average of all

Table 1
Patient Characteristics by Survival to Hospital Discharge.

	Survival to hospital discharge			
	No (N = 87)	Yes (N = 77)	Overall (N = 164)	P-value
Age				0.038[a]
< 1 year	45 (51.7%)	53 (68.8%)	98 (59.8%)	
> =1 year	42 (48.3%)	24 (31.2%)	66 (40.2%)	
Sex				0.158[a]
Male	43 (49.4%)	47 (61.0%)	90 (54.9%)	
Female	44 (50.6%)	30 (39.0%)	74 (45.1%)	
Race				0.248[a]
Unknown or Not Reported	14 (16.1%)	23 (29.9%)	37 (22.6%)	
White	45 (51.7%)	37 (48.1%)	82 (50.0%)	
Black or African American	25 (28.7%)	12 (15.6%)	37 (22.6%)	
Other	3 (3.4%)	5 (6.5%)	8 (4.9%)	
Preexisting conditions				
Respiratory insufficiency	73 (83.9%)	59 (76.6%)	132 (80.5%)	0.324[a]
Hypotension	77 (88.5%)	51 (66.2%)	128 (78.0%)	< .001[a]
Congestive heart failure	12 (13.8%)	7 (9.1%)	19 (11.6%)	0.465[a]
Pneumonia	5 (5.7%)	8 (10.4%)	13 (7.9%)	0.386[a]
Sepsis	24 (27.6%)	20 (26.0%)	44 (26.8%)	0.861[a]
Renal insufficiency	16 (18.4%)	8 (10.4%)	24 (14.6%)	0.186[a]
Malignancy	4 (4.6%)	1 (1.3%)	5 (3.0%)	0.372[a]
Congenital heart disease	44 (50.6%)	55 (71.4%)	99 (60.4%)	0.007[a]
Illness Category				0.090[a]
Surgical cardiac	39 (44.8%)	49 (63.6%)	88 (53.7%)	
Medical cardiac	17 (19.5%)	8 (10.4%)	25 (15.2%)	
Surgical non-cardiac	8 (9.2%)	5 (6.5%)	13 (7.9%)	
Medical non-cardiac	23 (26.4%)	14 (18.2%)	37 (22.6%)	
Unknown	0 (0.0%)	1 (1.3%)	1 (0.6%)	
Initial cardiac rhythm				0.068[a]
Asystole/PEA	29 (33.3%)	19 (24.7%)	48 (29.3%)	
VF/VT	14 (16.1%)	5 (6.5%)	19 (11.6%)	
Bradycardia with pulses	43 (49.4%)	48 (62.3%)	91 (55.5%)	
Unknown	1 (1.1%)	5 (6.5%)	6 (3.7%)	
Baseline PCPC score				0.452[b]
1 – Normal	45 (51.7%)	32 (41.6%)	77 (47.0%)	
2 – Mild disability	21 (24.1%)	26 (33.8%)	47 (28.7%)	
3 – Moderate disability	10 (11.5%)	13 (16.9%)	23 (14.0%)	
4 – Severe disability	7 (8.0%)	6 (7.8%)	13 (7.9%)	
5 – Coma/vegetative state	4 (4.6%)	0 (0.0%)	4 (2.4%)	
Baseline total FSS	7.0 [6.0,11.0]	8.0 [6.0,11.0]	8.0 [6.0,11.0]	0.120[b]
Interventions in place				
Vascular access	83 (95.4%)	72 (93.5%)	155 (94.5%)	0.736[a]
Arterial catheter	87 (100.0%)	76 (98.7%)	163 (99.4%)	0.470[a]
Central venous catheter	76 (87.4%)	66 (85.7%)	142 (86.6%)	0.821[a]
Vasoactive infusion	75 (86.2%)	53 (68.8%)	128 (78.0%)	0.008[a]
Invasive mechanical ventilation	77 (88.5%)	57 (74.0%)	134 (81.7%)	0.025[a]
Immediate Cause				
Hypotension	61 (70.1%)	49 (63.6%)	110 (67.1%)	0.408[a]
Arrhythmia	17 (19.5%)	14 (18.2%)	31 (18.9%)	0.845[a]
Respiratory decompensation	38 (43.7%)	34 (44.2%)	72 (43.9%)	1.000[a]
CPR Time Category				0.337[a]
Weekday	51 (58.6%)	51 (66.2%)	102 (62.2%)	
Weeknight/Weekend	36 (41.4%)	26 (33.8%)	62 (37.8%)	
Duration of CPR (minutes)	17.5 [4.0,38.0]	5.0 [2.0,13.0]	8.0 [3.0,27.0]	< .001[b]
Epinephrine	78 (89.7%)	65 (84.4%)	143 (87.2%)	0.355[a]
Total number of epinephrine doses	3.0 [2.0,7.0]	2.0 [1.0,3.0]	3.0 [1.0,5.0]	< .001[b]
Calcium	50 (57.5%)	28 (36.4%)	78 (47.6%)	0.008[a]
Sodium bicarbonate	57 (65.5%)	36 (46.8%)	93 (56.7%)	0.018[a]

[a] Fisher's Exact Test is used for 2 × 2 tables. Categorical variables are summarized using n (%).
[b] The Wilcoxon rank-sum test is used for ordinal variables. Continuous variables are summarized using median [Q1,Q3].

the available epochs was calculated (event-level average). Interruptions in compression delivery were defined as any interruption in compression delivery > 1.5 s (i.e., a compression rate < 40). Compliance with American Heart Association (AHA) Guidelines was defined as a compression rate of 100–120 per minute [21]. Of note, CPR recording defibrillators were not commonly used in the Network at the time of this study. As such, other important CPR quality variables such as compression depth [11] and release velocity [9] were not able to be considered in the analysis.

Outcomes

The prospectively selected primary outcome was survival to hospital discharge of index events. Secondary outcomes included: 1) return of spontaneous circulation (ROSC) of all events; 2) diastolic blood pressure (mmHg); 3) systolic blood pressure (mmHg); and 4) survival with favorable neurological outcome (PCPC 1–3 or no worsening) [17,18] of index events.

Table 2
Compression Rate & Chest Compression Fraction by Survival to Hospital Discharge.

	Survival to Hospital Discharge			
	No	Yes	Overall	P-value
Event Average Compression Rate	124.4 [114.9,138.1]	127.1 [110.8,140.3]	125.6 [114.3,139.4]	0.774[b]
Percent of Events: Rate 100–120	39.1%	26.0%	32.9%	0.096[a]
Percent of Minutes: Rate 100–120	33.5%	31.2%	32.6%	0.396[c]
Event Average CCF	0.92 [0.84,0.97]	0.91 [0.84,0.96]	0.92 [0.84,0.97]	0.437[b]

[a] Fisher's exact test is used for comparison of categorical variables.
[b] The Wilcoxon rank-sum test is used for comparison of continuous variables. Continuous variables are summarized using median [Q1,Q3].
[c] The association between percent of minutes in guidelines and survival to hospital discharge was assessed using a modified Poisson model assuming an AR [1] correlation structure for minutes within an event.

Table 3
Multivariable Association Between Minute-Level Compression Rate and Blood Pressures.

	Diastolic blood pressure[c]		Systolic blood pressure[d]	
	Effect estimate (95% CI)	P-value	Effect estimate (95% CI)	P-value
Chest compression rate (per minute)[a]	−0.02 (−0.06, 0.03)	0.427	−0.17 (−0.27, −0.07)	< 0.001
Chest compression rate (per minute)[b]		0.148		0.083
80– < 100 (n = 57)	−1.33 (−3.53, 0.87)	0.237	2.55 (-4.57, 9.68)	0.483
100–120 (n = 323)	Reference		Reference	
> 120–140 (n = 350)	0.15 (−1.08, 1.38)	0.813	−4.07 (−7.17, −0.97)	0.010
> 140 (n = 204)	1.62 (−0.31, 3.56)	0.099	−4.57 (−9.63, 0.50)	0.077

[a] Chest compression rate is analyzed as a continuous predictor and an AR-1 correlation structure is assumed to control for minute-level correlations within events. In the continuous models, minutes of CPR with compression rates less than 100 are excluded because the linearity assumption was only satisfied for rates greater than or equal to 100.
[b] Chest compression rate is analyzed as a categorical predictor and an AR-1 correlation structure is assumed to control for minute-level correlations within events. Every minute is included in the categorical models.
[c] The DBP models adjust for vasopressor administration, fluid bolus, sex, CPR location (PICU/CICU), arrhythmia as an immediate cause, respiratory decompensation as an immediate cause, and age (< 1 year, > =1 year).
[d] The SBP models adjust for vasopressor administration, fluid bolus, initial cardiac rhythm, vascular access, non-invasive ventilation, respiratory decompensation as an immediate cause, and age (< 1 year, > –1 year).

Statistical analysis

Patient and event characteristics were summarized using frequencies and percentages or median and interquartile ranges (IQR). Differences in these characteristics between those who did and did not survive to discharge were examined using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables (Table 1). Minute-level averages were used to determine the association between arterial blood pressure and compression rate, while event-level averages were used for the survival outcome models. The reference group in all models was a rate of 100–120 per minute (Guideline recommendations) [21]. Guideline recommendation for CCF of 0.80 was also utilized [21,22]. In all models, compression rate was categorized into 4 groups: < 100; 100–120; > 120–140; and > 140 per minute. Modified Poisson regression models were used to calculate relative risks (RRs) of achieving the patient outcome of interest across rate categories (Table 4). Survival models were adjusted for age [23], initial cardiac rhythm [24], illness category [25], and time of CPR [26], which were specified a priori based on previously established associations with in-hospital cardiac arrest outcomes. Backward selection with an exit criterion of $p > 0.1$ was then used for inclusion of other candidate variables. For arterial blood pressures, mixed effects linear regression models were used with an AR-1 correlation structure to account for the correlation between minutes of an event (Table 3). Blood pressure models were adjusted for fluid bolus and vasopressor administration during arrest, and backward selection with an exit criterion of $p > 0.1$ was used to consider additional covariates. Site was considered as a potential confounder in all models due to known differences in survival rates across the clinical sites in the network [27]. A mixed effects linear regression model with site as the fixed effect and an AR-1 correlation structure for minutes within an event was used to determine if there was significant variability in the average minute-level compression rate between sites. Similarly, a modified Poisson regression model with an AR-1 correlation structure and site as a fixed effect was used to determine if site was associated with higher likelihood of a minute of CPR having an average rate within Guidelines. Analyses of survival used only index events, while blood pressure and ROSC analyses included all events. Relative risks are presented with their 95% confidence intervals (CIs). P-values are reported based on a 2-sided alternative and considered statistically significant when less than 0.05.

Results

Between July 2013 and June 2016, there were 244 index CPR events in patients who received at least 1 min of chest compressions and who had an arterial line in place at the time of the arrest making them eligible for inclusion in PICqCPR. Of these, 80 subjects were excluded due to inability to determine arterial diastolic blood pressure (n = 36) or inability to determine starts and stops in chest compressions (n = 44), leaving 164 (67%) patients in the analytical cohort. The range of events reported per site was 4–70. The subjects for this secondary analysis are the same 164 patients who were included in the main study. Please see Fig. 1 for more details.

Patient and index event characteristics are contained in Table 1. More than half of the patients (98/164; 60%) were < 1 year old and

Table 4
Multivariable Association of Recommended Chest Compression Rates with Outcomes.

	Adjusted Relative Risk of Outcome (95% CI)	P-value
ROSC[a]		
Rate in Guidelines		
Yes	Reference	
No	1.02 (0.83, 1.25)	0.876
Rate Category		
< 100	1.34 (0.98,1.82)	0.069
100–120 (Guidelines)	Reference	
> 120–140	0.92 (0.72, 1.18)	0.511
> 140	1.13 (0.89,1.43)	0.322
Survival to Hospital Discharge[b]		
Rate in Guidelines		
Yes	Reference	
No	1.27 (0.84, 1.92)	0.257
Rate Category		
< 100	1.92 (1.13, 3.29)	0.017
100–120 (Guidelines)	Reference	
> 120–140	1.15 (0.74, 1.80)	0.527
> 140	1.31 (0.79, 2.18)	0.293
Survival with Favorable Neuro[c]		
Rate in Guidelines	Reference	
Yes		
No	1.54 (0.96, 2.49)	0.246
Rate Category		
< 100	2.12 (1.09, 4.13)	0.027
100–120 (Guidelines)	Reference	
> 120–140	1.42 (0.85, 2.37)	0.177
> 140	1.62 (0.93, 2.82)	0.085

[a] Results are based on a modified Poisson model adjusting for age (< 1 year, > = 1 year), initial cardiac rhythm, illness category, time of CPR (night/weekend), baseline PCPC score, and vascular access. All CPR events are considered for this analysis.

[b] Results are based on a modified Poisson model adjusting for age (< 1 year, > = 1 year), initial cardiac rhythm, illness category, time of CPR (night/weekend), vasoactive infusion, and invasive mechanical ventilation. All index CPR events are considered for this analysis.

[c] Results are based on a modified Poisson model adjusting for age (< 1 year, > = 1 year), initial cardiac rhythm, illness category, time of CPR (night/weekend), and vasoactive infusion. All index CPR events are considered for this analysis.

more than half were also classified as cardiac surgical patients (88/164; 54%). Respiratory insufficiency (132/164; 80%), hypotension (128/164; 78%), and congenital heart disease (99/164; 60%) were the most common pre-existing conditions. Hypotension (110/164; 67%) and respiratory decompensation (72/164; 44%) were common immediate causes of arrest. Among the pre-arrest patient characteristics, pre-existing hypotension was associated with a significantly lower rate of survival to hospital discharge and congenital heart disease with a higher rate. Among the index event characteristics, lower survival rates were associated with vasoactive infusions and invasive mechanical ventilation in place at the time of event, longer CPR duration, number of epinephrine doses, and the administration of either calcium or sodium bicarbonate during CPR. The characteristics and outcomes of the 164 patients included in the main study, and in this secondary analysis, were similar to those excluded [16].

Outcomes are summarized in Fig. 1. Ninety percent of patients survived the event (68% with ROSC; 22% by extracorporeal life support during CPR (E-CPR)). Forty seven percent survived to hospital discharge and 43% survived to discharge with favorable neurologic outcome. Among the 77 patients surviving to discharge, 70 (91%) had favorable neurologic outcome. Outcomes of subcohort requiring E-CPR are in Supplementary Table 1.

The summaries of compression rate and CCF are contained in Table 2. The median event-level average compression rate was 125.6 [IQR 114.3, 139.4]. Percentage of events with average compression rate within Guideline recommendations was 32.9%. Percentage of minutes with average compression rate within Guideline recommendations was 32.6%. The median CCF was 0.92 [IQR 0.84, 0.97]. Neither average rate nor CCF was different between those who did and did not survive to hospital discharge.

Across sites, there was significant variability in average delivered compression rates ($p = 0.001$). Additionally, there was a trend of association between site and likelihood of an event achieving Guideline recommendations for rate ($p = 0.058$). Please see Supplementary Fig. 1 for a graphical representation of the variability in compression rates across this cohort.

The association between compression rates and arterial blood pressures is summarized in Table 3. In the top part of the table, compression rate was modeled as a continuous variable. Among rates ≥100 per minute, there is a statistically significant decline in systolic blood pressure (point estimate 1.7 mmHg; CI95 2.7, 0.7; $p < 0.001$) for every

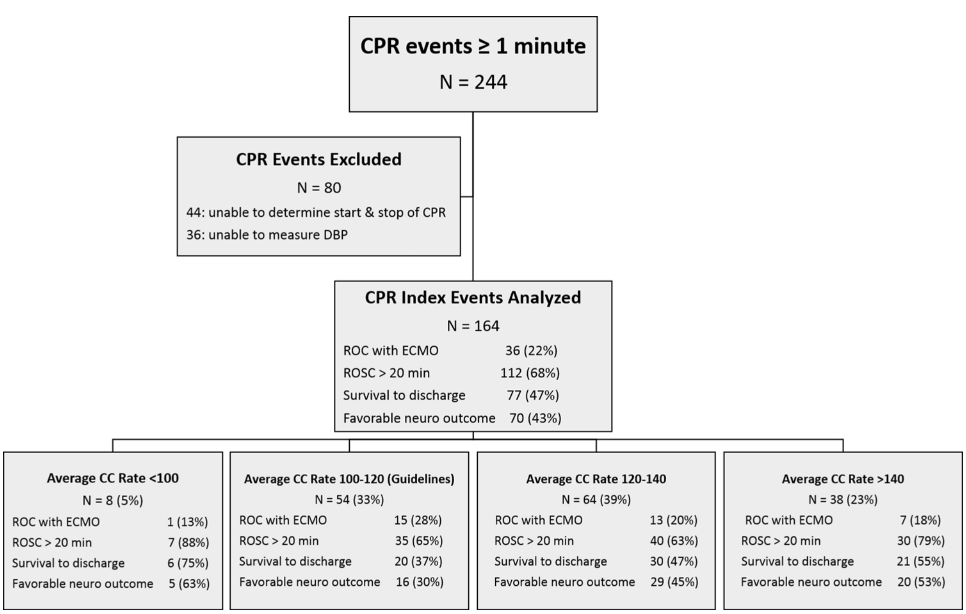

Fig. 1. Utstein-style flow diagram of patients included in this secondary analysis of the Pediatric Intensive Care Quality of Cardiopulmonary Resuscitation (PICqCPR) study. ROSC indicates Return of Spontaneous Circulation; ROC, return of circulation with extracorporeal support; neuro, neurological; favorable neuro outcome, Pediatric Cerebral Performance Category of 1–3 or no worse.

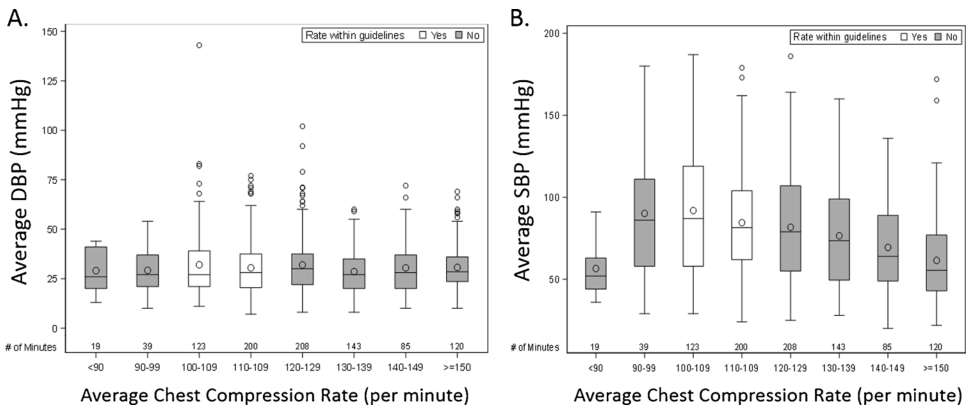

Fig. 2. Box plot minute-level average diastolic blood pressures (A) and systolic blood pressures (B) across compression rate categories. DBP indicates diastolic blood pressure, SBP, systolic blood pressure. Circles inside of each box represent the mean BP. The horizontal line inside of each box represents the median BP. The bottom and top edges of the box indicate the interquartile range (IQR). The whiskers that extend from each box indicate the range of values that are outside of the IQR (up to a distance of 1.5*IQR from the box). Any points that are more than 1.5*IQR from the box are considered outliers and are represented by circles beyond the edge of the whiskers.

10 compression per minute increase in rate. In the bottom part of the table, chest compression rate was modeled as a categorical predictor with Guideline recommendations (100–120 per minute) as the reference category. In this model, compared to Guidelines, systolic blood pressure was lower when compressions were performed between > 120–140/min (point estimate -4.07; CI95 −7.17, −0.97; p = 0.010) and tended to be lower when > 140/min (point estimate −4.57; CI95 −9.63, 0.50; p = 0.077). In neither model was there a significant relationship between diastolic blood pressure and compression rate. Please see Fig. 2 for a graphical representation of the relationship between minute-level average compression rates and average diastolic (A) and systolic (B) blood pressures.

The association between compression rates and outcomes is summarized in Table 4. Compared to Guidelines, a rate between 80–100 per minute was associated with a higher rate of survival to hospital discharge (aRR 1.92, CI95 1.13, 3.29, p = 0.017) and survival with favorable neurological outcome (aRR 2.12, CI95 1.09, 4.13, p = 0.027). Of note, among the 8 patients in this category, 6 (75%) had average rates ≥90 per minute (median of category: 94.6 per minute).

Discussion

In this study, event-level average compression rates were frequently outside Guideline recommendations, with nearly 70% of events not achieving the target. Across study sites, there was significant variability in the rate at which compressions were delivered (p = 0.001) and a trend towards some sites being more likely to achieve Guidelines compared to others (0.058). These data establish that rates exceeding Guideline recommendations are associated with mildly decreased systolic blood pressure, but not differences in diastolic blood pressure or survival outcomes. Compared to Guidelines, a rate between 80- < 100 per minute was associated with increased rates of survival, but not differences in blood pressures during CPR.

There has been a growing emphasis on the delivery of high quality CPR to improve outcomes from cardiac arrest [22]. Unfortunately, there is little data collected from children during cardiac arrest to support pediatric evidence-based guidelines. As many current CPR recording defibrillators are either not approved for infants or use pads that are too large for most infants, even the limited data that exists regarding pediatric CPR quality has been collected during the resuscitation of older children and adolescents [13]. By using monitor waveforms, this study overcomes these technological limitations.

Animal and adult out-of-hospital cardiac arrest studies have demonstrated that faster compression rates (> 120/min) may be associated with decreased coronary perfusion pressures [28] and lower survival rates [4,29]. Although of questionable clinical significance (~4 mmHg change in systolic blood pressure), our results similarly demonstrate a potentially detrimental physiologic consequence at faster rates (Fig. 2b). We propose two possible mechanisms. First, during compression, the generated arterial pressure is related to the amount of blood available for ejection during the compression phase. If compressions are delivered too quickly, diastolic filling time is reduced and the amount of blood available for the next compression phase may be limited. In addition, other studies have demonstrated an inverse relationship between compression depth and rate (i.e., higher rates lead to shallower compressions). Given the relationship between compression depth/force and arterial pressure [30,31], it is not surprising that faster rates would lead to lower arterial pressures, particularly systolic pressure, if depth was compromised. In the end, irrespective of the underlying mechanism, these data provide some evidence that rescuers should be cautious when providing faster compressions. As mean arterial pressure, mathematically defined as [(2× diastolic pressure) + systolic pressure]/3, is a primary determinant of cerebral perfusion pressure and cerebral blood flow, it is reasonable to speculate that lower systolic blood pressures during CPR could lead to lower cerebral perfusion and have clinical implications.

While a compression rate between 80– < 100 per minute was associated with improved survival, this statistical finding must be interpreted with caution given the following factors. First, there were only 8 patients in this category and as such, despite statistical significance, it is difficult to make definitive conclusions in regards to an optimal compression rate applicable to all pediatric patients. Second, the median rate in this category was ~95 per minute (within 5 per minute of Guidelines). A reasonable interpretation of our data therefore could be that rates of "approximately 100 per minute" as per 2005 Guidelines [32] should be recommended or that no change be made. Finally, in the main PICqCPR paper, *threshold* diastolic blood pressure targets (25 mmHg in infants, 30 mmHg in older children) were associated with improved outcomes [16]. Therefore, we speculate that providers in this cohort may have been focusing on blood pressures rather than rescuer-centric targets such as compression rate. Although diastolic pressures were similar across rate categories (Fig. 2), a slightly higher percentage of patients achieved the diastolic thresholds associated with survival when rates were between 80–100 (63%) compared to Guidelines (54%; difference not statistically significant; data not shown). This may explain part of the observed survival difference and is consistent with a growing body of translational literature supporting a hemodynamic-directed approach to resuscitation [33,34]. Coupled with the strong association of diastolic blood pressure and outcomes in the main PICqCPR manuscript, we believe that these data should be used to highlight the importance of prioritizing physiologic targets over rescuer-centric targets [35].

This investigation has strengths worth noting. Prior reports of pediatric CPR quality have utilized CPR recording defibrillators [3,11–14], and as such, have two main limitations. First, many infants are too small to accommodate the chest pads/sensors that are used to record quality data [36]. In a series of younger children at The Children's Hospital of Philadelphia (n = 8), all patients were at least 1 year of age [12]. In contrast, more than half of the patients in this report are < 1 year of age. In addition, placement of the sensors themselves can take up to 5 min after the start of compressions. Therefore, previous reports have likely either missed data from the initial minutes of the resuscitation or, worse, failed to include entire events. The magnitude of the number of potential missed events in these prior reports is highlighted by the fact that 37 (18.6%) events were less than 3 min in this investigation.

This study also has limitations. First, there may be concern that our findings are not generalizable because all patients had an arterial line in place at the time of arrest; however, more than 95% of pediatric in-hospital cardiac arrests now occur in ICUs, and over half will have an arterial line in place at the time of the arrest [37]. Second, other important CPR quality variables (compression depth [11], release velocity [9], ventilation rate [38]) and quality of post-arrest care [39,40] are not evaluated. While inclusion of CCF did not substantially affect our results (data not shown), the contribution of depth to this association remains unknown highlighting the need for further research in this area. Finally, this study was conducted in a network comprised of large academic pediatric ICUs and may represent a "best-case" scenario.

Conclusions

Compliance with Guideline recommendations for rate was not common in this multi-center cohort with substantial variability in compression rates across the sites. Rates exceeding Guidelines were associated with mildly decreased systolic blood pressure, but not diastolic pressure or survival. Slightly lower rates were associated with improved outcomes. These data do not support a pediatric compression rate of 100–120 per minute during in-hospital resuscitations.

Conflict of interest

The authors report no conflicts of interest related specifically to this manuscript. Unrelated disclosures include the following: Robert M. Sutton reports grant funding from the National Institutes of Health (NIH); Murray M. Pollack reports grant funding from the NIH and the Department of Defense, collaborative projects with Cerner Corporation, and philanthropy from Mallinckrodt Pharmaceuticals; Frank W. Moler reports NIH funding paid to his institution; Daniel A. Notterman reports grant funding from the NIH; and Christopher J. Newth reports consulting services for both Philips Research of North America and Medtronics.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2018.07.015.

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