

Predictors of Pediatric In-Hospital Recurrent Cardiac Arrest

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Abstract

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In-hospital pediatric cardiac arrest is an important cause of morbidity and mortality. Approximately 16,000 children receive cardiopulmonary resuscitation (CPR) in the United States each year. Patients who suffer more than one cardiac arrest event are at a particularly increased risk of mortality, with survival to hospital discharge estimated to be 41-50%. Identification of patients who are likely to suffer a recurrent cardiac arrest has important implications for the clinician at the bedside. These high risk patients may benefit from more aggressive post-arrest therapies, including Extracorporeal Life Support. We performed a retrospective cohort study of pediatric patients (age < 18 years) who survived a cardiac arrest while in the Emergency Department or during inpatient admission at Seattle Children's Hospital from February 1, 2012 to September 18, 2019. Data were extracted from the Electronic Data Warehouse, Code Blue Database, and from individual patient charts. There were 259 patients identified who suffered at least one cardiac arrest and met all inclusion and exclusion criteria, 55 of these patients (21 percent) experienced a recurrent arrest. Prolonged duration of CPR was associated with an increased risk of recurrent arrest, with a RR of RR 2.2 (95% CI 0.9 - 5.5) for 21-50 minutes and RR 5.1 (95% CI 3.6 - 7.1) for >50 minutes. There was little or no association between recurrent arrest and unit of admission, primary diagnosis, organ dysfunction or the presence of acidosis preceding the initial arrest. Further work is required to determine whether there are other factors that can be used to identify patients in whom recurrent arrest is likely to occur.

Introduction

In-hospital pediatric cardiac arrest is an important cause of morbidity and mortality. Approximately 16,000 children receive cardiopulmonary resuscitation (CPR) in the United States each year[1]. When children experience a cardiac arrest while admitted to a hospital, survival to hospital discharge is estimated to be between 24-53%[1, 2]. Mortality is particularly high in patients who suffer more than one cardiac arrest event [3]. Gupta et al found that survival to hospital discharge was lower in patients with a recurrent arrest compared to those with a single arrest, 41% vs 53%, respectively [3].

Identification of patients who are likely to suffer a recurrent cardiac arrest has important implications for the clinician at the bedside of a patient with an initial arrest. The approach to management of the post-arrest patient is evolving, with many pediatric centers now utilizing Extracorporeal Life Support (ECLS) during and after cardiac arrest [2, 4, 5]. It can be a challenge to determine who is likely to obtain more benefit than harm from ECLS and what point in their course is the optimal time to initiate ECLS. Part of the decision to initiate ECLS therapy is a judgment concerning the likely trajectory of the illness. If there are features strongly associated with recurrent arrest, then these could be useful in helping clinicians identify their highest risk patients for whom ECLS may provide benefit.

Methods

Study Design:

We performed a retrospective cohort study of pediatric patients (age < 18 years) who survived a cardiac arrest while in the Emergency Department or during inpatient admission at Seattle Children's Hospital from February 1, 2012 to September 18, 2019. Patients were included for analysis if their initial arrest occurred at any time during inpatient admission or in the Emergency Department. Events were excluded if CPR for the initial arrest began prior to arrival to the Emergency Department. Additionally, since ECLS provides cardiac and respiratory support making cardiac arrest exceedingly unlikely, patients were excluded if they received ECLS either during or after their initial arrest event. This study was approved by the Seattle Children's Hospital Institutional Review Board (Study ID: 2123).

Data Extraction:

Demographic, clinical and laboratory data were extracted from the Seattle Children's Hospital Electronic Data Warehouse (EDW), which stores data from the Electronic Medical Record. The Code Blue Database was used to identify patients who sustained a cardiac arrest and to provide details of the arrest including duration of CPR. Diagnosis information was obtained from data submitted by Seattle Children's Hospital to the VPS database. Individual patient charts were reviewed when required to obtain data missing from the above sources.

Outcome Measure:

Recurrent arrest was defined as a second arrest involving receipt of CPR after the initial one, with at least 20 minutes of spontaneous circulation between the two events.

Statistical Analysis:

The relative risk (RR) of recurrent arrest was calculated, with 95% confidence intervals (CI), for multiple demographic and clinical factors. The presence of all exposures and characteristics to be considered were those that were ascertained at or before the beginning of the first arrest. For the purpose of assessing the presence of organ dysfunction, acute kidney injury was defined as serum creatinine > 1.5 times the upper limit of normal for age[6]. Hepatic dysfunction was defined by total bilirubin > 4 mg/dL or ALT 2 times the upper limit of normal for age and thrombocytopenia was defined as platelet count $< 80,000/\text{mm}^3$ [7]. Laboratory values used to assess the presence of acute kidney injury, hepatic dysfunction and thrombocytopenia were considered for the 48 hour period preceding the first arrest. Blood gas analyses, including pH, serum lactate and pCO₂ values, were obtained from the 24 hours preceding the first arrest. For purposes of this analysis, the most abnormal blood gas values were selected from each subject. For analysis, patients with moderate and severe derangements in their pH, lactate or pCO₂ were compared to patients with normal values. Hypotension was defined as mean arterial pressure < 5 th percentile for age in the 12 hours preceding the first arrest, and hypoxia was defined as oxygen saturation less than 88% in the 4 hours preceding the first arrest. Statistical analysis was performed using R-Studio Version 1.1.463.

Results:

There were 259 patients identified who suffered at least one cardiac arrest and met all inclusion and exclusion criteria. Of these patients, 55 experienced a recurrent arrest (Table 1). The study population was 55% male, and the majority of patients (71%) were less than 1 year of age at the time of their first event.

Table 1. Patient Demographic Characteristics

		Total Patients	Number with Recurrent Arrest	Recurrent Arrest Cumulative Incidence [^]	RR	95% CI
Number		259	55	21		
Sex						
	Female	115	32	28	Ref	-
	Male	144	24	17	0.6	0.4 - 1.0
Age						
	< 3 months	111	16	14	Ref	-
	3 months to 1 year	72	18	25	1.7	0.9 - 3.2
	1 to < 4 years	39	10	26	1.8	0.9 - 3.6
	4 to < 12 years	21	3	14	1.0	0.3 - 3.1
	12 to < 18 years	16	8	50	3.5	1.8 - 6.8
[^] per 100 with an initial arrest event; *Median (IQR); RR = Relative Risk of recurrent arrest in patients with the characteristic compared to those without; 95% CI = 95% Confidence Interval						

Male sex was associated with a lower RR of recurrent arrest (0.6, 95% CI 0.4 – 1.0). Risk of recurrent arrest was higher in both the 3 month to 1 year and 1 to 4 year age groups compared to those under 3 months, RR 1.7 (95% CI 0.9 - 3.2) and 1.8 (95% CI 0.9 - 3.6) respectively. Patients 12 to < 18 years of age had a RR of recurrent arrest of 3.5 (95% CI 1.8 - 6.8) compared to patients under 3 months.

The risk of recurrent arrest in patients with organ failure is displayed in Table 2. Patients who had pre-arrest acute kidney injury had a RR of 2.4 (95% CI 1.1 - 4.7) for recurrent arrest. There was a suggestion that hepatic dysfunction, thrombocytopenia, and hypoxia were associated with a lower risk of recurrent

arrest, with RRs of 0.4 (95% CI 0.1 - 1.5), 0.6 (95% CI 0.3 - 1.4), and 0.7 (95% CI 0.4 - 1.7), respectively.

Hypotension bore little relation to the risk of recurrent arrest, RR 1.2 (95% CI 0.6 - 2.1).

Table 2. Measures of Association between Organ Failure and Recurrent Arrest

	Total Patients	Number with Recurrent Arrest	Recurrent Arrest Cumulative Incidence [^]	RR	95% CI	Number Missing
Acute Kidney Injury	10	5	50	2.4	1.1 - 4.7	93
Hepatic Dysfunction	30	3	10	0.4	0.1 - 1.5	214
Thrombocytopenia	33	5	15	0.6	0.3 - 1.4	116
Hypotension	99	23	23	1.2	0.6 - 2.1	95
Hypoxia	134	23	17	0.7	0.4 - 1.7	18

[^]per 100 with an initial arrest event; RR = Relative Risk of recurrent arrest in patients with the characteristic compared to those without; 95% CI = 95% Confidence Interval;

Table 3. Measures of Association between Clinical Features and Recurrent Arrest

	Total Patients	Number with Recurrent Arrest	Recurrent Arrest Cumulative Incidence [^]	RR	95% CI	Number Missing
Unit						0
PICU	91	22	24	Ref	-	
CICU	97	22	23	0.9	0.6 - 1.6	
NICU	67	10	15	0.6	0.3 - 1.2	
Inpatient Unit	4	1	25	1.0	0.2 - 5.9	
Primary Diagnosis						0
Cardiovascular	86	16	19	Ref	-	
Respiratory	84	25	30	1.6	0.9 - 2.8	
Infection	16	3	19	1.0	0.3 - 3.1	
Prematurity	40	7	18	0.9	0.4 - 2.1	
Congenital Anomaly	12	1	8	0.4	0.1 - 3.1	
Miscellaneous	21	3	11	0.8	0.2 - 2.4	
Compression Duration*						5
1-3 Minutes	137	27	20	Ref	-	
4-10 Minutes	80	17	21	1.1	0.6 - 1.9	
11-20 Minutes	28	5	18	0.9	0.4 - 2.1	
21-50 Minutes	7	3	43	2.2	0.9 - 5.5	
> 50 Minutes	1	1	100	5.1	3.6 - 7.1	

[^]per 100 with an initial arrest event; *Duration of the first cardiac arrest event; RR = Relative Risk of recurrent arrest in patients with the characteristic compared to those without; 95% CI = 95% Confidence Interval

Table 3 displays the association between unit of admission, primary diagnosis and duration of CPR and recurrent arrest. Admission to the neonatal intensive care unit (NICU) was associated with a relatively low risk of recurrent arrest, RR 0.6 (0.3 - 1.2); the risk of recurrent arrest was similar in the other units. Risk of recurrent arrest was similar among the primary diagnosis categories, with the exception of primary respiratory diagnoses (RR 1.6, 95% CI 0.9 - 2.8) and congenital anomalies (RR 0.4, 95% CI 0.1 - 3.1). Patients with >20 minutes of CPR in their first arrest had higher risk of a second arrest than did patients whose initial CPR lasted 20 or fewer minutes, with an RR of 2.2 (95% CI 0.9 - 5.5) for 21-50 minutes and of 5.1 (95% CI 3.6 - 7.1) for >50 minutes.

Patients with acidosis, even when severe, had similar risk of recurrent arrest as those with a normal pH (Table 4). Elevated serum lactate was associated with a 30%-50% lower risk of recurrent arrest, but the small number of patients with these values argues for a cautious interpretation. There was a suggestion that severe respiratory acidosis, with pCO₂ > 69, was associated with an increased risk of recurrent arrest (RR 1.5 95% CI 0.7 - 3.3).

Table 4. Measures of Association between Degree of Acidosis and Recurrent Arrest

		Total Patients	Number with Recurrent Arrest	Recurrent Arrest Cumulative Incidence [^]	RR	95% CI	Number Missing
Acidosis							71
	None	53	11	21	Ref	-	
	Moderate (pH 7.15 - 7.35)	90	17	19	0.9	0.5 - 1.8	
	Severe (pH < 7.15)	45	11	24	1.2	0.6 - 2.5	
Lactate							157
	Normal	56	11	20	Ref	-	
	2.3 - 4.0 mmol/L	11	1	9	0.5	0.1 - 3.2	
	> 4.0 mmol/L	35	5	14	0.7	0.3 - 1.9	
pCO₂							88
	Normal	48	9	19	Ref	-	
	46 - 69 mmHg	88	17	19	1.0	0.5 - 2.0	
	> 69 mmHg	37	11	30	1.5	0.7 - 3.3	
[^] per 100 with an initial arrest event; RR = Relative Risk of recurrent arrest in patients with the characteristic compared to those without; 95% CI = 95% Confidence Interval							

Discussion:

In this study of hospitalized pediatric patients who sustained an initial cardiac arrest, the cumulative incidence of recurrent arrest during hospitalization was 21 per 100. The only strong predictor of recurrent arrest was a relatively long duration of the initial arrest: there was no clear altered risk associated with patient characteristics, even those indicative of a relatively more serious condition. One possible explanation is that clinicians may have identified these patients as potentially higher risk and initiated more aggressive therapies to prevent a subsequent arrest.

If identifiable, patients at increased risk for a poor outcome may benefit from ECLS in the post-arrest period. In fact, de Mos, et al found that receiving ELCS therapy in the post-arrest period was associated with increased survival to hospital discharge[8]. They also demonstrated that there are pre-arrest clinical factors, including organ dysfunction and hypotension requiring vasoactive infusions, that are associated with increased mortality[8]. Our data suggest that patients with prolonged duration of CPR may be at increased risk for recurrent arrest. Potentially, this may be the group of patients for whom the benefits of ECLS therapy outweighs the harm.

One strength of this study is the breadth of diagnoses considered. Patients were included from all locations in the hospital, including the Pediatric, Cardiac and Neonatal ICUs, making the results more generalizable. Another strength is that the use of data extracted in bulk from the electronic medical record allowed us to obtain detailed information about a wide variety of clinical variables.

This study has several important limitations, the first of which is that some variables had a high proportion of missing data. Since the data were collected retrospectively, it was not possible to prevent or correct this. Second, all of the patients included were from a single quaternary pediatric center, so the results of this study may not be generalizable to some other settings. The relatively small number of patients limited our ability to detect any but the strongest associations. All factors included in this analysis were assessed at the time of the index arrest event. While this provides information for the clinician at the bedside about their patient's risk of recurrent arrest without having to wait for further evolution of their clinical status, it meant that we could not examine predictors of recurrent arrest that were present after treatment for the initial arrest had been completed. Lastly, since this study was limited to patients who had the potential to

have a second arrest, patients who received ECLS during or after their initial arrest were excluded. Although this group of patients was small (18 total), there may be important differences between patients who did and did not receive ECLS.

Conclusions:

This study observed a cumulative incidence of recurrent arrest during hospitalization of 21 per 100 patients with an initial cardiac arrest. There is some evidence that longer duration of the initial arrest is associated with increased risk of a recurrent arrest. The small number of patients in this study may have prevented the identification of associations of smaller magnitude. Further work is required to determine whether there are other factors that can be used to identify patients at increased risk of recurrent arrest.

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