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Clinical paper

Factors associated with survival and neurologic outcome after in-hospital cardiac arrest in children: A cohort study

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Abstract

Aim: In-hospital paediatric cardiopulmonary resuscitation (CPR) survival has been improving in high-income countries. This study aimed to analyse factors associated with survival and neurological outcome after paediatric CPR in a middle-income country.

Methods: This observational study of in-hospital cardiac arrest using Utstein-style registry included patients <18 years old submitted to CPR between 2015 and 2020, at a high-complexity hospital. Outcomes were survival and neurological status assessed using Paediatric Cerebral Performance Categories score at prearrest, discharge, and after 180 days.

Results: Of 323 patients who underwent CPR, 108 (33.4%) survived to discharge and 93 (28.8%) after 180 days. In multivariable analysis, lower survival at discharge was associated with liver disease (OR 0.060, CI 0.007–0.510, $p = 0.010$); vasoactive drug infusion before cardiac arrest (OR 0.145, CI 0.065–0.325, $p < 0.001$); shock as the immediate cause (OR 0.183, CI 0.069–0.486, $p = 0.001$); resuscitation > 30 min (OR 0.070, CI 0.014–0.344, $p = 0.001$); and bicarbonate administration during CPR (OR 0.318, CI 0.130–0.780, $p = 0.01$). The same factors remained associated with lower survival after 180 days. Neurological outcome was analysed in the 93 survivors after 180 days following CPR. Prearrest neurological dysfunction was observed in 31.4%, and neurological prognosis was favourable in 79.7% at discharge and similar after 180 days.

Conclusion: In-hospital paediatric cardiac arrest patients with complex chronic conditions had lower survival associated with liver disease, shock as cause of cardiac arrest, vasoactive drug infusion before cardiac arrest, bicarbonate administration during CPR, and prolonged resuscitation. Most survivors had favourable neurological outcome.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, In-hospital cardiac arrest, Pediatric, Prognostic factors, Neurological outcome

Introduction

Cardiac arrest is an infrequent event in the paediatric population compared to that in adults.[1,2] The estimated annual incidence in the United States is 292,000 cases in adults and 15,200 cases in children, posing a major challenge for conducting paediatric studies with robust data.[2]

The literature reports great variation in paediatric cardiac arrest outcomes due to different populations analysed, hospital and department characteristics, different outcomes, level of development between countries, and study periods.[1,3–7] However, there is a trend toward improved survival to discharge rate as high as 43% to 45%, in high-income countries.[8,9] In addition to survival, reports on neurological prognosis have gained increasing importance in paediatric resuscitation studies.[1,3,9–13]

An increased paediatric population with pre-existing chronic conditions has also been observed, reaching more than 50% of patients in paediatric intensive care.[14,15] Another subgroup of the paediatric population with increasing importance is patients with complex chronic conditions, defined as any condition expected to last at least 12 months, involving one major organ or with systemic involvement, requiring specialized follow-up, or involving hospitalization in a tertiary centre.[16] This population has a high mortality rate and a greater need for intensive care and length of stay[17]; however, the factors associated with the prognosis of cardiac arrest in children with complex chronic conditions are unclear.

Most studies on in-hospital paediatric cardiac arrest involve large cardiopulmonary resuscitation (CPR) registries, multicentre studies,

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and single-centre studies with voluntary participation, with data especially concentrated in high-income countries.[3,4,18–25] The epidemiology of paediatric cardiac arrest was identified by the International Liaison Committee on Resuscitation as a priority area for larger studies.[26]

The primary objective of this study was to evaluate the factors associated with survival at discharge and after 180 days. The secondary objective was to analyse the neurological outcome.

Methods

Design, setting and patients

This observational study used data derived from the hospital cardiac arrest record that followed the Utstein style[27] and had been filled out by the professionals responsible for patient care. The Paediatric Cerebral Performance Category (PCPC) score was used to assess neurological function through the analysis of medical records and interviews with professionals and family members. Neurological function was classified as favourable (Paediatric Cerebral Performance Category 1 or 2 or no change from baseline) or unfavourable (Paediatric Cerebral Performance Category $\geq$ 3). Only the index event was considered.

The data were collected during the period between January 1, 2015 and December 31, 2020 from a single center, which is a quaternary university public paediatric hospital with a rapid response team and a paediatric early warning system. Extracorporeal cardiopulmonary resuscitation is not offered during CPR. It is located in Sao Paulo, Brazil, in the biggest hospital complex of the country.

The study was approved by the local ethics and research committee, CAAE: 29237420.7.0000.0068. A presumed consent form was used due to the difficulty in obtaining a signature in extreme emergency situations.[28–30]

Participants

The study population included patients <18 years of age undergoing in-hospital cardiac arrest. The exclusion criteria were patients who did not receive CPR, out of hospital cardiac arrest, children with sur-

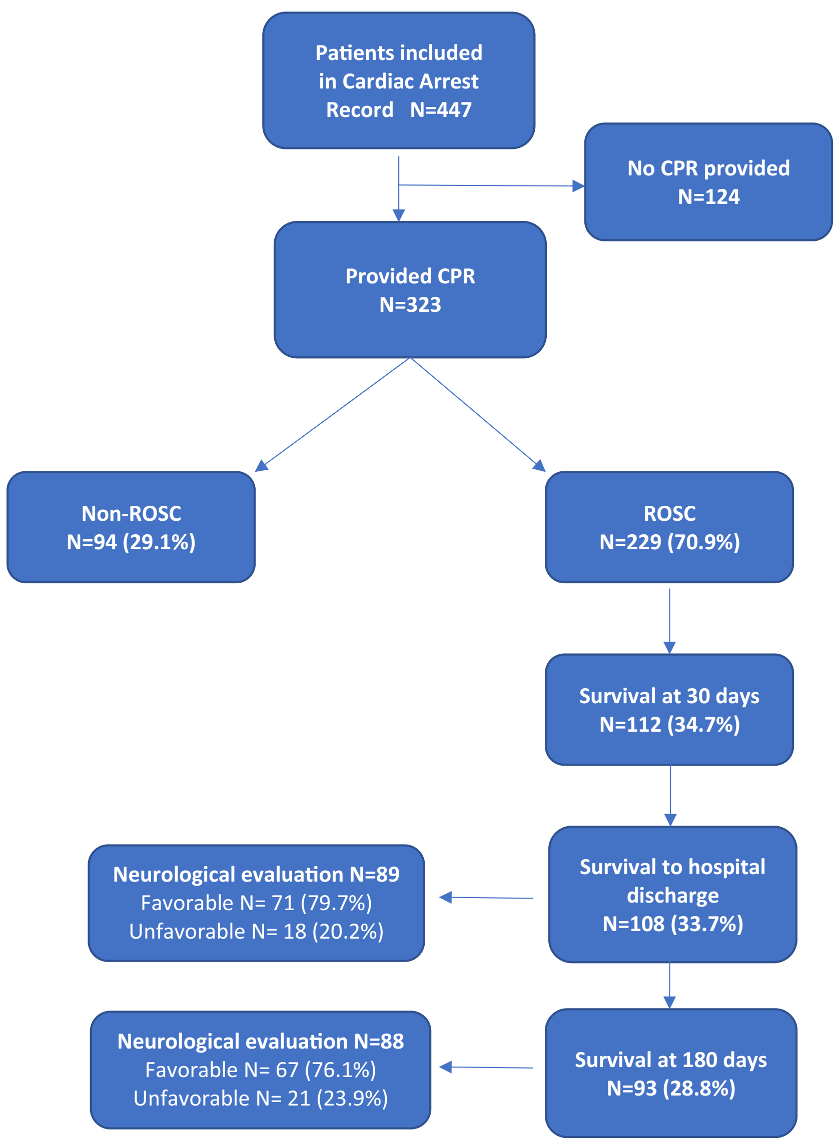

Fig. 1 – Patient inclusion flowchart and neurological outcome. CPR: cardiopulmonary resuscitation, ROSC: return of spontaneous circulation.

gical cardiac diseases, trauma patients, and cardiac arrest in the delivery room. Trauma patients and patients with surgical heart diseases were treated in other sectors of the hospital complex.

Of the initial 447 patients, 323 were eligible, corresponding to the study population.

Independent variables

The data on the following variables were collected: sex, age, day of the week, period of the day and year when the cardiac arrest occurred, complex chronic conditions category, event location, interventions in place at time of cardiac arrest (mechanical ventilation, vasoactive drug infusion), immediate cause of cardiac arrest, duration of CPR attempt, initial cardiac rhythm, and drugs used during CPR (adrenaline, bicarbonate, and calcium). Paediatric Cerebral Performance Category score was evaluated in the periods prearrest, at discharge, and after 180 days. Dose, time, and interval of adrenaline administration; CPR quality parameters; and post-cardiac arrest care variables were not analysed.

Outcomes

Outcomes included survival and neurological status at hospital discharge and after 180 days. Neurological function was assessed using the Paediatric Cerebral Performance Category score prearrest, at discharge, and after 180 days.

Statistical analyses

Statistical analyses were conducted using IBM SPSS software version 24 and R software version 3.5. Outcomes were compared between groups using the Pearson's chi-square test or Fisher's exact test for categorical variables. Univariable and multivariable logistic regression analyses were performed to assess the effect of each one of the factors on survival to hospital discharge and survival at 180 days. All individual factors with statistical significance in the univariable analysis and *p*-value <0.10 were eligible for inclusion in the logistic regression model. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for each model. *P* values less than 0.05 were considered significant.

Results

Of 323 patients who underwent CPR, 229 (70.9%) achieved return of spontaneous circulation (ROSC), 112 (34.7%) survived after 30 days, 109 (33.7%) to discharge, and 93 (28.8%) after 180 days (Fig. 1).

The characteristics of the study population are presented in Table 1. The following variables showed statistically significant differences: complex chronic conditions category, event location, day of the week and time of cardiac arrest, interventions prior to CPR (vasoactive drug infusion and mechanical ventilation), immediate car-

Table 1 – Characteristics of survivors versus non-survivors at hospital discharge.

Characteristics	Total n (%) N = 323	Survival to hospital discharge: Survivors n (%) N = 109	No survivors n (%) N = 214	*P*-value
Year				
2015	65 (20.1)	24 (22.0)	41 (19.2)	0.19
2016	64 (19.8)	21 (19.3)	43 (20.1)	
2017	59 (18.3)	15 (13.8)	44 (20.6)	
2018	43 (13.3)	10 (9.2)	33 (15.4)	
2019	47 (14.6)	20 (18.3)	27 (12.6)	
2020	45 (13.9)	19 (17.4)	26 (12.1)	
Age group				
<1 month	74 (22.9)	19 (17.4)	55 (25.7)	0.06
≥1 month–1 year	119 (36.8)	50 (45.9)	69 (32.2)	
≥1–12 years	107 (33.1)	35 (32.1)	72 (33.6)	
≥12 years old	23 (7.1)	5 (4.6)	18 (8.4)	
Sex				
Female	164 (50.8)	61 (56)	103 (48.1)	0.18
Male	159 (49.2)	48 (44)	111 (51.9)	
Complex chronic condition				
No	12 (3.7)	8 (7.3)	4 (1.9)	**0.01**
Yes	311 (96.3)	101 (92.7)	210 (98.1)	
Disease categories				
Prenatal condition or complications	83 (25.7)	26 (23.9)	57 (26.6)	**0.002**
Hepatic	77 (23.8)	14 (12.8)	63 (29.4)	
Genetic or metabolic	59 (18.3)	21 (19.3)	38 (17.8)	
Oncohematologic or immunologic	27 (8.4)	10 (9.2)	17 (7.9)	
Other	65 (20.1)	30 (27.5)	35 (16.4)	
Event location				
PICU	259 (80.2)	77 (70.6)	182 (85.0)	**0.005**
Emergency department	29 (9.0)	11 (10.1)	18 (8.4)	
OR/Endoscopy/Diagnostic area	25 (7.7)	15 (13.8)	10 (4.7)	
Wards	10 (3.1)	6 (5.5)	4 (1.9)	

(*continued on next page*)

Table 1 (continued)

Characteristics	Total n (%) N = 323	Survival to hospital discharge Survivors n (%) N = 109	No survivors n (%) N = 214	*P*-value
Period of the week				
Weekday	237 (73.4)	83 (76.1)	154 (72.0)	0.42
Weekend	86 (26.6)	26 (23.9)	60 (28.0)	
Period of the day				
Day (7 am–6:59 pm)	184 (57.0)	77 (70.6)	107 (50.0)	**<0.001**
Night (7 pm–6:59 am)	139 (43.0)	32 (29.4)	107 (50.0)	
Witnessed				
No	2 (0.6)	1 (0.9)	1 (0.5)	0.62
Yes	321 (99.4)	108 (99.1)	213 (99.5)	
Previous interventions				
Mechanical ventilation				
No	88 (27.2)	43 (39.4)	45 (21.0)	**0.002**
Yes	232 (71.8)	65 (59.6)	167 (78.0)	
Unknown	3 (0.9)	1 (0.9)	2 (0.9)	
Vasoactive drugs				
No	168 (52.0)	90 (82.6)	78 (36.4)	**<0.001**
Yes	152 (47.1)	18 (16.5)	134 (62.6)	
Unknown	3 (0.9)	1 (0.9)	2 (0.9)	
Immediate cause				
Respiratory	153 (47.4)	78 (71.6)	75 (35.0)	**<0.001**
Shock	121 (37.5)	10 (9.2)	111 (51.9)	
Metabolic	32 (9.9)	9 (8.3)	23 (10.7)	
Arrhythmia	8 (2.5)	5 (4.6)	3 (1.4)	
Unknown	9 (2.8)	7 (6.4)	2 (0.9)	
Rhythm				
Bradycardia	181 (56.0)	69 (63.3)	112 (52.3)	0.16
PEA	77 (23.8)	24 (22.0)	53 (24.8)	
Asystole	49 (15.2)	10 (9.2)	39 (18.2)	
VT/VF	10 (3.1)	3 (2.8)	7 (3.3)	
Unknown	6 (1.9)	3 (2.8)	3 (1.4)	
CPR duration				
Up to 5 min	130 (40.2)	65 (59.6)	65 (30.4)	**<0.001**
>5–15 min	87 (26.9)	28 (25.7)	59 (27.6)	
>15–30 min	61 (18.9)	12 (11)	49 (22.9)	
>30 min	42 (13.0)	3 (2.8)	39 (18.2)	
Unknown	3 (0.9)	1 (0.9)	2 (0.9)	
Epinephrine				
No	38 (11.8)	25 (22.9)	13 (6.1)	**<0.001**
Yes	285 (88.2)	84 (77.1)	201 (93.9)	
Bicarbonate				
No	186 (57.6)	89 (81.7)	97 (45.3)	**<0.001**
Yes	137 (42.4)	20 (18.3)	117 (54.7)	
Calcium				
No	226 (70.0)	91 (83.5)	135 (63.1)	**<0.001**
Yes	97 (30.0)	18 (16.5)	79 (36.9)	

Subtitles PICU, paediatric intensive care unit; OR, operating room; PEA, pulseless electrical activity; VT, pulseless ventricular taquicardia; VF, ventricular fibrilation; CPR, cardiopulmonary resuscitation. Significant values in bold.

diac arrest cause, CPR duration, and drugs given during CPR (adrenaline, bicarbonate, and calcium).

Patients <1 year old (59.7%) constituted the dominant population. Nearly the entire sample (96.3%) had a complex chronic conditions, the most frequent being prenatal conditions and complications (25.7%) and liver diseases (23.8%), followed by genetic-metabolic diseases (18.3%) and onco-hematologic and immunological diseases (8.4%).

The intensive care unit (ICU) was the location with the highest number of CPR occurrences (80.2%), followed by those in the emergency room (9%), operating room (7.7%), and wards (3.1%). CPR events were proportionally similar between weekdays and weekends, and 57% were during the daytime period.

Of the interventions in place prior to CPR, it is noteworthy that most patients (71.8%) were under mechanical ventilation and nearly half (47.1%) were on vasoactive drug support, reflecting the severity of the patient's condition. The primary immediate causes were respiratory (47.4%) and shock-related (37.5%), followed by metabolic (9.9%) and arrhythmias (2.5%).

Bradycardia, pulseless electrical activity, and asystole were the most frequent initial rhythms, and the presence of shockable rhythms was rare (3.1%). Short-duration CPR (up to 15 minutes) occurred in

Table 2 – Regression analysis for characteristics associated with survival to hospital discharge.

Characteristics	Univariate			Multivariate		
	OR	CI (95%)	*P*-value	OR	CI (95%)	*P*-value
Age group						
<1 month	0.477	[0.252; 0.901]	**0.02**	0.954	[0.349; 2.609]	0.92
≥1 month–<1 year	1.000	–	–	1.000	–	–
≥1 year–<12 years	0.671	[0.389; 1.155]	0.15	0.997	[0.421; 2.361]	0.99
≥12 years old	0.383	[0.133; 1.102]	0.07	0.341	[0.068; 1.724]	0.19
Sex						
Female	1.000	–	–			
Male	0.730	[0.459; 1.161]	0.18			
Complex chronic conditions						
No	1.000	–	–			
Yes	0.240	[0.071; 0.817]	**0.02**			
Disease categories						
Absent	1.000	–	–	1.000	–	–
Hepatic	0.111	[0.029; 0.421]	**0.001**	0.060	[0.007; 0.510]	**0.010**
Prenatal condition or complications	0.228	[0.063; 0.826]	**0.02**	0.248	[0.030; 2.036]	0.19
Other	0.429	[0.117; 1.566]	0.20	0.119	[0.015; 0.933]	**0.04**
Oncohematologic or immunologic	0.294	[0.070; 1.232]	0.09	0.288	[0.031; 2.632]	0.27
Genetic or metabolic	0.276	[0.074; 1.027]	0.05	0.134	[0.016; 1.190]	0.06
Event location						
PICU	1.000	–	–	1.000	–	–
Wards	3.545	[0.973; 12.917]	0.05	2.094	[0.229; 19.134]	0.51
Emergency department	1.444	[0.652; 3.202]	0.36	0.796	[0.232; 2.737]	0.71
OR/Endoscopy/Diagnostic area	3.545	[1.525; 8.240]	**0.003**	18.977	[3.832; 93.976]	**<0.001**
Period of the week						
Weekday	1.000	–	–			
Weekend	0.804	[0.472; 1.369]	0.42			
Period of the day						
Day (7 h–18 h59)	1.000	–	–	1.000	–	–
Night (7 pm–6.59am)	0.416	[0.254; 0.679]	**<0.001**	0.890	[0.418; 1.894]	0.76
Previous interventions						
Mechanical ventilation						
No	1.000	–	–	1.000	–	–
Yes	0.407	[0.245; 0.676]	**0.001**	0.721	[0.322; 1.610]	0.42
Vasoactive drugs						
No	1.000	–	–	1.000	–	–
Yes	0.116	[0.065; 0.207]	**<0.001**	0.145	[0.065; 0.325]	**<0.001**
Immediate cause						
Respiratory	1.000	–	–	1.000	–	–
Shock/hypotension	0.087	[0.042; 0.178]	**<0.001**	0.183	[0.069; 0.486]	**0.001**
Metabolic/Arrhythmia/Sudden/Unknown	0.721	[0.377; 1.379]	0.32	1.739	[0.632; 4.784]	0.28
Rhythm						
Bradycardia	1.000	–	–	1.000	–	–
Assistolia	0.416	[0.195; 0.887]	**0.02**	0.911	[0.310; 2.682]	0.86
PEA	0.735	[0.417; 1.297]	0.28	1.393	[0.567; 3.422]	0.47
VT/VF	0.696	[0.174; 2.780]	0.60	0.391	[0.044; 3.474]	0.39
Unknown	1.623	[0.319; 8.269]	0.56	0.781	[0.051; 12.050]	0.85
CPR duration						
Up to 5 min	1.000	–	–	1.000	–	–
>5–15 min	0.475	[0.269; 0.836]	**0.010**	0.807	[0.353; 1.845]	0.61
>15–30 min	0.245	[0.119; 0.503]	**<0.001**	0.317	[0.106; 0.950]	0.04
>30 min	0.077	[0.023; 0.261]	**<0.001**	0.070	[0.014; 0.344]	**0.001**
Epinephrine						
No	1.000	–	–	1.000	–	–
Yes	0.217	[0.106; 0.445]	**<0.001**	0.517	[0.171; 1.561]	0.24
Bicarbonate						
No	1.000	–	–	1.000	–	–
Yes	0.186	[0.107; 0.324]	**<0.001**	0.318	[0.130; 0.780]	**0.01**
Calcium						
No	1.000	–	–	1.000	–	–
Yes	0.338	[0.190; 0.602]	**<0.001**	1.022	[0.403; 2.589]	0.96

95% CI indicates 95% confidence interval; OR, odds ratio; PICU, paediatric intensive care unit; OR; operating room; PEA, pulseless electrical activity; VT, pulseless ventricular tachycardia; VF, ventricular fibrillation. Significant values in bold.

Table 3 – Regression analysis for characteristics associated with survival at 180 days.

Characteristics	Univariate			Multivariate		
	OR	CI (95%)	*P*-value	OR	CI (95%)	*P*-value
Age group						
<1 month	0.612	[0.314; 1.192]	0.14	1.603	[0.574; 4.474]	0.36
≥1 month–<1 year	1.000	–	–	1.000	–	–
≥1 year–<12 years	0.928	[0.527; 1.633]	0.79	1.588	[0.669; 3.769]	0.29
≥12 years old	0.570	[0.197; 1.652]	0.30	0.651	[0.135; 3.130]	0.59
Sex						
Female	1.000	–	–	1.000	–	–
Male	0.610	[0.374; 0.995]	**0.04**	0.554	[0.280; 1.097]	0.09
Complex chronic conditions						
No	1.000	–	–	–	–	–
Yes	0.221	[0.063; 0.775]	**0.01**	–	–	–
Disease categories						
No	1.000	–	–	1.000	–	–
Hepatic	0.105	[0.027; 0.417]	**0.001**	0.070	[0.007; 0.693]	**0.02**
Prenatal condition or complications	0.178	[0.047; 0.674]	**0.01**	0.159	[0.016; 1.534]	0.11
Other	0.406	[0.108; 1.526]	0.18	0.122	[0.013; 1.120]	0.06
Oncohematologic or immunologic	0.336	[0.078; 1.441]	0.14	0.310	[0.030; 3.220]	0.32
Genetic or metabolic	0.251	[0.065; 0.965]	**0.04**	0.131	[0.014; 1.266]	0.07
Event location						
PICU	1.000	–	–	1.000	–	–
Wards	4.669	[1.276; 17.084]	**0.02**	4.550	[0.474; 43.628]	0.18
Emergency department	1.902	[0.852; 4.246]	0.11	1.291	[0.368; 4.530]	0.69
OR/Endoscopy/Diagnostic area	3.962	[1.711; 9.176]	**0.001**	11.858	[2.540; 55.349]	**0.002**
Period of the week						
Weekday	1.000	–	–			
Weekend	0.920	[0.531; 1.593]	0.76			
Period of the day						
Day (7 am – 6:59 pm)	1.000	–	–	1.000	–	–
Night (7 pm – 6:59 am)	0.416	[0.248; 0.699]	**0.001**	0.762	[0.355; 1.635]	0.48
Previous interventions						
Mechanical ventilation						
No	1.000	–	–	1.000	–	–
Yes	0.492	[0.292; 0.831]	**0.008**	1.037	[0.464; 2.317]	0.93
Vasoactive drugs						
No	1.000	–	–			
Yes	0.136	[0.075; 0.249]	**<0.001**	0.192	[0.085; 0.437]	**<0.001**
Immediate cause						
Respiratory	1.000	–	–	1.000	–	–
Shock/hypotension	0.088	[0.040; 0.194]	**<0.001**	0.163	[0.057; 0.472]	**0.001**
Metabolic/Arrhythmia/Sudden/Unknown	0.719	[0.370; 1.397]	0.33	1.271	[0.470; 3.436]	0.63
Rhythm						
Bradycardia	1.000	–	–	1.000	–	–
Assistolia	0.394	[0.173; 0.893]	**0.02**	0.628	[0.210; 1.879]	0.40
PEA	0.756	[0.419; 1.365]	0.35	1.034	[0.429; 2.491]	0.94
TV/FV	0.864	[0.216; 3.464]	0.83	0.345	[0.037; 3.250]	0.35
Unknown	1.345	[0.219; 8.267]	0.74	0.787	[0.031; 19.699]	0.88
CPR duration						
Up to 5 min	1.000	–	–	1.000	–	–
>5–15 min	0.523	[0.291; 0.942]	**0.03**	0.978	[0.431; 2.217]	0.95
>15–30 min	0.331	[0.161; 0.682]	**0.003**	0.513	[0.167; 1.571]	0.24
>30 min	0.068	[0.016; 0.292]	**<0.001**	0.048	[0.007; 0.340]	**0.002**
Epinephrine						
No	1.000	–	–	1.000	–	–
Yes	0.229	[0.113; 0.466]	**<0.001**	0.502	[0.175; 1.445]	0.20
Bicarbonate						
No	1.000	–	–	1.000	–	–
Yes	0.198	[0.110; 0.355]	**<0.001**	0.347	[0.138; 0.870]	**0.02**
Calcium						
No	1.000	–	–	1.000	–	–
Yes	0.372	[0.203; 0.680]	**0.001**	1.285	[0.503; 3.280]	0.60

95% CI indicates 95% confidence interval; OR, odds ratio; PICU, paediatric intensive care unit; OR, operating room; PEA, pulseless electrical activity; VT, pulseless ventricular tachycardia; VF, ventricular fibrillation. Significant values in bold.

most events (67.1%), although the rate of prolonged CPR (>30 minutes) was not negligible (13.3%).

Adrenaline was used in the vast majority (88.2%) of patients. Bicarbonate and calcium, which are not routinely recommended by CPR guidelines, were used in 42.4% and 30% of patients, respectively.

Factors associated with survival to discharge

Table 2 presents the univariable analysis. The following factors were significantly associated with lower survival to discharge: age <1 month; liver disease; prenatal conditions and complications; occurrence at night;, interventions prior to CPR;, shock as the immediate cause; asystole as the initial rhythm; CPR duration >5 minutes; and use of adrenaline, bicarbonate, or calcium during CPR.

Multivariable analysis (Table 2) found lower survival to discharge to be significantly associated with pre-existing liver disease, vasoactive drug support before cardiac arrest, shock as the immediate cause, CPR prolonged duration, and use of bicarbonate during CPR.

Factors associated with survival after 180 days

Table 3 shows the factors associated with survival after 180 days found in univariable analysis. Male sex; liver disease; genetic and metabolic disease; prenatal conditions or complications; occurrence at night; interventions in place at time of event (mechanical ventilation and vasoactive drug infusion); shock as the immediate cause; asystole as initial rhythm; CPR duration >5 minutes; and use of adrenaline, bicarbonate, or calcium during CPR were significantly associated with lower survival after 180 days. Multivariable analysis identified following variables significantly associated with lower survival after 180 days: pre-existing liver disease, vasoactive drug support before cardiac arrest, shock as the immediate cause, CPR prolonged duration, and use of bicarbonate during CPR.

Neurological outcome

Table 4 and Fig. 1 shows the neurological outcome in the 93 survivors after 180 days. Approximately-one-third already presented prearrest neurological dysfunction. Between the prearrest and discharge period, 20.2% of patients had an unfavourable prognosis. Neurological outcome was similar between discharge and after 180 days. Twenty-three patients with severe dysfunction prearrest (Paediatric Cerebral Performance Category 4) remained stable after 180 days. Neurological outcome was mostly favourable at discharge (79.7%) and after 180 days (76.1%).

Univariable and multivariable analysis was conducted to evaluate factors associated with good neurological prognosis was carried out in the 93 survivors after 180 days. In multivariable analysis, factors associated with favourable neurological prognosis age >1 year (OR: 23.894, 95%CI 2.735–208.735, p = 0.004) and non-administration of vasoactive drugs pre-CPR (OR: 4.518, 95%CI 1.116–18.291, p = 0.03) (Supplemental Table 1).

Discussion

This study analysed the association of a set of factors with paediatric CPR survival in patients with complex chronic conditions in a high-complexity hospital. Prior liver disease, vasoactive drug support before CA, shock as the immediate cause, prolonged CPR, and use of bicarbonate were significantly associated with lower survival both at discharge and after 180 days. Most patients had a favourable neurological prognosis at discharge and after 180 days.

This study is characterized by a robust sample of patients with complex chronic conditions (96.3%) in a middle-income country, where literature data are scarce. Patients with complex chronic conditions have a higher frequency of hospitalization,[17] which is related with life expectancy currently increasing, likely as result of early diagnosis and technological advances, especially in cardiorespiratory support. This population should be highlighted in studies on in-hospital CPR from now on.

Paediatric in-hospital CPR outcomes greatly vary according to different services and between countries (Table 5). Inequality in cardiac arrest care, which depends on training, expertise, human resources, equipment, ICU beds, and multidisciplinary team along with the variability in human development indexes may explain the different outcomes.

However, rates of survival to discharge (33.7%) and after 180 days (29.2%) as shown in this study are aligned with the literature from high-income countries (Table 5). Additionally, there was an overall improvement in survival when comparing a similar study previously conducted in the same hospital with the current data (ROSC from 64% to 70.9%; survival to discharge 16.3–33.7%; survival after 180 days 15.5–29.2%, respectively).[3]

In-hospital paediatric cardiac arrest typically occurs in patients with pre-existing diseases, who account for 71.0% to 90.9% of cases.[3–5,20,31–33] In the present study, 96.3% of patients had complex chronic conditions, reinforcing the literature findings on the increased prevalence in this population.[17] The prognosis of cardiac arrest appears to be influenced by the complex chronic conditions category, and thus further studies must address this issue.

Liver disease was the most frequent condition noted in the current study, having been associated with lower rates of survival to discharge and after 180 days. Previous studies in the same hospital have already reported liver disease as the most common condition.[3,34] These findings can be attributed to the fact that the hospital

Table 4 – Neurological outcome.

PCPC	Pre-arrest N %		Hospital Discharge N %		180 days N %	
1	56	60.2%	31	33.3%	30	32.3%
2	7	7.5%	15	16.1%	11	11.8%
3	5	5.4%	5	5.4%	8	8.6%
4	23	24.7%	41	44.1%	41	44.1%
Unknown	2	2.2%	1	1.1%	3	3.2%
Total	**93**	**100.0%**	**93**	**100.0%**	**93**	**100.0%**

PCPC, pediatric cerebral performance categories; N, number of patients.

Table 5 – Characterization of pediatric in-hospital CPR (adaptation of López-Herce, under authorization).

Author	Country	Year	Study Type	N	Setting	ROSC (%)	Survival to discharge (%)	Good neurological survival (%)	6 months or 1 year survival (%)
Slonin[48]	USA	1997	Prospective	205	PICU	UNK	13.7	UNK	UNK
Suominen[24]	Finland	2000	Retrospective	118	In-hospital	62.7	19.5	12.7	17.8
Reis[3]	Brazil	2002	Prospective	129	In-hospital	64	16.2	89.5	14.7
Guay[49]	Canada	2004	Retrospective	203	In-hospital	73.8	40.8	23.4	26
Rodriguez-Nuñes[50]	Spain	2006	Prospective	116	PICU	59.5	35.3	31	34.5
Tibballs[19]	Australia	2006	Prospective	111	In-hospital	76	36	UNK	34
Nadkarni[1]	USA,Canada	2006	Prospective	880	In-hospital	52	27	18	UNK
de Mos[51]	Canada	2006	Retrospective	91	PICU	82	25	18	UNK
Meaney[38]	USA	2006	Prospective	411	PICU	48.9	21.4	14	UNK
Wu[52]	China	2009	Retrospective	316	In-hospital	72.2	20.9	15.5	UNK
Olotu[53]	Kenya	2009	Prospective	114	In-hospital	UNK	22	ND	UNK
Moreno[54]	Argentina	2010	Prospective	132	PICU	53	19.7	16.6	UNK
Berens[55]	USA	2011	Retrospective	257	In-hospital	56.8	31.1	19.8	UNK
Matos[39]	USA	2013	Retrospective	3419	In-hospital	63.7	27.9	19	UNK
Girotra[11]	USA	2013	Retrospective	1031	In-hospital	UNK	34.8	61	UNK
Zeng[7]	China	2013	Prospective	174	In-hospital	62.1	28.2	86	12.1
López-Herce[4]	Multinational	2013	Prospective	502	In-hospital	69.5	39.2	34.8	UNK
López-Herce[40]	Spain	2014	Prospective	200	In-hospital	74	41	77.9	UNK
Straney[42]	Australia, New Zealand	2015	Prospective	677	PICU	UNK	63.7	UNK	UNK
Rathore[12]	India	2016	Prospective	314	In-hospital	64.6	14	77	11.1
Gupta[46]	USA	2017	Retrospective	154	PICU	100	66.6	94.3	UNK
Andersen[23]	USA	2017	Prospective	182	In-hospital	UNK	53.8	UNK	UNK
Sutton[10]	USA	2018	Prospective	164	PICU	90	47	75.7	UNK
Edward-Jackson[57]	Malawi	2019	Prospective	135	In-hospital	6	0	0	0
Mustafa[58]	England	2021	Retrospective	1528	PICU	UNK	61.9	UNK	UNK
Hamzah[59]	USA	2021	Retrospective	20654	In-hospital	UNK	39.8	UNK	UNK
Lee[33]	China	2022	Retrospective	233	PICU	74.8	25	21.9	UNK
Shimoda-Sakano	Brazil	2022	Prospective	323	In-hospital	70.9	33.7	79.7	28.8

CPR, cardiopulmonary resuscitation; N, number of patients; ROSC, return of spontaneous circulation; PICU, pediatric intensive care unit; UNK, unknown.

is a reference in liver transplantation and receive severely ill patients from all over the country. Delayed diagnosis and difficulty in accessing the hospital due to the continental size of Brazil may explain the greater severity.

Although comparison with other studies depends on institutional characteristics, data from children and adults also reported lower survival in cirrhotic patients[35,36] and unfavourable neurological prognosis.[37]

The administration of vasoactive drugs before cardiac arrest was associated with lower survival to hospital discharge and after 180 days along with poorer neurological prognosis. Other authors also have observed the same association with lower survival to hospital discharge[12,33,38], as well as poorer neurological outcome.[33] The use of vasoactive drug support may reflect patient condition and the association with lower survival rates may be a marker of severity rather than cause-and-effect relationship.

The main causes of cardiac arrest were respiratory (47.4%) and shock (37.5%), aligned to the literature.[1,3,31,39] Shock associated with lower survival to hospital discharge and after 180 days is confirmed by other studies.[23,40] The increasing number of children surviving with severe chronic diseases may explain the mortality due to shock.

The present study showed that the longer the CPR, the lower the survival rate at discharge and after 180 days, both in univariable and multivariable analysis. This influence of CPR duration on prognosis was also observed by other authors.[3,4,9,24,31,39,41,42] A multicentre registry reported a drop of 2.1% per minute in survival to discharge and of 1.2% per minute in favourable outcome in events which CPR duration was inferior to 15 min.[39] However, it is possible to obtain a good prognosis, even in prolonged CPR. Studies including CPR duration greater than 30 minutes showed favourable neurological outcome in 60% to 89% of CPR events.[9,39] In addition, survival rates of 16.6% has been observed in patients undergoing CPR lasting longer than 35 min.[39]

CPR duration is a variable that is influenced by pre-cardiac arrest and intra-CPR events, and thus should be considered as an important prognostic factor. A child with chronic disease, who has shock and cardiac arrest in asystole, is expected to have longer CPR than a child who develops symptomatic bradycardia due to asphyxia and recover with ventilation, chest compression and one adrenaline dose.

The analysis of adrenaline's role in survival is complex and could not be explored in this study. Data on the time to the first dose, doses interval, and the number of doses are important in the analysis and were not collected in this study. In addition, other factors such as CPR duration and the initial rhythm of cardiac arrest should be considered. Holmberg et al. described in children receiving CPR for bradycardia with poor perfusion that adrenaline was associated with worse outcomes and this, at least partially, explains how complex it is to analyze the influence of adrenaline on survival.[60]

The use of bicarbonate during CPR was frequent and associated with lower survival to hospital discharge and after 180 days. In a meta-analysis, the use of bicarbonate during in-hospital paediatric cardiac arrest was also frequent (43.7–65.6%) and associated with lower survival to hospital discharge.[43] Despite not being routinely recommended by paediatric resuscitation guidelines,[44,45] it is likely indicated in prolonged cardiac arrest in patients with high complexity or due to lower adherence to advanced life support recommendations.

Neurological outcome was favourable in 76.1% of survivors after 180 days and this result is confirmed by others studies.[3,4,11,31,42,46] Pre-cardiac arrest neurological dysfunction in complex chronic conditions carriers is expected and was present in about one-third (31.4%) of patients. Significant worsening of neurological function (20.2%) occurred between prearrest and discharge periods, but not between discharge and 180-day periods.

Patients with severe prearrest dysfunction (Paediatric Cerebral Performance Category 4) remained unchanged after 180 days. This group may not have had any Paediatric Cerebral Performance Category changes or this score is not sensitive enough to detect worsening brain function in patients with previous severe involvement. The International Liaison Committee on Resuscitation, through the Paediatric Core Outcome Set for Cardiac Arrest (P-COSCA) initiative, suggests the use of the Paediatric Cerebral Performance Category score, despite its limitations, for being validated and extensively used in paediatric CPR studies and for the possibility of being applied to children from birth to 18 years of age.[47]

Among the strengths of this study, some must be highlighted: the study included paediatric patients with complex chronic conditions, an increasingly important population; it was conducted in a middle-income country where epidemiological studies are scarce; it is a robust sample for a single centre; included Paediatric Cerebral Performance Category evaluation prearrest and post-cardiac arrest; and compared data from the current study with a previous one carried out in the same hospital.

Some of the limitations were those inherent to the performance of a study in a single centre, albeit the local validity remains, which may reflect the reality of tertiary and quaternary hospitals in middle-income countries. Although the recording of all CPR have been encouraged, it is not possible to guarantee that data regarding all eligible patients were recorded. Additionally, only the index event was considered, i.e., the first CPR performed in the hospital, and other cardiac arrest events may have negatively influenced survival and neurological outcome. Patients with trauma and surgical cardiac diseases have very specific characteristics and were not included, which may have influenced the comparison with other studies.

Conclusions

In-hospital paediatric cardiac arrest in patients with complex chronic conditions had lower survival to discharge and after 180 days associated with liver disease, shock as immediate cause of the arrest, vasoactive drug support before cardiac arrest, bicarbonate administration during CPR, and prolonged CPR attempt. Neurological outcome was favourable in most patients and similar in the evaluations performed at discharge and after 180 days.

Declaration of conflicts of interest

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Ethics and patient consent

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Collaborators

Tania M Shimoda-Sakano was responsible for data acquisition, analysed data, drafted the article and reviewed the manuscript.

Amelia G Reis was responsible for the conceptualization and designed the study, coordinated and supervised data collection, carried out the initial analyses and critically reviewed the manuscript.

Edison F Paiva supervised data collection, analysed the data, critically reviewed and helped to draft the manuscript.

Claudio Schvartsman revised the data and critically reviewed the manuscript.

All authors approved the final article as submitted, and agree to be accountable for all aspects of the work.

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Tania M Shimoda-Sakano was responsible for data acquisition, analyzed data, drafted the article and reviewed the manuscript.

Amelia G Reis was responsible for the conceptualization and designed the study, coordinated and supervised data collection, carried out the initial analyses and critically reviewed and the manuscript.

Paiva EF supervised data collection, analysed the data, critically reviewed and helped to draft the manuscript.

Schvartsman C revised the data and critically reviewed the manuscript.

All authors approved the final article as submitted, and agree to be accountable for all aspects of the work.

Appendix A. Supplementary material

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