Critical Care Unit Characteristics and Extracorporeal Cardiopulmonary Resuscitation Survival in the Pediatric Cardiac Population: Retrospective Analysis of the Virtual Pediatric System Database

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OBJECTIVES: Existing literature provides limited data about ICU characteristics and pediatric extracorporeal cardiopulmonary resuscitation (E-CPR) outcomes. We aimed to evaluate the associations between patient and ICU characteristics, and outcomes after E-CPR in the pediatric cardiac population.

DESIGN: Retrospective analysis of the Virtual Pediatric System database (VPS, LLC, Los Angeles, CA).

SETTING: PICUs categorized as either cardiac-only versus mixed ICU cohort type.

PATIENTS: Consecutive cardiac patients less than 18 years old experiencing cardiac arrest in the ICU and resuscitated using E-CPR.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Event and time-stamp filtering identified E-CPR events. Patient, hospital, and event-related variables were aggregated for independent and multivariable mixed effects logistic regression to assess the association between ICU cohort type and survival. Among ICU admissions in the VPS database, 2010–2018, the prevalence of E-CPR was 0.07%. A total of 671 E-CPR events (650 patients) comprised the final cohort; congenital heart disease (84%) was the most common diagnosis versus acquired heart diseases. The majority of E-CPR events occurred in mixed ICUs (67%, $n = 449$) and in ICUs with greater than 20 licensed bed capacity (65%, $n = 436$). Survival to hospital discharge was 51% for the overall cohort. Independent logistic regression failed to reveal any association between survival to hospital discharge and ICU type (ICU type: cardiac ICU, odds ratio [OR], 1.01; 95% CI, 0.71–1.44; $p = 0.95$). However, multivariable logistic regression revealed an association between cardiac surgical patients and greater odds for survival (OR, 2.03; 95% CI, 1.40–2.95; $p < 0.001$). Also, there was an association between ICUs with capacity greater than 20 (vs not) and lower survival odds (OR, 0.65; 95% CI, 0.43–0.96).

CONCLUSIONS: The overall prevalence of E-CPR among critically ill children with cardiac disease observed in the VPS database is low. We failed to identify an association between ICU cohort type and survival. Further investigation into organizational factors is warranted.

KEY WORDS: congenital heart disease; extracorporeal cardiopulmonary resuscitation; pediatrics

Introduced over 40 years ago as a rescue modality for failed conventional cardiopulmonary resuscitation (CPR) after post-cardiotomy cardiac arrest in children undergoing congenital heart surgery, extracorporeal CPR

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RESEARCH IN CONTEXT

- Extracorporeal cardiopulmonary resuscitation (E-CPR) in the pediatric cardiac population has been utilized for over 40 years, yet survival outcomes remain unchanged over the last decade.
- Our understanding of the complex interplay of patient/event E-CPR characteristics with hospital and ICU ecosystems is limited and in need of a paradigm shift to account for unmeasured influences on outcomes.
- The inclusion of ICU structural factors such as ICU size and cohort type warrant further investigation.

(E-CPR) continues to demonstrate survival benefit and increased utilization in the pediatric cardiac population and beyond (1–4). Although E-CPR for the pediatric cardiac population is now endorsed in resuscitation guidelines (5), survival rates after E-CPR have remained relatively unchanged over the last decade (4, 6, 7). Even though support from the international resuscitation science community for the use of E-CPR remains steadfast for select groups such as children with underlying cardiac disease, our understanding of factors associated with survival after cardiac arrest and E-CPR beyond those commonly reported Utstein patient-level characteristics remains limited (8, 9).

In North America, most E-CPR reports come from dedicated cardiac ICUs (CICUs)—both single-center and multicenter—with few reports from other ICU models (e.g., mixed cardiac and general pediatric critical care units). Although associations between patient-level and event-level factors (i.e., surgical vs medical cardiac illness categories, CPR duration and timing during day vs night) and outcomes after E-CPR have been demonstrated through the use of large clinical registries of cardiac arrest and/or cardiac critical care such as the American Heart Association's Get With the Guidelines-Resuscitation and the Pediatric Cardiac Critical Care Consortium (PC4) (3, 6, 10), critical care unit-level characteristics, and the potential associations with survival have not been reported. To date, no studies compare survival after E-CPR between ICUs of varying capacity and cohort types. We therefore sought to leverage standardized cardiac and alternative model PICU clinical data from the Virtual Pediatric System North American database (VPS, LLC, Los Angeles, CA). Our primary hypothesis is that ICU type (CICU vs mixed/PICU) is associated with E-CPR survival for surgical and medical cardiac patients resuscitated with E-CPR.

METHODS

The Institutional Review Board of Baylor College of Medicine as well as the feasibility committee and the research committee of VPS waived need for informed consent and approved use of the registry data for analysis (Protocol H-43584; approval date May 21, 2021; title: E-CPR in the Pediatric Population: An In-Depth Analysis of Outcome Variability from the Virtual Pediatric System Database). All research procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

The VPS database is dedicated to standardized data sharing among PICUs and is used to track outcomes, measure quality, and conduct research. VPS has over 135 contributing hospital units and contains over 1.8 million patient admissions. It uses a standardized data reporting form to collect patient characteristics and conditions, details of the critical illness, interventions, processes of care, and outcomes. VPS neither endorsed nor restricted our interpretation of these data. Certified data abstractors from participating institutions record information about each ICU patient from medical charts and submit data to the VPS using a standardized form. Each patient is given a unique code and de-identified data are then submitted to a central repository in compliance with the HIPAA. The VPS, LLC provides oversight for data collection, integrity, analysis, and reporting through staff, a science advisory board, and an executive database steering committee. A trained site coordinator reviews the data for the database. Periodic validation maintains a high inter-rater reliability (> 95%) (10).

This study included all index cardiac arrests for all ICU encounters submitted to the VPS system between January 1, 2010, and October 30, 2018, in patients less than 18 years old. In the VPS registry, CPR is defined as a resuscitation event requiring chest compressions and/or defibrillation and is listed as a procedure type with unique start time date stamp. Cardiopulmonary bypass (CPB) and extracorporeal membrane oxygenation

(ECMO) are also listed as procedure types with specific time stamps. Because E-CPR is not listed as a unique procedure or event, we defined an E-CPR event a priori as a CPR event in which the patient was supported on ECMO or CPB within 2 hours of initiation of CPR. VPS captures CPR duration, which is defined as the time chest compressions and/or defibrillation began to return of spontaneous circulation (ROSC) and/or initiation of ECMO support. Sustained ROSC is deemed to have occurred when chest compressions are not required for 20 consecutive minutes and signs of circulation persist. Patients who were placed on ECMO less than 20 minutes after ROSC were not included. For patients having multiple E-CPR events, only the index (first) E-CPR event was considered for analysis, like the Extracorporeal Life Support Organization, which defines E-CPR as being utilized when conventional CPR is unsuccessful in achieving sustained ROSC. Patients admitted to the ICU for primary indication of trauma as well as patients who go onto ECMO greater than 2 hours after cessation of CPR were excluded.

Patient and ICU admission characteristics included underlying illness categorization/cardiac status, primary diagnosis, discharge disposition, cardiac arrest event data, and all cardiac data such as procedure codes and dates. In addition, ICU level features were captured including licensed bad capacity, average annual ICU admission volume, training program status, and region. We collected diagnoses information for all cases and used only the primary diagnosis if there were multiple diagnoses listed for a patient. We classified primary diagnosis into cardiovascular, respiratory, neurologic, and infectious. Cardiac medical patients were identified if no cardiothoracic surgical procedure was performed at any point in the hospitalization prior to the CPR event while cardiac surgical patients were those with a documented cardiothoracic surgical procedure prior to the CPR event. Variables with greater than 10% missing data were not considered for regression analysis for survival outcome.

We grouped ICU types into two distinct categories: dedicated CICU and combined PICU/mixed type. A combined PICU/mixed unit was defined as an ICU in which children with both cardiac and noncardiac illnesses are cared for by the same medical team in the same space. Assumed differences in physician and nursing training and staffing models between dedicated CICUs and mixed/PICUs informed the decision to combine PICU and mixed type units thereby creating a dichotomous exposure variable that would reflect these differences in provider team coverage for patient populations.

We utilized survival to hospital discharge as the primary outcome, defined as discharge from the ECMO center to either home or another facility. Patient characteristics and outcomes for both critical care unit types were reported as medians with 25th and 75th percentiles, and/or with accompanying frequencies with percentages. We compared characteristics and outcomes by diagnosis group using quantile regression, chi-square test and Fisher exact test. We used independent and multivariable mixed effects logistic regression, accounting for correlation within hospital and patient to assess the association between characteristics and survival. The multivariable model includes all factors with a p value of less than 0.10 in the independent logistic regression and is then reduced by excluding factors due to collinearity if needed (assessed using variance inflation factor) and further reducing the model until all variables have a p value of less than 0.05. We performed all the analyses using Stata v 15 (StatCorp LLC, College Station, TX).

RESULTS

Over 1 million unique ICU admissions were reported to the VPS database over the 9-year study period, 2010–2019, of which 12,931 index cardiac arrest events were identified (1.3% prevalence) for 11,853 patients. Of these cardiac arrest events, 671 met inclusion criteria representing 650 unique patients with 5.2% (671/12,931) of cardiac arrest events progressing to E-CPR (**Fig. 1**). Of the 671 patients, 84% had underlying congenital heart disease (CHD). Most of the cohort was categorized as cardiac surgical (n = 400, 60%), while the remainder were categorized as cardiac medical (n = 271, 40%). Most admissions had a single E-CPR event (95.8%), and 28 admissions had more than one E-CPR event.

Patient level demographics, arrest event characteristics, and ICU level factors for the entire cardiac E-CPR cohort are detailed in **Table 1**. These events are also stratified by ICU type, CICU versus mixed, and reveal significant differences in comorbidities (e.g., infection),

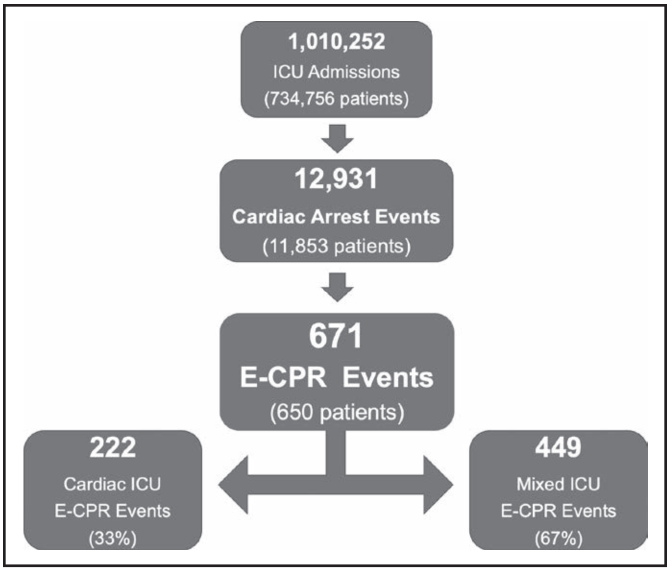

Figure 1. Event selection flow diagram. E-CPR = extracorporeal cardiopulmonary resuscitation.

AT THE BEDSIDE

- Survival to discharge after E-CPR across the Virtual Pediatric System registry ICUs was not associated with ICU cohort type (mixed ICU/PICU vs dedicated cardiac ICU).
- Patient-level factors and ICU bed capacity were associated with survival after E-CPR in the pediatric cardiac population.
- Further work is warranted to evaluate the potential for novel and unmeasured organizational/personnel explanatory factors associated with E-CPR outcomes in children with underlying cardiac disease.

CPR duration, licensed bed capacity and annual ICU admission volume, geographic distribution, and presence of fellowship training program between the ICU types. Outcomes after E-CPR reveal fewer differences between ICU types with no significant differences observed for ECMO duration, mechanical ventilation duration, or survival to hospital discharge on univariate analysis (**Table 2**).

Use of E-CPR in cardiac surgical patients, versus other patients, was associated with greater odds of survival to hospital discharge (odds ratio [OR], 1.40; 95% CI, 1.02–1.92; $p = 0.037$). We failed to identify an association between ICU type and improved survival to discharge (**Table 3**); however, on multivariable analysis greater ICU capacity was associated with lesser odds of survival to discharge (OR, 0.65; 95% CI, 0.43–0.96; $p = 0.032$). Cardiac patient category (surgical vs medical) remained significantly associated with greater odds of survival (OR, 2.03; 95% CI, 1.40–2.95; $p < 0.001$).

DISCUSSION

Our analysis of pediatric cardiac patients requiring E-CPR as reported to VPS revealed a low prevalence of ECMO utilization and confirms prior research suggesting patient level factors (i.e., cardiac surgical status) remain key explanatory factors in survival outcomes. Although we were unable to demonstrate significant associations between critical care cohort type and survival outcomes. In addition, several secondary outcomes evaluated in this analysis failed to reveal differences between critical care unit types including ECMO duration and mechanical ventilation duration.

While the cohorting of pediatric cardiac patients into dedicated CICUs began over 4 decades ago, evidence to support improved outcomes by this practice is limited (11, 12) and often confounded by patient-level and institutional factors such as annual admission and surgical volume (13–18). Single center and retrospective clinical/administrative database analyses of pediatric E-CPR outcomes have revealed improved outcomes for cardiac patients compared with noncardiac patients who are rescued from failed conventional CPR (2, 3, 6, 19–22). However, contradictory evidence also exists suggesting underlying illness category may have less of a role in outcome (7, 23, 24). These prior reports have approached E-CPR outcomes analyses by utilizing the illness categorization (i.e., cardiac vs noncardiac or surgical cardiac vs medical cardiac), rather than geography or care model (3, 23). Therefore, we approached this analysis from the perspective of organizational unit or ICU type. Although the sample size is skewed towards mixed/PICUs, the distribution of patient ages, those with medical versus surgical disease as well as those with documented CHD was found to be similar between unit types. In the VPS database, we failed to find an associated survival benefit for patients needing E-CPR cared for in dedicated CICUs as opposed to mixed/PICUs. We hope to explore potential mechanisms for this finding.

TABLE 1.

Baseline Patient, Event, and ICU Characteristics of Cardiac Patient Population, Stratified by ICU Type

Variable	Overall Cohort ($n = 671$), n (%)	Cardiac ICU ($n = 222$), n (%)	Mixed/PICU ($n = 449$), n (%)	p
Patient and event level factors				
Age				0.12
Neonate	274 (41)	103 (46)	171 (38)	
Infant (30 d to 2 yr)	252 (38)	80 (36)	172 (38)	
Child (2–12 yr)	101 (15)	25 (11)	76 (17)	
Adolescent (12–18 yr)	44 (7)	14 (960)	30 (5)	
Gender, male	348 (52)	122 (55)	226 (50)	0.29
Weight at admission, kg, median (IQR)	4.2 (3.1–9.5)	4.0 (3.0–7.5)	4.6 (3.2–10.4)	0.15
Cardiac patient category				0.28
Medical	271 (40)	83 (37)	188 (42)	
Surgical	400 (60)	139 (63)	261 (58)	
Comorbidities[a]				
Congenital heart disease	564 (84)	194 (87)	370 (82)	0.12
Infection	235 (35)	57 (26)	178 (40)	< 0.001
Neurologic	326 (49)	106 (48)	220 (49)	0.81
Respiratory	511 (76)	165 (74)	346 (77)	0.44
Event characteristics				
CPR duration, min, median (IQR)	45 (30–68)	50 (35–72)	43 (28–65)	0.006
Defibrillation during event	32 (5)	10 (5)	22 (5)	1.00
Intubation during event	116 (17)	38 (17)	78 (17)	1.00
Extracorporeal CPR day/time				
Night (11:00 PM–6:59 AM)	171 (26)	57 (27)	114 (26)	0.78
Weekend (Friday 11 PM–Monday 6:59 AM)	162 (25)	52 (24)	110 (25)	1.00
ICU level factors				
Licensed bed capacity				< 0.001
≤ 20	235 (35)	136 (61)	99 (22)	
> 20	436 (65)	86 (39)	350 (78)	
Average annual ICU admission volume				< 0.001
0–500	89 (13)	87 (39)	2 (< 1)	
501–1,000	268 (40)	131 (59)	137 (31)	
1,001–1,500	123 (18)	4 (2)	119 (27)	
1,501–2,000	68 (10)	0 (0)	68 (15)	
> 2,000	123 (18)	0 (0)	123 (27)	
Fellowship training, yes	492 (73)	198 (89)	294 (66)	< 0.001

(*Continued*)

TABLE 1. (*Continued*)
Baseline Patient, Event, and ICU Characteristics of Cardiac Patient Population, Stratified by ICU Type

Variable	Overall Cohort ($n = 671$), n (%)	Cardiac ICU ($n = 222$), n (%)	Mixed/PICU ($n = 449$), n (%)	p
Region				< 0.001
International	28 (4)	10 (5)	18 (4)	
Mid-West	315 (47)	83 (37)	232 (52)	
North-East	32 (5)	13 (6)	19 (4)	
South	189 (28)	41 (19)	148 (33)	
West	107 (16)	75 (34)	32 (7)	

CPR = cardiopulmonary resuscitation, IQR = interquartile range.

[a]Comorbidities are not mutually exclusive such that an individual ICU admission may have more than one comorbidity identified in the database.

TABLE 2.
Extracorporeal Cardiopulmonary Resuscitation Outcomes Stratified by ICU Type

Variable	Overall Cohort ($n = 671$), n (%)	Cardiac ICU ($n = 222$), n (%)	Mixed/PICU ($n = 449$), n (%)	p
Extracorporeal membrane oxygenation duration, hr	91 (49–153)	91 (56–159)	90 (44–148)	0.98
Mechanical ventilation duration, d	14 (6–31)	14 (7–27)	14 (5–34)	0.92
Length of ICU stay, d, median (interquartile range)	21 (8–50)	20 (11–40)	22 (8–53)	0.61
Survival to hospital discharge	342 (51)	113 (51)	229 (51)	1.00
Brain death[a]	14 (7)	6 (8)	8 (7)	0.79
Withdrawal of life sustaining therapy	221 (41)	71 (42)	150 (41)	0.78

[a]Brain death data is available for $n = 189$ of the 329 deaths.

In a study of the Kids' Inpatient Database, the prevalence of E-CPR utilization was 0.9% of CPR events between 2000 and 2006 (23), whereas our analysis of the VPS database revealed as a significantly higher utilization rate of E-CPR among CPR events (5.2%) between 2010 and 2018. This either could be related to differences in reporting between the two databases or could be related to a true increase in prevalence of E-CPR utilization over time. Furthermore, we demonstrate significant variability in E-CPR utilization across ICUs of varying size and academic type that have not been reported in prior studies.

Previous single-center reports have described outcomes following E-CPR in dedicated CICUs (21, 25, 26). Our study examined E-CPR outcomes from one of the largest multicenter PICU databases with a survival to hospital discharge like the rates in prior reports. We also we found that overall survival following E-CPR was equal between ICU types (CICU and PICU/mixed unit; both 51%). In leveraging the large VPS multicenter database, we acknowledge that an inherent selection bias may exists, which influence outcomes. In particular, mixed/PICU units that are capable of providing E-CPR and participate in VPS may differ from similar ICU types that do not participate in the database, and therefore limit the generalizability of the findings. The necessary multidisciplinary commitment of resources and expertise for the development and maintenance of an E-CPR program within mixed/PICU types also minimizes potential differences in care models with dedicated CICUs.

Although we failed to identify any association between survival and ICU cohort types, we pursued a secondary analysis evaluating ICU licensed bed capacity and its association with survival. In our analysis, a dichotomous breakdown of licensed bed capacity revealed lower odds of survival for ICUs with greater than 20 beds in comparison to those units with less than or equal to

TABLE 3.
Independent and Multivariable Logistic Regressions for Survival to Hospital Discharge

Variable	OR (95% CI)	*p*
Independent[a]		
Male	1.14 (0.84–1.55)	0.39
Age (reference: neonate)		0.76
Infant (30 d to 2 yr)	0.99 (0.70–1.40)	0.97
Child (2–12 yr)	0.95 (0.60–1.50)	0.82
Adolescent (12–18 yr)	0.71 (0.37–1.35)	0.29
Weight (per 1 kg increase)	1.00 (0.99–1.01)	0.49
ICU type (reference: mixed/PICU)		
Cardiac ICU	1.01 (0.71–1.44)	0.95
Licensed bed capacity (reference: ≤ 20 beds)		
> 20	0.71 (0.49–1.01)	0.056
Fellowship training, yes	0.91 (0.61–1.35)	0.64
Average annual ICU admission volume (reference: 0–500)		0.59
501–1,000	0.87 (0.52–1.47)	0.61
1,001–1,500	0.67 (0.38–1.18)	0.17
1,501–2,000	0.77 (0.39–1.52)	0.46
> 2,000	0.72 (0.41–1.26)	0.25
Region (reference: international)		0.55
Mid-West	1.59 (0.71–3.53)	0.26
North-East	1.18 (0.42–3.33)	0.76
South	1.31 (0.58–2.98)	0.52
West	1.16 (0.49–2.75)	0.74
Cardiac patient category (reference: medical)		
Surgical	1.40 (1.02–1.92)	0.037
Comorbidities		
Congenital heart disease	0.56 (0.37–0.87)	0.009
Infection	1.20 (0.86–1.66)	0.29
Neurological	0.70 (0.51–0.95)	0.021
Respiratory	1.47 (1.01–2.14)	0.045
E-CPR day/time		
Night (11:00 PM–6:59 AM; $n = 659$)	0.72 (0.51–1.03)	0.069
Weekend (Friday 11 PM–Monday 6:59 AM; $n = 659$)	0.76 (0.53–1.08)	0.13
Multivariable ($n = 659$)		
ICU beds (reference: ≤ 20 beds)		
> 20	0.65 (0.43–0.96)	0.032
Cardiac patient category (reference: medical)		
Surgical	2.03 (1.40–2.95)	< 0.001
Comorbidity: neurological	0.67 (0.49–0.93)	0.017
Comorbidity: respiratory	1.52 (1.02–2.26)	0.04
Comorbidity: congenital heart disease	0.35 (0.21–0.58)	< 0.001
E-CPR day/time: night (11:00 PM–6:59 AM)	0.67 (0.47–0.97)	0.035

E-CPR = extracorporeal cardiopulmonary resuscitation, OR = odds ratio.

[a]Total $n = 671$ unless otherwise specified.

20 beds. This observation seems at odds with the idea that high volume practice is associated with better outcomes (16)—here number of beds is being used as a surrogate marker of cardiac surgical case volume. While surgical volume is aligned with larger ICU capacity, our understanding of the observed survival association for smaller ICUs and those with mixed cohort models is more limited. A recent analysis of the PC4 database revealed a significant association between ICU average bed occupancy and cardiac arrest rates in the pediatric cardiac population (8). Although these authors found no associations between average daily occupancy and survival after cardiac arrest (i.e., rescue), the evaluation of non-Utstein factors such as bed capacity and staffing and their role in cardiac arrest prevalence and outcomes served as an impetus for the current investigation. Nonpatient level factors such as nurse/doctor:patient ratios, ICU strain in the form of higher admission/discharge volumes, and personnel training/experience level are challenging to measure and may vary across ICUs of different bed capacities, thus serving as important potentially modifiable factors to be included in future outcomes analyses in the cardiac arrest and E-CPR populations (8, 18, 27).

Our study had several limitations. Like other registry-based retrospective studies, limitations exist in regard to data entry and validity. Since VPS is a well-established database with periodic, random data quality reviews, we did not come across a significant level of missingness within the dataset. Since we defined E-CPR a priori based on time stamps related to initiation of CPR event and initiation of ECMO, it is possible that some E-CPR events were not included in the analysis. Since deploying ECMO during CPR is a resource-intensive event, we defined the E-CPR event using 2-hour rather than 1-hour cutoff to include most E-CPR events from the database. Also, although we were able to report CICU versus PICU/mixed unit outcomes of E-CPR, this ICU-specific database does not capture E-CPR occurring in non-ICU settings such as the operating room, cardiac catheterization laboratory, emergency room, or acute care ward. This limits our ability to generalize survival outcome differences for E-CPR occurring across in-hospital settings, especially events outside the ICU environment.

CONCLUSIONS

The overall prevalence of E-CPR among critically ill children with cardiac disease in the VPS database is low with significant variability in utilization across ICUs of varying size and patient cohort type. Patient and arrest-level characteristics remained associated with survival although ICU cohort type was not found to have an impact on survival. Further investigation into the impact of, yet, unmeasured organizational factors is warranted to further explore influences on outcomes after E-CPR in the pediatric cardiac population.

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