

# Ventilation Rates and Pediatric In-Hospital Cardiac Arrest Survival Outcomes

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**Objectives:** The objective of this study was to associate ventilation rates during in-hospital cardiopulmonary resuscitation with 1) arterial blood pressure during cardiopulmonary resuscitation and 2) survival outcomes.

**Design:** Prospective, multicenter observational study.

**Setting:** Pediatric and pediatric cardiac ICUs of the Collaborative Pediatric Critical Care Research Network.

**Patients:** Intubated children ( $\geq 37$  wk gestation and  $< 19$  yr old) who received at least 1 minute of cardiopulmonary resuscitation.

**Interventions:** None.

**Measurements and Main Results:** Arterial blood pressure and ventilation rate (breaths/min) were manually extracted from arterial line and capnogram waveforms. Guideline rate was defined as  $10 \pm 2$  breaths/min; high ventilation rate as greater than

or equal to 30 breaths/min in children less than 1 year old, and greater than or equal to 25 breaths/min in older children. The primary outcome was survival to hospital discharge. Regression models using Firth penalized likelihood assessed the association between ventilation rates and outcomes. Ventilation rates were available for 52 events (47 patients). More than half of patients (30/47; 64%) were less than 1 year old. Eighteen patients (38%) survived to discharge. Median event-level average ventilation rate was 29.8 breaths/min (interquartile range, 23.8–35.7). No event-level average ventilation rate was within guidelines; 30 events (58%) had high ventilation rates. The only significant association between ventilation rate and arterial blood pressure occurred in children 1 year old or older and was present for systolic blood pressure only (−17.8 mm Hg/10 breaths/min; 95% CI, −27.6 to −8.1;  $p < 0.01$ ). High ventilation rates were associated with a higher odds of survival to discharge (odds ratio, 4.73;  $p = 0.029$ ). This association was stable after individually controlling for location (adjusted odds ratio, 5.97;  $p = 0.022$ ), initial rhythm (adjusted odds ratio, 3.87;  $p = 0.066$ ), and time of day (adjusted odds ratio, 4.12;  $p = 0.049$ ).

**Conclusions:** In this multicenter cohort, ventilation rates exceeding guidelines were common. Among the range of rates delivered, higher rates were associated with improved survival to hospital discharge. (*Crit Care Med* 2019; XX:00–00)

**Key Words:** cardiac arrest; cardiopulmonary resuscitation; pediatric; ventilation

More than 10,000 children receive cardiopulmonary resuscitation (CPR) annually in the United States (1, 2). Despite improving survival rates over the last 2 decades, more than half of these children do not survive to hospital discharge (3). Neurologic morbidity is common among survivors (1).

Current CPR guidelines recommend a ventilation rate of 10 breaths/min (breaths/min) for both children and adults, despite children having much higher ventilation rates at baseline (4) and more pediatric arrests being associated with respiratory deterioration (3, 5, 6). The decision to recommend a uniform rate was partly to simplify training, but also because adult models of cardiac arrest have demonstrated that excessive ventilation has a detrimental effect on hemodynamics and survival (7). Given the excessive ventilation during pediatric resuscitation (8–10), if higher ventilation rates are truly detrimental, ventilation rate could be targeted to improve pediatric cardiac arrest outcomes.

The Pediatric Intensive Care Unit Quality of CPR (PICqCPR) (11) study conducted by the Collaborative Pediatric Critical Care Research Network (CPCCRN) (12) provides a unique opportunity to evaluate ventilation rates during CPR. This study collected data on pediatric cardiac arrests in the Network ICUs over a 3-year period. Using this dataset, the primary objective of this investigation was to associate ventilation rates during pediatric CPR with survival outcomes.

## MATERIALS AND METHODS

### Setting and Design

Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the CPCCRN conducts investigations related to pediatric critical care practice (12). The clinical sites are supported by a data coordinating center (DCC) at the University of Utah. 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 physiologic targets—invasive arterial blood pressures (BPs) and end-tidal carbon dioxide (EtCO<sub>2</sub>)—and cardiac arrest survival outcomes during ICU resuscitation attempts. The results of the main PICqCPR analyses have been previously reported (11, 13). This study represents a secondary retrospective analysis of the prospective observational PICqCPR study.

PICqCPR was approved with waiver of informed consent by the Institutional Review Board at each clinical site and the DCC. Trained research coordinators collected Utstein-style standardized cardiac arrest and CPR data (14). Neurologic status was assessed using the pediatric cerebral performance category (PCPC) (15) and Functional Status Scale (16, 17). See previous publication for more details regarding the methods of the PICqCPR study (11).

### Patient Population

Children greater than or equal to 37 weeks gestation and less than 19 years old with an invasive airway in place at the time of the arrest and who received chest compressions for at least 1 minute with EtCO<sub>2</sub> monitoring before and during CPR in a CPCCRN ICU were eligible. At least 1 minute of continuous quantitative capnography data and at least one additional waveform to allow determination of starts and stops in CPR (i.e., artifact from central venous pressure, respiratory plethysmography, or electrocardiogram) were also required. Subjects were excluded if the first compression was not captured or if ventilation rate could not be determined from the capnogram waveform (e.g., disconnection of monitor, artifact from compressions). Subjects with passive pulmonary blood flow (i.e., hypoplastic left heart subjects status post-cavopulmonary shunting) were also excluded because they may be more susceptible to the detrimental hemodynamic effects of increased intrathoracic pressure associated with excessive ventilation.

### Measurements

The first 10 minutes of CPR data were collected. Ventilation rates and arterial BPs were manually extracted from EtCO<sub>2</sub> and arterial waveform printouts (PlotDigitizer, Version 2.0; University of South Alabama, Mobile, AL). The investigators analyzing the waveforms, who were blinded to patient outcome, reviewed all the waveforms together to ensure consensus of ventilation rate determination (physician: R.M.S.; engineer: W.P.L.). This manual process mitigates known difficulties with automated ventilation detection via capnography (18, 19). For each 1-minute epoch, the following data points were extracted:

1) the number of ventilations; 2) the time (seconds) that compressions were not being performed (pause time); 3) total time (seconds) that ventilation rate could not be determined (“missing” data due to EtCO<sub>2</sub> interruption); and 4) in the subset with arterial line and capnography waveform data, mean systolic BP, and diastolic BP (mm Hg). Ventilation rate was defined as follows: number of ventilations/“CPR time.” CPR time was defined as follows: epoch length (1 min) – (pause time + missing data time). Only ventilations delivered during CPR time were used to calculate the average rate. Chest compression fraction (CCF; proportion of time compressions are performed during arrest) was defined as follows:  $1 - (\text{pause time} / [60 - \text{missing data time}])$ . For each minute of CPR, an average of ventilation rate, chest compression rate, CCF, systolic BP, and diastolic BP was calculated (minute-level average), and then for each event, the average of all the available epochs was calculated (event-level average). American Heart Association (AHA) Guideline rate was defined as  $10 \pm 2$  breaths/min (20), high ventilation rates as greater than or equal to 30 breaths/min in children less than 1 year of age, and greater than or equal to 25 breaths/min in older children (8, 21).

### Outcomes

The primary outcome was survival to hospital discharge of index events. Secondary outcomes included the following: 1) return of spontaneous circulation (ROSC) of all events; 2) systolic BP (mm Hg); 3) diastolic BP (mm Hg); and 4) survival with favorable neurologic outcome (PCPC 1–3 or no worsening from baseline) of index events (14, 15).

### Statistical Analysis

Patient and event characteristics were summarized using frequencies and percentages or median and interquartile ranges (IQRs). Differences in these characteristics between those who did and did not survive to discharge were examined using Fisher exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Logistic regression models were used to evaluate the association between event-level average ventilation rates and patient outcomes. To test the stability of the association between ventilation rate categories and survival, models were individually adjusted for specified a priori covariates based on previous associations with outcomes (initial cardiac rhythm [22], location [PICU vs cardiac ICU (23)], and time of CPR [24]). This approach was chosen to avoid overfitting the model in the setting of a small cohort of patients and used Firth likelihood penalty. The association between minute-level average ventilation rates and BPs was investigated using generalized estimating equations with an first order autoregressive (AR-1) correlation structure to account for the correlation between minutes of an event. In an attempt to identify an optimal ventilation rate, both receiver operating characteristic (ROC) and cubic spline curves were constructed. Restricted cubic splines were formed using three knots at the 10th, 50th, and 90th percentiles. Odds ratios (ORs) are presented with their 95% CIs; *p* values are two-sided and considered significant when less than 0.05.

### RESULTS

Between July 2013 and June 2016, there were 47 patients (52 events) who met all inclusion and exclusion criteria. Our analytic cohort includes the four patients with hypoplastic left heart syndrome (one preoperative, three status post stage I repair) that were excluded from the main EtCO<sub>2</sub> PICQ-CPR study (13). All patients received asynchronous ventilations during CPR (20). Ventilation rate could be determined from the capnography waveform data for all events. Of these 47 patients, 26 had both arterial line and capnography data. The range of events reported per clinical site was 1–17 across the seven clinical sites. ROSC was achieved in 36 of 52 events (69%); survival to discharge was achieved in 18 of 47 index events (38%). All survivors had a favorable neurologic outcome.

Patient and index event characteristics and their univariable association with survival to discharge are contained in **Tables 1 and 2**, respectively. More than half of the patients (30/47; 64%) were less than 1 year old, male (25/47; 53%), and classified as cardiac patients (32/47; 68%). Respiratory insufficiency (36/47; 77%) and hypotension (39/47; 83%) were the most common pre-existing conditions. Hypotension (35/47; 74%) was also the most common immediate cause of arrest, followed by respiratory decompensation (13/47; 28%). Median duration of CPR was 6 minutes (IQR, 2–22). Among the prearrest patient characteristics, there was a trend toward higher survival in patients with congenital heart disease (*p* = 0.07). Among the index event characteristics, location of arrest, initial rhythm, duration of CPR, number of epinephrine doses, and the administration of sodium bicarbonate during CPR were associated with survival on univariable analysis. Patient and event characteristics (index and recurrent arrests) and their univariable association with ROSC are contained in **Supplemental Tables 1 and 2** (Supplemental Digital Content 1, <http://links.lww.com/CCM/E781>), respectively. Pre-existing hypotension, time of day, duration of CPR, number of epinephrine doses, calcium administration, and sodium bicarbonate administration were associated with ROSC.

The summaries of ventilation rate, compression rate, and CCF for index events and their univariable association with survival to discharge are contained in **Supplemental Table 3** (Supplemental Digital Content 1, <http://links.lww.com/CCM/E781>). Among index events, the median event-level average ventilation rate for all patients was 30.1 breaths/min (IQR, 23.4–37.4), 32 breaths/min (26.9–37.4) for children less than 1 year of age, and 26.1 breaths/min (20.4–35.6) for older children. No events achieved guideline recommendations (range, 14.2–62.0 breaths/min). More than half of the index events (29/47; 62%) met the definition of high ventilation rates. Of index events, median event-level average ventilation rates were significantly higher in patients who survived to hospital discharge compared with those who did not (33.0 breaths/min [29.6–37.8 breaths/min] vs 26.9 breaths/min [20.2–35.6 breaths/min]; *p* = 0.043). Neither average compression rate nor CCF was different between those who did and did not survive to hospital discharge. Please see **Supplemental Table 4** (Supplemental

**TABLE 1. Prearrest Characteristics by Survival to Hospital Discharge**

Prearrest Characteristic	Overall (n = 47)	Survival to Hospital Discharge		p
		Yes (n = 18)	No (n = 29)	
Age, yr, n (%)				0.135 <sup>a</sup>
< 1	30 (64)	14 (78)	16 (55)	
≥ 1	17 (36)	4 (22)	13 (45)	
Male, n (%)	25 (53)	11 (61)	14 (48)	0.549 <sup>a</sup>
Race, n (%)				0.449 <sup>a</sup>
White	20 (43)	9 (50)	11 (38)	
Black or African American	10 (21)	2 (11)	8 (28)	
Other	4 (9)	2 (11)	2 (7)	
Preexisting conditions, n (%)				
Respiratory insufficiency	36 (77)	13 (72)	23 (79)	0.726 <sup>a</sup>
Hypotension	39 (83)	15 (83)	24 (83)	1.000 <sup>a</sup>
Not reported	13 (28)	5 (28)	8 (28)	
Congestive heart failure	7 (15)	4 (22)	3 (10)	0.403 <sup>a</sup>
Pneumonia	3 (6)	1 (6)	2 (7)	1.000 <sup>a</sup>
Sepsis	6 (13)	3 (17)	3 (10)	0.662 <sup>a</sup>
Renal insufficiency	10 (21)	4 (22)	6 (21)	1.000 <sup>a</sup>
Malignancy	1 (2)	0 (0)	1 (3)	1.000 <sup>a</sup>
Congenital heart disease	28 (60)	14 (78)	14 (48)	0.068 <sup>a</sup>
Illness category, n (%)				0.008 <sup>a</sup>
Surgical cardiac	18 (38)	12 (67)	6 (21)	
Medical cardiac	14 (30)	2 (11)	12 (41)	
Surgical noncardiac	3 (6)	0 (0)	3 (10)	
Medical noncardiac	12 (26)	4 (22)	8 (28)	
Baseline pediatric cerebral performance category, n (%)				0.293 <sup>b</sup>
Normal	24 (51)	10 (56)	14 (48)	
Mild disability	14 (30)	7 (39)	7 (24)	
Moderate disability	7 (15)	1 (6)	6 (21)	
Severe disability	1 (2)	0 (0)	1 (3)	
Coma/vegetative state	1 (2)	0 (0)	1 (3)	
Baseline Functional Status Scale, median (interquartile range)	6.0 (6.0–9.0)	7.0 (6.0–9.0)	6.0 (6.0–10.0)	0.355 <sup>b</sup>

<sup>a</sup>Fisher exact test.<sup>b</sup>Wilcoxon rank-sum test.

Digital Content 1, <http://links.lww.com/CCM/E781>) for these same summaries for all events and their association with ROSC. Median event-level average ventilation rates were significantly higher in events that achieved ROSC compared with those that did not (31.1 breaths/min [25.6–39.2 breaths/min] vs 24.5 breaths/min [16.7–32.5 breaths/min];  $p = 0.017$ ).

The association between minute-level average ventilation rates and arterial BPs is depicted in **Figure 1** (diastolic BP:

Fig. 1, A and B; systolic BP: Fig. 1, C and D). For children less than 1 year old (Fig. 1, A and C), there was no association between ventilation rate and either diastolic BP (–1.8 mm Hg per 10 breaths/min increase; 95% CI, –3.9 to 0.3;  $p = 0.10$ ) or systolic BP (–3.3 mm Hg per 10 breaths/min increase; 95% CI, –6.8 to 0.2;  $p = 0.06$ ). For children 1 year old or older (Fig. 1, B and D), there was no association between ventilation rate and diastolic BP (–3.1 mm Hg per 10 breaths/min increase;

**TABLE 2. Event Characteristics by Survival to Hospital Discharge**

Event Characteristic	Overall ( <i>n</i> = 47)	Survival to Hospital Discharge		<i>p</i>
		Yes ( <i>n</i> = 18)	No ( <i>n</i> = 29)	
Location of CPR event, <i>n</i> (%)				0.006 <sup>b</sup>
PICU	20 (43)	3 (17)	17 (59)	
Cardiac ICU	27 (57)	15 (83)	12 (41)	
Immediate cause, <sup>a</sup> <i>n</i> (%)				
Hypotension	35 (74)	15 (83)	20 (69)	0.324 <sup>b</sup>
Respiratory decompensation	13 (28)	4 (22)	9 (31)	0.739 <sup>b</sup>
Arrhythmia	8 (17)	2 (11)	6 (21)	0.692 <sup>b</sup>
First documented rhythm, <i>n</i> (%)				0.020 <sup>b</sup>
Asystole/PEA	8 (17)	0 (0)	8 (28)	
VF/VT	4 (9)	1 (6)	3 (10)	
Bradycardia with poor perfusion	35 (74)	17 (94)	18 (62)	
Duration of CPR (min)	6.0 (2.0–22.0)	3.0 (2.0–6.0)	11.0 (5.0–24.0)	0.006 <sup>c</sup>
Duration of CPR (min) category, <i>n</i> (%)				0.023 <sup>c</sup>
1–15	33 (70)	16 (89)	17 (59)	
16–35	9 (19)	2 (11)	7 (24)	
> 35	5 (11)	0 (0)	5 (17)	
Interventions in place, <i>n</i> (%)				
Vascular access	32 (68)	11 (61)	21 (72)	0.524 <sup>b</sup>
Arterial catheter	34 (72)	14 (78)	20 (69)	0.739 <sup>b</sup>
Central venous catheter	40 (85)	18 (100)	22 (76)	0.034 <sup>b</sup>
Vasoactive infusion	36 (77)	14 (78)	22 (76)	1.000 <sup>b</sup>
Time, <sup>d</sup> <i>n</i> (%)				0.063 <sup>b</sup>
Weekday	27 (57)	13 (72)	14 (48)	
Weeknight	11 (23)	1 (6)	10 (34)	
Weekend	9 (19)	4 (22)	5 (17)	
Pharmacologic interventions				
Epinephrine, <sup>e</sup> <i>n</i> (%)	45 (96)	18 (100)	27 (93)	0.517 <sup>b</sup>
No. of doses (when used)	2.0 (1.0–4.0)	1.0 (1.0–3.0)	3.0 (1.0–6.0)	0.013 <sup>c</sup>
Calcium, <i>n</i> (%)	18 (38)	6 (33)	12 (41)	0.759 <sup>b</sup>
Sodium bicarbonate, <i>n</i> (%)	27 (57)	6 (33)	21 (72)	0.015 <sup>b</sup>

CPR = cardiopulmonary resuscitation.

<sup>a</sup>Immediate causes are not mutually exclusive.

<sup>b</sup>Fisher exact test.

<sup>c</sup>Wilcoxon rank-sum test.

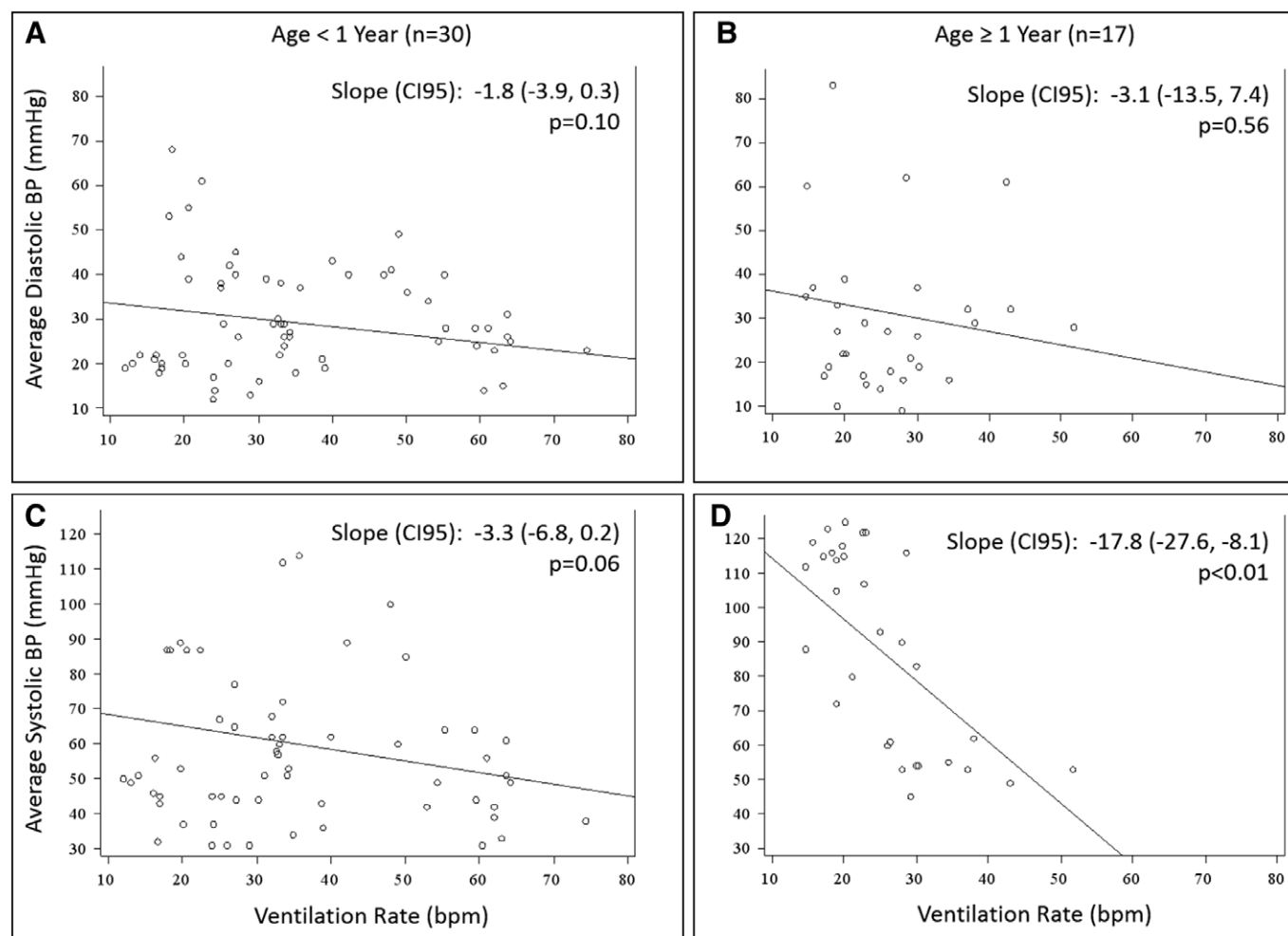
<sup>d</sup>Weekdays are Monday–Friday, 07:00 AM–22:59 PM; weeknights are Monday–Friday, 23:00 PM–06:59 AM; and weekends are Saturday–Sunday.

<sup>e</sup>The comparison of number of epinephrine doses is based only on index events for which epinephrine was used.

95% CI, –13.5 to 7.4; *p* = 0.56); however, systolic BP dropped significantly as ventilation rates increased (–17.8 mm Hg per 10 breaths/min increase; 95% CI, –27.6 to –8.1; *p* < 0.01).

The association between event-level average ventilation rate and survival to discharge as evaluated by ROC area under the

curve (AUC) (**Fig. 2, A and B**) and cubic spline analysis (**Fig. 2, C and D**) is depicted in Figure 2. For children less than 1 year old (**Fig. 2, A and C**), the AUC (**Fig. 2A**) for event-level average ventilation rate was 0.701 (95% CI, 0.501–0.901; optimal rate, 29.63 breaths/min; sensitivity, 0.93; specificity, 0.56). Cubic spline



**Figure 1.** Scatterplot of minute-level average ventilation rates versus diastolic (**A** and **B**) and systolic (**C** and **D**) blood pressures (BPs). Children less than 1 yr old (**A** and **C**), and older children greater than or equal to 1 yr old (**B** and **D**). Estimates for slope represent change in BP for each 10 breaths/min (bpm) increase in ventilation rate. All estimates from generalized estimating equations to control for minutes within a cardiopulmonary resuscitation event for the same patient.

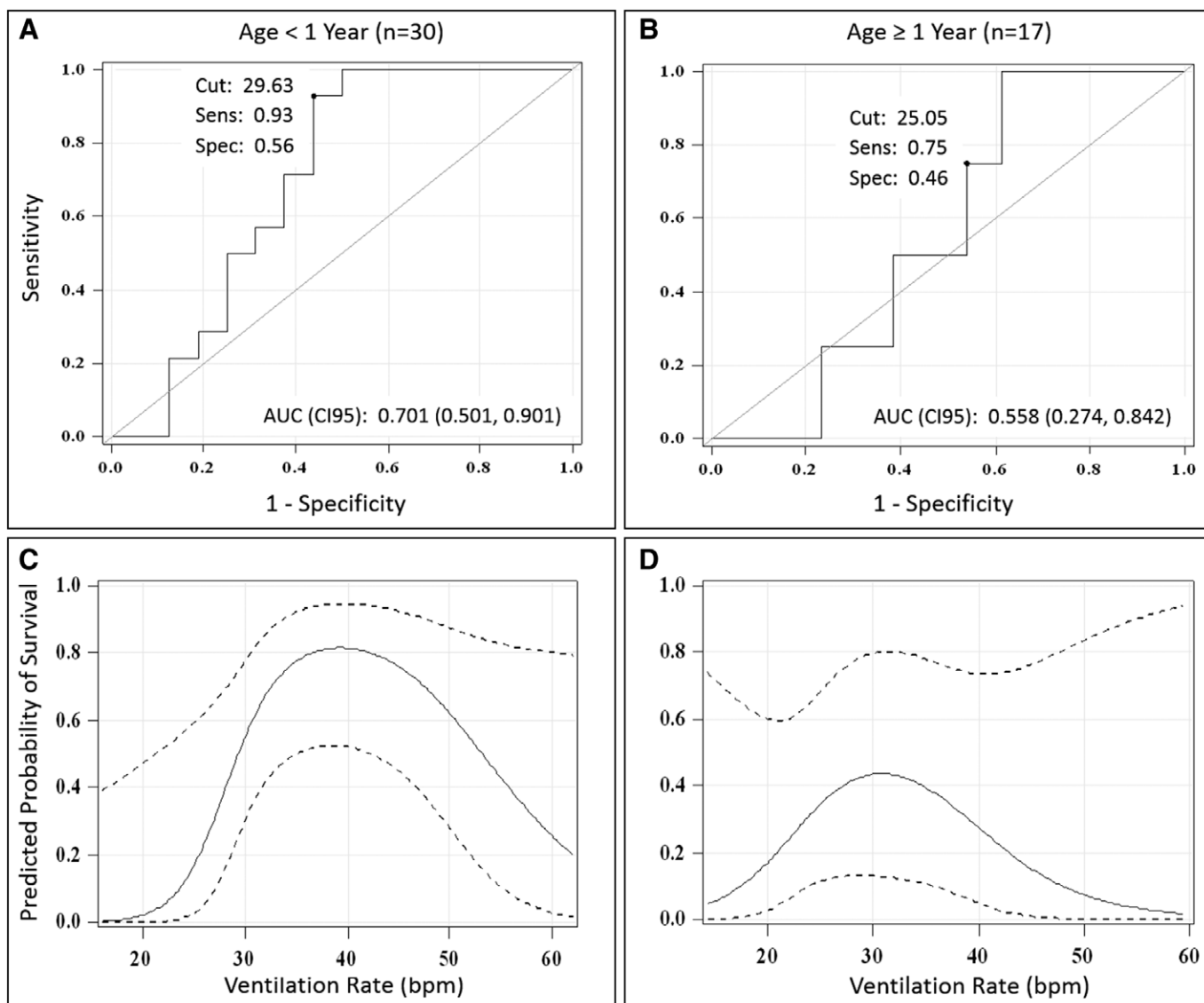
analysis (Fig. 2C) suggested stable survival rates between 30 and 50 breaths/min. For children 1 year old or older (Fig. 2, B and D), the AUC (Fig. 2B) for event-level average ventilation rate was 0.558 (95% CI, 0.274–0.842; optimal rate, 25.05 breaths/min; sensitivity, 0.75; specificity, 0.46). Cubic spline analysis (Fig. 2D) suggested stable survival rates between 25 and 35 breaths/min.

The association between high ventilation rates and outcomes is in **Table 3**. Among index events, high ventilation rates were associated with improved rates of survival to discharge and survival with favorable neurologic outcome (OR, 4.73; 95% CI, 1.17–19.13;  $p = 0.029$ ) compared with lower ventilation rates, associations that were stable after controlling for location (adjusted OR [aOR], 5.97;  $p = 0.022$ ), initial rhythm (aOR, 3.87;  $p = 0.066$ ), and time of day (aOR, 4.12;  $p = 0.049$ ). Among all events, high ventilation rates were associated with improved rates of ROSC (OR, 4.64; 95% CI, 1.32–16.27;  $p = 0.017$ ) compared with lower rates, an association that was stable after controlling for location (aOR, 4.45;  $p = 0.02$ ), initial rhythm (aOR, 4.09;  $p = 0.03$ ), and time of day (aOR, 5.17;  $p = 0.015$ ).

## DISCUSSION

In this multicenter study, none of these 52 CPR events achieved an event-level average ventilation rate within guidelines. High ventilation rates ( $\geq 30$  breaths/min in children  $< 1$  yr old and  $\geq 25$  breaths/min in older children) were common and associated with improved rates of ROSC and survival compared with lower rates. No patient received a ventilation rate within guidelines; therefore, it remains unclear as to whether a rate at 10 breaths/min could improve outcomes. However, these data do not suggest that slightly higher rates (children  $< 1$  yr old:  $\approx 30$ –50 breaths/min; older children:  $\approx 25$ –35 breaths/min) are detrimental to outcomes and, in fact, may be beneficial among PICU patients who have an invasive airway in place at the time of the arrest.

A recent AHA scientific statement highlights the importance of evidence-based CPR targets to improve outcomes from cardiac arrest (25). To date, an imbalance in this research area exists with more investigation into the chest compression aspect of CPR (i.e., depth [26–28], rate [29–31], release velocity [32, 33]) when compared with ventilations. Current



**Figure 2.** Evaluation of optimal ventilation rates using receiver operating characteristic area under the curve (AUC; **A** and **B**) and cubic spline analysis (**C** and **D**). Children less than 1 yr old (**A** and **C**), and older children greater than or equal to 1 yr old (**B** and **D**). *Solid line* in AUC analysis signifies the predicted survival rate, whereas the *dotted line* represents the 95% CI. bpm = breaths/min, Cut = optimal cut point, Sens = sensitivity, Spec = specificity.

**TABLE 3. Odds Ratio Estimates for High Ventilation Rate With Outcomes**

Model <sup>a</sup>	Return of Spontaneous Circulation, OR (95% CI)	p	Survival to Hospital Discharge, OR (95% CI)	p	Survival With Favorable Neurologic Outcome, OR (95% CI)	p
Unadjusted	4.64 (1.32–16.27)	0.017	4.73 (1.17–19.13)	0.029	4.73 (1.17–19.13)	0.029
Adjusted for cardiac ICU vs PICU	4.45 (1.27–15.60)	0.020	5.97 (1.29–27.67)	0.022	5.97 (1.29–27.67)	0.022
Adjusted for initial rhythm	4.09 (1.14–14.63)	0.030	3.87 (0.91–16.40)	0.066	3.87 (0.91–16.40)	0.066
Adjusted for weekday vs weeknight/weekend	5.17 (1.38–19.36)	0.015	4.12 (1.00–16.88)	0.049	4.12 (1.00–16.88)	0.049

OR = odds ratio.

<sup>a</sup>All models estimate the odds of the outcome for ventilation rate ≥ 30 breaths/min for infants < 1 yr and ≥ 25 breaths/min for children ≥ 1 yr. Estimates are from logistic regression models with Firth penalized likelihood.

guidelines recommend a ventilation rate of 10 breaths/min across all age groups (20) partly to simplify training, but also to avoid the risk of excessive ventilation increasing intrathoracic pressure, decreasing venous return, and worsening hemodynamics (7, 21). **To our knowledge, this study is the first clinical study to associate ventilation rates with survival and, given our findings, indicate that pediatric ventilation guidelines require re-evaluation.**

The high-quality CPR in this research network should be considered when interpreting our findings. In the PICQcPR study (11), 62% of patients achieved the diastolic BP targets associated with improved survival ( $\geq 25$  mm Hg in infants  $<1$  yr old,  $\geq 30$  mm Hg in older children). Similarly, the CPR quality data (CCF  $> 90\%$ ; compression rate within 10/min of guidelines) support this contention. Therefore, one interpretation of our results could be that in the setting of high-quality chest compressions, ventilation rates higher than currently recommended may be beneficial.

Children may also simply benefit from higher ventilation rates than currently recommended. Children have higher baseline ventilation rates (4), and their cardiac arrests are more likely to be triggered by a respiratory deterioration (5). As such, higher rates may be necessary to restore adequate oxygenation and ventilation during CPR (34). In addition, hypoxia and acidosis impede myocardial resuscitability (35, 36) and decrease likelihood of successful defibrillation (37). Therefore, in the setting of respiratory acidosis, an increase in ventilation rate could be used to improve the likelihood of resuscitation success when adequate hemodynamics alone do not attain ROSC. In light of our findings that **higher ventilation rates are associated with lower systolic BPs in older children (and a trend toward lower diastolic [ $p = 0.10$ ] and systolic [ $p = 0.06$ ] BPs in children  $< 1$  yr old), any increase in ventilation rate should caution the rescuer to pay strict attention to any adverse effects on hemodynamics.** Such an approach would be consistent with the growing body of literature supporting physiologic-directed resuscitation (38–43).

This study has limitations. First, conclusions based on our small sample size are inherently fragile. For example, after adjustment for initial rhythm,  $p$  value increased to 0.066 even though the magnitude of the association was stable (aOR, 3.87–5.97). Further, our small sample size also does not allow for us to perform potentially important subgroup analyses (e.g., pre-existing conditions). Second, there may be concern that our findings are not generalizable given the characteristics of our cohort (**i.e., intubated ICU patients, 68% classified as cardiac patients**). However, not only do more than 95% of pediatric in-hospital cardiac arrests occur in ICUs (44), but nearly half ( $\approx 40\%$ ) will be classified as medical or surgical cardiac (23) and almost three-quarters will have invasive mechanical ventilation in place at the time of the arrest (44). Third, we do not have blood gas data available to evaluate the association between ventilation rates and intra-arrest oxygenation or ventilation. Therefore, although supported by translational data (34), our proposed mechanism as to why children may benefit from higher ventilation rates remains speculative. Fourth,

the effect that **other ventilation variables (e.g., positive end-expiratory pressure, tidal volume, and minute volume) have on oxygenation and ventilation during CPR and on survival outcomes were not registered in our study.** This is an important limitation. Fifth, we did not collect granular data regarding the specific nature of the type of congenital heart disease present in these patients. Finally, CPR recording defibrillators were not commonly used in the Network; therefore, compression depth (27, 28) and release velocity (32, 33) were not available for analysis.

## CONCLUSIONS

In this ICU study of children with an invasive airway, no patient received guideline recommended ventilation rates during CPR. High ventilation rates ( $\geq 30$  breaths/min in children  $< 1$  yr old and  $\geq 25$  breaths/min in older children) were common and associated with improved outcomes compared with lower rates. However, further study is necessary to confirm these findings and to elucidate the potential physiologic mechanisms underlying these findings.

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