J Pediatr (Rio J). 2020;96(4):409−421

Jornal de Pediatria

www.jped.com.br

REVIEW ARTICLE

Epidemiology of pediatric cardiopulmonary resuscitation☆,☆☆

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Received 1 July 2019; accepted 31 July 2019
Available online 30 September 2019

KEYWORDS
Cardiopulmonary resuscitation;
Cardiopulmonary arrest;
Ventricular fibrillation;
Pulseless ventricular tachycardia;
Asystole;
Pulseless electrical activity

Abstract
Objective: To analyze the main epidemiological aspects of prehospital and hospital pediatric cardiopulmonary resuscitation and the impact of scientific evidence on survival.
Source of data: This was a narrative review of the literature published at PubMed/MEDLINE until January 2019 including original and review articles, systematic reviews, meta-analyses, annals of congresses, and manual search of selected articles.
Synthesis of data: The prehospital and hospital settings have different characteristics and prognoses. Pediatric prehospital cardiopulmonary arrest has a three-fold lower survival rate than cardiopulmonary arrest in the hospital setting, occurring mostly at home and in children under 1 year. Higher survival appears to be associated with age progression, shockable rhythm, emergency medical care, use of automatic external defibrillator, high-quality early life support, telephone dispatcher-assisted cardiopulmonary resuscitation, and is strongly associated with witnessed cardiopulmonary arrest. In the hospital setting, a higher incidence was observed in children under 1 year of age, and mortality increased with age. Higher survival was observed with shorter cardiopulmonary resuscitation duration, occurrence on weekdays and during daytime, initial shockable rhythm, and previous monitoring. Despite the poor prognosis of pediatric cardiopulmonary resuscitation, an increase in survival has been observed in recent years, with good neurological prognosis in the hospital setting.

☆ Please cite this article as: Shimoda-Sakano TM, Schvartsman C, Reis AG. Epidemiology of pediatric cardiopulmonary resuscitation. J Pediatr (Rio J). 2020;96:409−21.
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https://doi.org/10.1016/j.jped.2019.08.004

Conclusions: A great progress in the science of pediatric cardiopulmonary resuscitation has been observed, especially in developed countries. The recognition of the epidemiological aspects that influence cardiopulmonary resuscitation survival may direct efforts towards more effective actions; thus, studies in emerging and less favored countries remains a priority regarding the knowledge of local factors.

PALAVRAS-CHAVE
Ressuscitação cardiopulmonar;
Parada cardiorrespiratória;
Fibrilação ventricular;
Taquicardia ventricular sem pulso;
Assistolia;
Atividade elétrica sem pulso

Epidemiologia da ressuscitação cardiopulmonar pediátrica

Resumo
Objetivo: Analisar os principais aspectos epidemiológicos da ressuscitação cardiopulmonar pediátrica pré-hospitalar e hospitalar e o impacto das evidências científicas na sobrevida.
Fonte de dados: Revisão narrativa da literatura publicada Pubmed/Medline até janeiro de 2019, inclusive artigos originais e de revisão, revisões sistemáticas, metanálises, anais de Congresso, além de busca manual dos artigos selecionados.
Síntese dos dados: Os cenários pré-hospitalar e hospitalar apresentam características e prognósticos distintos. A parada cardiorrespiratória pré-hospitalar pediátrica apresenta sobrevida três vezes menor do que a hospitalar, ocorre em sua maioria nas residências e nos menores de um ano. A maior sobrevida parece estar associada a progressão da idade, ritmo chocável, atendimento por serviço médico de emergência, uso de desfibrilador externo automático, suporte básico de vida precoce de alta qualidade e orientação de ressuscitação cardiopulmonar via telefônica por atendente e está fortemente associada com parada cardiorrespiratória presenciada. No cenário hospitalar, observou-se maior incidência em menores de um ano e mortalidade crescente com a idade. Maior sobrevida foi observada quanto menor duração da ressuscitação cardiopulmonar, ocorrência em dias da semana e período diurno, ritmo chocável inicial e monitorização prévia. Apesar do prognóstico reservado da ressuscitação cardiopulmonar pediátrica, observou-se nos últimos anos incremento da sobrevida com bom prognóstico neurológico no cenário hospitalar.
Conclusões: Houve grande avanço na ciência da ressuscitação cardiopulmonar pediátrica, especialmente em países desenvolvidos. O reconhecimento dos aspectos epidemiológicos que influenciam a sobrevida da ressuscitação cardiopulmonar pode direcionar esforços para ações mais efetivas. Assim, a pesquisa em países emergentes e menos favorecidos persiste como prioridade no conhecimento de fatores locais.

Introduction

Cardiopulmonary resuscitation (CPR) as it is currently known (chest compressions and artificial ventilation) was developed in 1960; since then, medical entities have been working on the progress of resuscitation science and in programs to disseminate this procedure, including the training of healthcare professionals and lay people. Despite major advances, pediatric cardiopulmonary arrest (CPA) still has a poor prognosis. Although in recent years there has been a trend towards increased survival of in-hospital pediatric CPA in developed countries, this has not been observed in prehospital CPA, where the morbidity and mortality rates remains high.[1,2]

Factors associated with CPA survival remain a topic of great interest in the literature, which mainly addresses adults in developed countries.[2] The epidemiological aspects associated with pediatric CPA are less clear and differ from those in adults regarding etiology and prognosis.[3,4]

The main CPR topics that must be studied were highlighted in a recent publication by the International Liaison Committee on Resuscitation (ILCOR), an entity that discusses the science of CPR and brings together specialists from several countries.[5] This document stressed the need for studies focusing on the epidemiology of pediatric CPA to detect variables that can influence survival and neurological prognosis. The Utstein style, developed in 1990 by ILCOR, aims to standardize terms and definitions for data collection during CPA and CPR,[6] and has since become the international standard for research data collection in this field.

In 2004, the Utstein style was revised, aiming to decrease its complexity, adapt the variables to the science of resuscitation,[7] and unify the hospital registry of CPA in adults and children. Since then, there has been a significant increase in resuscitation registries and clinical trials in several regions, notably in the United States, Europe, Asia, Australia, and Japan.[8] Increasing data have allowed

Table 1 Characteristics of pre hospital CPA according to age range.

	Overall	Infants	Children	Adolescents	Adults
Incidence (100,000 cases/year)	3.3-8.0	65.5–72	3.7	6.3	50–64.7
30-day survival (%)	8.1	1.4–2.6	7.8–16.1	7.7–9.3	9.3
Survival-hospital discharge (%)	1.1-20	3.3	9.1	8.9	1.1–10.6
Favorable neurological prognosis[a] (%)	1-12	1-2	4	11–16	2–10.7
Public place (%)	7-12	4	14	22–45	16
CPR in the community (%)	6–48.8	37	40	28	19
Initial rhythm asystole (%)	82–95	84	83	77	60
Initial rhythm VF (%)	5–11.7	4	5–22	15–51.2	23–33.7

[a] Studies evaluated 1 to 18 months after CPA.[2,10,11,15,19,21]

the comparison of the epidemiology in different regions,[2] CPA therapeutics, and outcomes,[9] in addition to identifying knowledge gaps and advancing the science of resuscitation.[5]

Therefore, this study aimed to review the epidemiology of pediatric CPR, highlighting the possible factors associated with CPA prognosis and survival trends. Due to the heterogeneity of the studies, the authors chose to perform a narrative review to interpret the literature. The post-CPR period was excluded from this review, due to its peculiar characteristics.

As the epidemiology of pediatric prehospital and in-hospital CPA is distinct, this review will present the factors associated with these two different scenarios.

Prehospital cardiopulmonary arrest

Prehospital CPA is rare in children and adolescents, occurring in 2.28 to 8.04/100,000, in contrast to adults, occurring in 50 to 126.57/100,000, and is associated with high mortality and severe neurological sequelae.[10–12] Pediatric CPA accounts for only 1.5 to 2.2% of total CPAs, according to recent Asian[13] and American[14] registry publications, respectively.

The survival in CPA in the prehospital and in-hospital settings is distinct and varies according to region and country.[2,15–17] A European registry in adults observed that 66% received CPR prior to prehospital care and 10.3% had survival at hospital discharge,[18] similar to that found in a multicenter North-American study that included adults and children.[15]

A systematic review including adults and children disclosed a wide variation in the incidence and outcome of CPA across the continents, with the highest incidence in North America (54.6/100,000) and the lowest in Asia (28.3/100,000). The lowest survival rate at hospital discharge was reported in Asia (2%), compared with Europe (9%), North America (6%), and Australia (11%).[2] This result can be attributed to the diversity among populations with distinct comorbidities, emergency medical service (EMS), definitions, study methodologies, local telecommunications system, incidence of VF as the initial rhythm, and registry differences.

The neurological prognosis in pediatric prehospital CPA is very guarded. An American pediatric study showed an overall survival at discharge of 8.6%, with 31% showing good neurological prognosis.[19] In Japan, the overall survival after one month was 8%, and good neurological prognosis after one month was observed in 1% of infants, 2% of children, and 11% of adolescents.[10] A pediatric study involving several Asian countries showed an overall survival with good prognosis of 3.7%.[13]

The standardization of the CPA data collection recommended by the Utstein-style allowed the identification of variations between communities and countries regarding the healthcare system, survival chain quality, patient-related factors, and CPA data collection.

The factors associated with survival in prehospital pediatric CPA have been the subject of many studies and will be discussed below.

Age

In pediatric patients, most CPA events occur in those younger than 1 year (44–64%),[10,11,20] and the incidence in this age range is close to that of adults.

A Swedish prospective study including adults and children (n = 40,503) observed, at shockable rhythms, higher survival rates after one month in those younger than 18 years (24.5%), intermediate in adults aged 18–35 years (21.2%), and lower rates in adults older than 35 years (13.6%; $p < 0.003$), a pattern similar to that observed in non-shockable rhythms (3.8%, 3.2%, and 1.6%, respectively, $p < 0.0001$). One-month survival rates were 2.6% in neonates, 7.8% in children, and 24.5% in adolescents when the initial rhythm was shockable. In non-shockable rhythms, one-month survival was 3.8% in children, 3.2% in young adults, 1.6% in adults (older than 35 years).[21] Pediatric multicenter studies have shown the same trend, with lower survival in infants (1.4–3.7%), followed by children (3.6–9.8%) and adolescents (8.9–16.3%).[11,13,20,22]

In Japan, a prospective observational study disclosed more favorable outcomes in children, when compared with adults, with a survival rate of 8% versus 5% and good neurological function in 2% versus 1%, respectively. In the same study, survival with good neurological prognosis was observed in 1% of infants, 4% of children, and 11% of adolescents.[10] Table 1 presents the main characteristics of prehospital CPA in different age groups.[10,11,15,19,21–28]

The better survival rates observed in adolescents can be attributed to a set of factors, such as the higher occurrence in public places, greater likelihood of being witnessed, increased prevalence of VF (ventricular fibrillation)/VT pulseless (ventricular tachycardia) initial rhythm,

Fig. 1 Pediatric Chain of Survival of the American Heart Association.[33]

and increased chance of automatic external defibrillator (AED) use.

Although the incidence and outcomes of prehospital CPA differ according to age, the variables associated with this observation are not fully understood.

Place of occurrence

Survival at hospital discharge after CPA that occurred in a prehospital setting is approximately three times lower when compared within-hospital CPA, due to delayed recognition and treatment.[17,29]

Most pediatric prehospital CPA events occur at home, and their occurrence in public places increases with age, ranging from 22% to 45% in adolescents.[10,30]

Some locations may show a peculiar survival rate due to the availability of AED and trained teams. A study carried out at 40 international airports disclosed a 32% survival rate for adults.[31] The São Paulo subway system, in Brazil, achieved a 43% survival rate at hospital discharge in adults, a significant figure in the pre hospital setting.[32]

The occurrence of CPA in public places, which are more likely to be witnessed, associated with the availability of AED and community trained in CPR, can positively influence survival.

Witnessed CPA and early CPR

The key elements of the pediatric survival chain include an integrated sequence of events: prevention, early CPR, EMS activation, advanced life support (ALS), and post-CPR care[33,34] (Fig. 1). Despite the increasing emphasis on early CPR, only 15–40% of prehospital pediatric CPA in developed countries undergo such maneuvers in the community, similar to what is observed adults.[4,10,24,30]

Most pediatric prehospital CPAs occur at home[13,21,30]; when there are trained family members, this is an opportunity to start early CPR. Pediatric CPA followed by CPR prior to the arrival of EMS are factors strongly associated with survival at hospital discharge, with good neurological prognosis (OR 4.74; 95% CI: 1.49–15.05).[35] Witnessed pediatric CPA occurs in 36–39.9% of the cases and CPR prior to the arrival of the EMS occurs in 49–49.2% of cases.[4,13,23,24,30,36,37]

The increased survival of patients with chronic diseases may be an opportunity to raise awareness and disseminate CPR training in the community, focusing on strategic individuals, such as family members, with a possible impact on pediatric CPA prognosis.

Etiology

Unlike adults, in which cardiac causes are frequent,[38] the main etiologies of prehospital CPA in children are sudden infant death syndrome (20–60%), trauma (19–53%), and respiratory causes (4–41%).[4,19,35,39]

In a study analyzing prehospital pediatric CPA admitted to the intensive care unit (ICU), it was observed that patients who presented a cardiac etiology showed survival with a good neurological prognosis in 65% of cases, in contrast to 39% when the etiology was non cardiac (OR 6.40; 95%CI: 1.65–24.76).[35]

Sudden death is one of the most frequent causes in infants[40] and, in these circumstances, the cardiac cause is probably underestimated, since the cardiovascular etiology, such as channel opathies,[41] which are hereditary diseases characterized by alteration in ion channels causing greater susceptibility to arrhythmias, may be present and undiagnosed.[21]

Survival in pediatric trauma victims (n = 2,299) is very low, around 1.1% at hospital discharge, and only 0.3% have a good neurological prognosis.[19] In turn, in cases of drowning, survival at discharge reaches 22.7%, of whom 6% have a good neurological prognosis.[4,11] Among the variables that affect the outcome of drowning, submersion duration, water temperature, and early start of CPR are noteworthy. Survival with intact neurological function has been described in prolonged submersion in freezing waters.[42]

Although the etiology can influence prognosis, the cause of pre hospital CPA is often presumed and difficult to confirm.

Telephone EMS dispatcher-assisted CPR guidance

Despite the importance of early CPR in the community, only one-third to one-half receives CPR in prehospital CPA.[43] Thus, the role of the EMS dispatcher through telephone-based CPR guidance may be relevant.

An observational study on prehospital pediatric CPA in Japan found that, when compared with its absence, specialized telephone guidance increased the rate of CPR performed in the community (68.7% vs. 27.8%), mouth-to-mouth ventilation (43.6 % vs. 18.4%), and one-month survival (19% vs. 11.2%); however, no significant effect was observed on the neurological outcome.[44] A more recent study in the same country corroborated previous findings. Telephone-based guidance increased CPR (OR 7.51; 95% CI: 6.60–8.57) and favorable neurological outcome after one month when compared with non-CPR performance (OR 1.81; 95%CI: 1.24–2.67).[43]

Thus, as the CPR performed in the community is a fundamental link in the pediatric survival chain, telephone-based guidance has the potential to trigger early CPR and may increase survival, with a good neurological prognosis.

Emergency medical service care

Prehospital CPA care by EMS appears to be associated with longer survival.[13,45] A pediatric study observed an association with longer survival after interventions in a prehospital environment, such as fluid administration (OR 1.73; 95% CI: 1.07–2.80) and attempts via intraosseous or intravenous route (OR 2.40; 95% CI: 1.20–4.81). As for the acquisition of advanced airway, it was not associated with survival (OR 0.69; 95% CI: 0.43–1.10), and drug use was associated with worse prognosis (OR 0.24; 95% CI: 0.15–0.39).[20] In turn, in a pediatric study carried out in Asian countries, the acquisition of advanced airway was positively associated with survival at hospital discharge in children younger than 13 years (OR 3.35; 95% CI: 1.23–9.13).[13]

Consequently, there is still no consensus on which maneuvers, in addition to high-quality chest compressions and AED use, should be part of prehospital CPR. Studying each of the possible prehospital interventions that may impact survival is desirable, but difficult to perform due to the difficulty in obtaining the number of cases of pediatric CPA with statistical power.

Rhythm

Non-shockable rhythms are those most often observed in prehospital pediatric CPA;[21,30,46] asystole is identified in 39–78% and PEA (pulseless electrical activity), in 10–31% of patients.[4,13,23,35,44]

Shockable rhythms are present in approximately 35% of adults[21]; their frequency is lower in pediatric patients and varies with age (5–11% in children and 19–21% in adolescents).[20,44] Shockable rhythm has been identified as one of the factors strongly associated with survival in prehospital CPA in adults and children.[10,19,21,23,30,35] A retrospective pan-Asian prehospital pediatric study involving 974 children under 17 years also observed this association (OR 20.29; 95%CI: 9.45–43.57).[13]

Although shockable rhythms, which are associated with better survival, are uncommon in the pediatric age group, this age group has higher survival than adults; the factors that determine this outcome remain unclear.

Early defibrillation

Rapid defibrillation is critical for the survival of patients with VF; consequently, the routine use of AED is indicated in all prehospital CPA according to the resuscitation guidelines.[8,33,47] A study including children aged 1–17 years found that shockable rhythms were less frequent in children younger than 8 years than in adults (11.6% vs. 23.7%), and the use of AED was 16.3% in children younger than 8 years versus 28.3% in adults.[28] Other studies have confirmed this observation.[13,22,30,45]

The availability of AED in public places associated with basic life support (BLS) training showed a strong association with survival, with good neurological prognosis in children in a Japanese study (OR 5.13; 95% CI: 2.64–9.96)[44] and in an Australian study (OR 4.74; 95% CI: 1.49–15.05). In this study, BLS training was associated with a tenfold increase in CPR and AED use in the community, and increased survival to high with good neurological prognosis, from 42% to 64% in the same period.[35]

Despite the increasing acknowledgement of the importance of BLS and early defibrillation, transposing the recommendation into effective dissemination in the community remains a major challenge.

Quality of basic life support

The principles of high-quality BLS include: minimizing compression interruption, avoiding hyperventilation, maintaining adequate compression frequency and depth, and allowing full chest return.[47] Based on the 2005 resuscitation guidelines,[48] there is an increasing emphasis on the importance of BLS, because high-quality CPR may be associated with longer survival.[45,49–52]

In shockable rhythms, a high compression fraction (proportion of time devoted to chest compression during CPR) was associated with higher survival in adults (OR 3.01; 95% CI: 1.37–6.58).[49] The depth of the compressions (higher than 38 mm) in adults was associated with survival at hospital discharge (OR1.45; 95% CI: 1.20–1.76).[51] However, most of these studies were performed in adults and in pediatric in-hospital CPA.

Several aspects of BLS have been evaluated. A prehospital CPA study in adults evaluated the rate of chest compression and found an association with the return of spontaneous circulation (ROSC); OR 0.78; 95% CI: 0.66–0.92, $p < 0.003$), but not with survival at hospital discharge (OR 0.82; 95% CI: 0.63–1.07, $p < 0.14$).[49]

A multicenter prospective study found several opportunities for improvement in prehospital pediatric CPR, as it detected poor adherence (22–58%) to CPR quality parameters.[45] Another relevant parameter is appropriate ventilation, as hyperventilation reduced coronary perfusion ($p = 0.03$) and survival ($p = 0.006$), even in teams trained in animal models.[53,54]

Adequate depth of compressions was observed in only 58% of CPR in pediatric patients, and no association with ROSC was observed.[45] Animal studies suggest that chest compression discontinuation results in an abrupt fall in coronary perfusion, and several chest compressions are required to resume adequate coronary perfusion pressure.[55]

Full chest return at the end of the compression allows the reduction of intrathoracic pressure, favoring preload and coronary perfusion, in addition to allowing passive air intake, fundamental factors to achieve ROSC.[56]

There is evidence that high-quality BLS is associated with increased survival; therefore, efforts to expand opportunities for improvement in the prehospital setting are essential.

In-hospital CPA

The standardization of the pediatric Utstein style occurred in 1995,[57] and encouraged the creation of CPR registries and databases. One example is the National Registry of Cardiopulmonary Resuscitation (NRCPR), which started in 2000to collect prospective data at various hospitals in the United States,[58] with the primary objective of improving CPR quality. This registry provided a robust database for the development of evidence-based guidelines, as well as data comparison across hospitals and implementation of improvement strategies. In 2010, the NRCPR was incorporated into the Get With The Guidelines—Resuscitation Registry (GWTG-R) program to facilitate the registration, analysis, implementation, and dissemination of the guidelines, as well as evidence-based practice.[8]

In-hospital pediatric CPA studies show a wide variability regarding prognosis, which can be explained by regional differences, study design, studied population, hospital characteristics and sector, rapid response team performance, and post-resuscitation care, among others (Table 2).

The Utstein style stimulated the research on in-hospital pediatric CPR, and the first pediatric study applying this standardization was developed in Brazil.[59] In a prospective multicenter observational study that included adults and children in emergency services, it was observed that most rhythms during CPA were non-shockable and survival at hospital discharge was higher in children than in adults (27% vs. 18%, OR 2.29; 95% CI: 1.95–2.68).[60] In turn, a more recent, multicenter retrospective study using the same database as the previous study found that survival at hospital discharge was similar between adults and children (23% vs. 20%).[61]

Considering the different hospital sectors, survival at hospital discharge was observed in 13.7–47% in pediatric ICU studies,[62–64] 12.8% in multicenter studies in pediatric emergency services,[65] and 37–39.2% when considering all hospital sectors.[66,67]

Studies evaluating survival at hospital discharge in less favored countries are scarce. In India, survival at hospital discharge was 14.5%, with 77.1% having a good neurological prognosis.[68] In Brazil, a database analysis showed a survival rate of 32.8% at discharge in a tertiary university pediatric hospital.[69]

In a tertiary university hospital in Africa, with limited resources, including shortage of trained staff, equipment (defibrillator), medications, and ICU beds, mortality was 100% within 24 h. The infectious etiology (malaria, sepsis) associated with peculiar comorbidities (HIV and malnutrition) contributed to this scenario, which impair all patient care (pre-, during, and post-CPR).[70]

Table 2 describes the outcomes of in-hospital pediatric CPA.[29,37,60,63,64,68–86] One-year survival ranged from 11.1 to 34.5% among the studies.[59,68,71–74] Several factors may be associated with in-hospital pediatric CPA survival and will be discussed below.

Age

The age range appears to influence the incidence of in-hospital CPA. A retrospective cohort study found a higher incidence in infants under 1 year, when compared with children and adolescents (0.79/1,000 vs. 0.56/1,000). Despite the higher incidence in this age group, infant mortality (46.8%) was significantly lower than in the other groups: 1 to 2 years, 3 to 5years, 6 to 11 years, and 12 to 17 years of age (58.8%, 57.7%, 64.8%, and 70%, respectively).[1]

A multicenter study carried out in a pediatric ICU observed a survival rate of 27% at hospital discharge in the neonatal period, 36% in infants, 19% in children aged 1 to 8 years, and 16% in children older than 8 years.[63] Lower survival was obtained in a pediatric tertiary center, with 17.8% in infants, 7.5% in children aged 1 to 4 years, and 3.4% in children older than 8 years.[69] Both studies showed lower survival with advancing age.

Analyses of long-term survival are scarce. A multicenter study indicated a one-year survival of 52.4% in children younger than 1 year, 43.4% in those aged 1 to 4 years, 41.7% in those aged 5 to 12 years, and 41% in those aged >13 years.[87]

Therefore, age appears to be a determining factor in prognosis; however, the factors associated with this observation are yet to be clarified.

CPR duration

Some authors have observed that the duration of pediatric in-hospital CPR was inversely related to survival.[42,59,82,84,87–89] A negative association was observed between CPR duration and survival (OR 0.95; 95% CI: 0.91–0.98). In prospective study carried out in a pediatric tertiary hospital in Brazil using the Utstein style.[59] A pediatric prospective study in the ICU observed survival at hospital discharge with CPR lasting less than 3 min of 66% and lasting longer than 30 min of 28%.[84] A multicenter registry showed a 2.1% per minute drop in survival at hospital discharge with CPR lasting less than 15 min and a 1.2% per minute drop in the favorable neurological outcome.[88] In turn, studies including prolonged pediatric CPA (longer than 30–35 min) showed a favorable neurological prognosis in 60–89% of cases.[84,88]

The longer the CPR duration, the longer the low cardiac output period, with potential organ damage. Increased survival at hospital discharge with favorable neurological prognosis despite prolonged duration has a multifactorial cause; the best quality-CPR and advances in post-CPA care are likely the determining factors.

Time and day of the week

The influence of the time and day of week on the outcome of CPA has been evaluated by some authors. A study in adults observed higher survival at daytime on weekdays (20.6%; 95% CI: 20.3–21%), when compared with night time and on weekends (17.4%; 95% CI: 16.8–18%); OR 1.15; 95% CI: 1.09–1.22).[90] A pediatric multicenter study also found lower survival rates at hospital discharge at night time, when compared with daytime (OR 0.88; 95%CI: 0.80–0.97; $p < 0.007$).[91]

The difference in the patient care processes between daytime and nighttime, such as lower nurse/patient ratio, presence of less experienced professionals, greater possibility of error, and reduced psychomotor skill performance may explain these results.[90]

Table 2 Characterization of studies on in-hospital pediatric CPA.

Author	Country	Year	Study type	Number of patients	Place	ROSC(%)	High survival (%)	Survival with good neurological prognosis (%)	One-year survival (%)
Slonin[62]	United States	1997	Prospective	205	ICU	NA	13,7	NA	NA
Suominen[71]	Finland	2000	Retrospective	118	Hospital	62.7	19.5	12.7	17.8
Reis[59]	Brazil	2002	Prospective	129	Hospital	64	16.2	15	14.7
Guay[72]	Canada	2004	Retrospective	203[a]	Hospital	73.8	40.8	23.4	26
Rodríguez-Nuñes[37]	Spain	2006	Prospective	116	ICU	59.5	35.3	31	34.5
Tibballs[73]	Australia	2006	Prospective	111	Hospital	76	36	NA	34
Nadkarni[60]	United States and Canada	2006	Prospective	880	Hospital	52	27	18	NA
de Mos[75]	Canada	2006	Retrospective	91	ICU	82	25	18	NA
Meaney[63]	United States	2006	Prospective	411	ICU	48.9	21.4	14	NA
Wu[76]	Taiwan	2009	Retrospective	316	Hospital	72.2	20.9	15.5	NA
Meert[77]	United States	2009	Retrospective	353[b]	Hospital	ND	48[a]	46[a]	NA
Olotu[78]	Kenya	2009	Prospective	114[c]	Hospital	ND	15.7% PCR	ND	NA
Berens[79]	United States	2011	Retrospective	257	Hospital	56.8	31.1	19.8	NA
Girotra[29]	United States	2013	Retrospective	1031	Hospital		34.8	61	NA
López-Herce[80]	Spain	2014	Prospective	200	Hospital	74	41	77.9	NA
Berg[81]	United States	2013	Prospective	5870 events	Hospital	72	39	95	NA
Zeng[74]	China	2013	Prospective	174	Hospital	62.1	28.2	86	12.1
RIBEPCI[82]	Multinational	2013	Prospective	502	Hospital	69.5	39.2	34.8	NA
Straney[83]	Australia, NewZealand	2015	Prospective	677	ICU	NA	63.7	NA	NA
Rathore[68]	India	2016	Prospective	314	Hospital	64.6	14	77	11.1
Berg[84]	United States	2016	Prospective	139	ICU	65	45	89	NA
Gupta[85]	United States	2017	Retrospective	154	ICU	100	66,6	94,3	NA
Andersen[86]	United States	2017	Prospective	182	Hospital	ND	53,8	NA	NA
Sutton[64]	United States	2018	Prospective	164	ICU	90	47	75,7	NA
Shimoda-Sakano, Annals[69]	Brazil	2018	Prospective	220	Hospital	70,1	28,7	NA	NA
Edward-Jackson[70]	Malawi (Africa)	2019	Prospective	135	Hospital	6	0	0	0

(Update and adaptation by Lopez Herce, with permission). NA, not available.
[a] Includes apnea patients, 55 CPA patients.
[b] Not including all CPA patients, only those with sustained ROSC.
[c] Includes newborns and children with apnea and CPA.

Hospital inpatient units need to develop mechanisms that allow the improvement and standardization of CPR care regardless of the time and day of the week.

Drug administration

Epinephrine is the most significant drug used during CPR. Despite its frequent use, its effectiveness, safety, and adequate dosage are not fully known.[92] Epinephrine has been used in CPR since 1960 due to the effect of increased coronary and cerebral perfusion pressure and increased possibility of ROSC and survival at hospital admission.[93] However, it might reduce microcirculatory flow, favor arrhythmias, and decrease cerebral blood flow.[92]

Studies comparing epinephrine *versus* placebo use found that the drug increases ROSC (RR 3.09; 95% CI: 2.82–3.89; n = 8,469) and survival at discharge (RR 1.44; 95% CI: 1.11–1.86; n = 8,538).[92,94,95] However, when considering the neurological prognosis, no difference was observed between the conventional dose of epinephrine and placebo (RR 1.22; 95%CI: 0.90–1.92).[94,95]

Another aspect of interest was the use of high doses compared to conventional doses of epinephrine in pediatric CPA.[96,97] In a prospective randomized pediatric study conducted in Brazil, it was found that the use of high-dose epinephrine after the conventional dose reduced 24 h survival in children (OR for death: 7.9; 97.5% CI: 0.9–72.5; p = 0.08).[96] A Cochrane review analyzing the use of epinephrine in pediatric CPA, when evaluating the use of the standard dose of epinephrine compared with high doses in pediatric CPA, failed to observe significant differences in ROSC (RR 1.13; 95% CI: 0.73–1.73), 24 h survival (RR 1.04; 95% CI: 0.76–1.43), and survival at discharge (RR 1.54; 95% CI: 0.17–13.66).[92]

The timing of first dose administration has been the subject of a recent study and appears to be of relevance for the outcomes.[98] A pediatric in-hospital CPA study found that, with non-shockable rhythms, delayed epinephrine administration was associated with lower chance of ROSC (RR per minute of delay: 0.97; 95% CI: 0.96–0.99), reduced survival at hospital discharge (RR per minute of delay: 0.95; 95% CI: 0.93–0.98), and neurological prognosis worsening (RR per minute of delay: 0.95; 95% CI: 0.91–0.99).[99]

The interval between epinephrine doses during CPR is another important aspect. A pediatric study[100] obtained a higher survival at hospital discharge in patients receiving epinephrine at intervals longer than three to five minutes (longer than five and shorter than eight minutes, OR 1.81; 95% CI: 1.26–2.59 and 8–10 min, OR 2.64; 95% CI: 1.53–4.55); 3–5 min is the interval recommended by the current 2015 resuscitation guidelines.

The number of epinephrine doses during PCR was inversely associated with shorter 12-month survival. The administration of more than four epinephrine doses was independently associated with shorter one-year survival (OR 0.52; 95% CI: 0.30–0.92).[87]

Epinephrine remains the most commonly used drug in CPA for increasing the rate of ROSC; however, its influence on long-term survival and neurological prognosis has yet to be proven.

Monitoring at the time of the event

Pre-CPR monitoring influences CPA survival in adults and children. A retrospective study in adults compared survival at discharge in places with and without telemetry (cardiac) monitoring and found rates of 20.8% versus 16.1%, respectively.[90] A pediatric study also observed a lower mortality rate when CPA occurred in a monitored environment (OR 0.51; 95% CI: 0.30–0.87, p = 0.01).[86]

The occurrence of CPA in emergency services, that is, in places with lower monitoring, is more frequent in less favored countries, probably due to the scarcity of ICU beds. Pediatric CPA in the ICU has better survival at discharge when compared to other hospital sectors (OR 0.38; 95% CI: 0.15–0.86),[82] possibly due to appropriate monitoring, resulting in early detection and intervention in the presence of clinical deterioration signs.

In Japan, there was a higher incidence of CPA in pediatric wards compared to the American database (27% vs. 14%), demonstrating a shortage of ICU beds; however, there was no significant difference in outcome.[101]

Monitoring allows the early diagnosis and early onset of CPR, with a likely favorable impact on the outcome of pediatric CPA.

CPR quality monitoring

The assessment of the quality and performance of CPR has allowed advances in science and clinical practice. The use of new technologies has allowed the monitoring of CPR parameters during care, and their use in clinical practice is recommended whenever available.[102] CPR monitoring categories can be classified into physiological (patient-dependent) and CPR performance (resuscitator-dependent).

CPR guidelines recommend uniformity of chest compressions according to age range, but this approach does not assess the individual response to CPR efforts.[52] Thus, adjusting CPR quality to physiological parameters through invasive hemodynamic assessment (invasive blood pressure and central venous pressure monitoring) and expired CO_2 ($EtCO_2$) through capnography may increase survival.[102–107]

Data on pediatric CPR quality are limited so far, and recommendations are based on expert consensus.[102] The value of $EtCO_2$appears to be directly associated with pulmonary flow, cardiac output and survival. The consensus on CPR quality recommends control of the performance to achieve $EtCO_2$ >20 mmHg, based on experimental studies and limited data in adults.[102] A recent review has emphasized that the $EtCO_2$'s evolution value can be more reliable than its static value during CPR.[103] Therefore, although all pediatric CPR guidelines recommend the use of capnography during PCA as a measure of compression quality, no pediatric studies have established its true role.

Observational studies analyzing diastolic blood pressure suggest an association with coronary perfusion pressure. A recent pediatric publication suggests that chest compressions may target minimal diastolic pressure and correspond to a performance measure that may determine CPR outcome.[104] In this study, survival at hospital discharge was 70% more frequent when the diastolic blood pressure was greater than or equal to 25 mmHg in infants and greater than or equal to 30 mmHg in children older than one year. Thus, based on animal studies and limited data in adults and children, it is reasonable to use physiological parameters to monitor and maximize CPR quality.[105]

High-quality CPR is also considered one of the determinants of survival in both prehospital and in-hospital settings.[106] A study in adults found that when chest compressions were less than 100/minute, there was a reduction from 72% to 42% in ROSC.[102] In turn, a pediatric study found that compression rates of 80–100/min (lower than that recommended by current guidelines),when compared with 100–120/min, led to higher survival at discharge (RR 1.92; 95% CI: 1.13–3.29, $p = 0.017$) and better neurological prognosis (RR 2.12; 95% CI: 1.09–4.13, $p = 0.027$).[64]

The control of CPR physiological and quality parameters is promising and may represent a change from conventional care, where pre-established quality parameters are recommended. Further studies are required to clarify the real role of CPR quality parameters and their respective target values.

Initial rhythm

The initial rhythm has been associated with the prehospital[10,30] and in-hospital[60,74,87] CPA outcome. In a study that analyzed the first documented rhythm, survival at discharge in shockable rhythms was higher in children than in adults, 24% versus 11% (OR 2.73; 95% CI: 2.23–3.32), respectively.[60]

Although shockable rhythms are not frequent in children, the presence of VF or pulseless VT as the initial rhythm represented higher chances of sustained ROSC (more than 20 min; 64.7% vs. 39.1%, $p < 0.046$) and higher survival at hospital discharge (58.8% vs. 21.7%, $p < 0.02$)[89] when compared to asystole and PEA. One-year survival was 64.7% in those with shockable rhythms, 56.5% in PEA, and 16.7% in asystole.[87]

The better prognosis in shockable rhythms involves their greater reversibility potential. Therefore, focusing efforts on early CPR, shockable rhythm recognition, and rapid defibrillation should remain a priority.

Immediate cause and underlying disease category

In-hospital pediatric CPA occurs mostly in patients with chronic diseases, accounting for 71% to 90.9% of cases.[59,82,87,89] The chronic disease category may be influenced by the analyzed region and may be associated with higher or lower mortality. In India, for instance, malnutrition was found in 65% of pediatric CPRs.[68]

The prognosis of CPR appears to be influenced by the associated chronic disease. In an international multicenter prospective pediatric study, onco hematological (OR 3.33; 95% CI: 1.60–6.98) and neurological (OR 5.19; 95%CI: 1.49–18.73) diseases led to higher mortality.[82]

Children with congenital or acquired heart disease represent a higher risk group for CPA.[85,108] A multicenter study in cardiac pediatric ICUs showed that the prevalence of CPA in non-surgical *vs.* surgical heart diseases was 50% higher, and survival was lower (37.7% vs. 62.5%, $p < 0.0001$, respectively).[108]

Regarding the most common preexisting causes of pediatric CPA, an American registry highlighted respiratory (58%), shock (36%), and heart failure (31%) as the most prevalent causes.[60] In contrast, a study in India identified sepsis (71%), respiratory diseases (39.5%), and neurological diseases (31.5%) as the most prevalent causes.[68]

A prospective Brazilian study carried out in a tertiary pediatric hospital found respiratory diseases as the main cause (61%), followed by shock (29%);[59] a more recent study at the same institution found a change in this distribution, with a decline in respiratory causes (56%) and an increase in shock (43%).[69]

Some studies have shown that conditions preceding the pediatric CPA were associated with increased mortality, such as hypotension (OR 3.26; 95% CI: 1.89–5.92, $p < 0.001$) and sepsis (OR 2.45; 95%CI: 1.52–3.97; $p < 0.001$).[86] Other studies reinforced this finding by observing that the use of vasoactive drugs[68,89] (OR 4.47; 95% CI: 1.72–9.37; $p < 0.001$)[68] and shock preceding the CPA[69,82,86] (OR 2.46; 95% CI: 1.52–3.97, $p < 0.001$)[85] indicated a guarded prognosis at CPR.

Variations in the etiology of CPA may reflect improvements in respiratory disease prevention and care, and the association of chronic diseases results in higher mortality from shock. Studying the role of each category of chronic disease in the incidence and prognosis of CPR is not an easy task, as it requires large multicenter studies with a large number of patients.

Prognostic trend for in-hospital pediatric CPA

Pediatric in-hospital CPA appears to exhibit distinct behaviors over time. When analyzing the trend of pediatric in-hospital CPA in the United States, an increase was observed in the incidence of CPA, from 0.57/1,000 in 1997 to 1.1/1,000 in 2012 ($p < 0.05$), with a decline in mortality over the same period, from 51% to 40% ($p < 0.05$).[1] Considering the intensive care setting, including 32 American services, survival at hospital discharge after pediatric CPA was 13.7% in the 1990s[62] and 22% in the 2000s.[63] A similar trend was observed in other countries, such as Spain, where a significant improvement in survival (from 25.9% to 41% in 10 years) was observed, most of them with a good neurological prognosis.[25,89] Data from a Brazilian tertiary pediatric hospital observed an increase in the rate of ROSC (64–70%) and survival at hospital discharge (19–32.8%) in 15 years.[59,69]

The trend towards increased survival in pediatric CPA in several services and countries is probably the result of multiple efforts involving improved quality of BLS, ALS, and post-CPA care as a result of the advancement of CPR science.

Conclusion

Prehospital pediatric CPA is a rare event, with shorter survival compared to the in-hospital setting and has a guarded neurological prognosis.

Conversely, pediatric in-hospital CPA has a longer survival than prehospital CPA due to early recognition associated with high-quality BLS, appropriate ALS and post-CPR care. In recent years, a trend towards improved pediatric CPA survival has been observed in some communities and hospitals, and survival with good neurological prognosis is more frequent in children than in adults.

The available epidemiological data on pediatric CPA are particularly concentrated in countries in North America, Europe, Asia, and Australia that participate in large international registries. Improvement in pediatric CPA outcomes depends on efforts to clarify factors associated with better survival with good neurological prognosis. To increase the knowledge in this area, epidemiological studies in pediatric hospitals located in disadvantaged areas remain a research priority and are fundamental for the implementation of prevention strategies, improvements in CPR performance, in addition to allowing the analysis of possible regional variations of CPR epidemiology among the different services and countries.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Martinez PA, Totapally BR. The epidemiology and outcomes of pediatric in-hospital cardiopulmonary arrest in the United States during 1997 to 2012. Resuscitation. 2016;105:177–81.
2. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: systematic review of 67 prospective studies. Resuscitation. 2010;81:1479–87.
3. Young KD, Seidel JS. Pediatric cardiopulmonary resuscitation: a collective review. Ann Emerg Med. 1999;33:195–205.
4. Donoghue AJ, Nadkarni V, Berg RA, Osmond MH, Wells G, Nesbitt L, et al. Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. Ann Emerg Med. 2005;46:512–22.
5. Kleinman ME, Perkins GD, Bhanji F, Billi JE, Bray JE, Callaway CW, et al. ILCOR scientific knowledge gaps and clinical research priorities for cardiopulmonary resuscitation and emergency cardiovascular care: a consensus statement. Resuscitation. 2018;127:132–46.
6. Cummins RO, Chamberlain DA, Abramson NS, Allen M, Baskett PJ, Becker L, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style. A statement for health professionals from a task force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. Circulation. 1991;84:960–75.
7. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, Inter American Heart Foundation, Resuscitation Council of Southern Africa). Resuscitation. 2004;63:233–49.
8. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, Inter American Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Circulation. 2015;132:1286–300.
9. Glover BM, Brown SP, Morrison L, Davis D, Kudenchuk PJ, Van Ottingham L, et al. Wide variability in drug use in out-of-hospital cardiac arrest: a report from the resuscitation outcomes consortium. Resuscitation. 2012;83:1324–30.
10. Nitta M, Iwami T, Kitamura T, Nadkarni VM, Berg RA, Shimizu N, et al. Age-specific differences in outcomes after out-of-hospital cardiac arrests. Pediatrics. 2011;128:e812–820.
11. Atkins DL. Cardiac arrest in children and young adults: we are making progress. Circulation. 2012;126:1325–7.
12. Meyer L, Stubbs B, Fahrenbruch C, Maeda C, Harmon K, Eisenberg M, et al. Incidence, causes, and survival trends from cardiovascular-related sudden cardiac arrest in children and young adults 0 to 35 years of age: a 30-year review. Circulation. 2012;126:1363–72.
13. Tham LP, Wah W, Phillips R, Shahidah N, Ng YY, Shin SD, et al. Epidemiology and outcome of paediatric out-of-hospital cardiac arrests: a paediatric sub-study of the Pan-Asian resuscitation outcomes study (PAROS). Resuscitation. 2018;125:111–7.
14. McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, et al. Out-of-hospital cardiac arrest surveillance –Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005–December 31, 2010. Morb Mortal Wkly Rep Surveill Summ Wash DC 2002. 2011;60:1–19.
15. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA. 2008;300:1423–31.
16. Nishiyama C, Brown SP, May S, Iwami T, Koster RW, Beesems SG, et al. Apples to apples or apples to oranges? International variation in reporting of process and outcome of care for out-of-hospital cardiac arrest. Resuscitation. 2014;85:1599–609.
17. Kendirli T, Erkek N, Köroğlu T, Yldzdaş D, Bayrakç B, Güzel A, et al. Cardiopulmonary resuscitation in children with in-hospital and out-of-hospital cardiopulmonary arrest: multicenter study from Turkey. Pediatr Emerg Care. 2015;31:748–52.
18. Gräsner J-T, Lefering R, Koster RW, Masterson S, Böttiger BW, Herlitz J, et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: a prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. Resuscitation. 2016;105:188–95.
19. Young KD, Gausche-Hill M, McClung CD, Lewis RJ. A prospective, population-based study of the epidemiology and outcome of out-of-hospital pediatric cardiopulmonary arrest. Pediatrics. 2004;114:157–64.
20. Tijssen JA, Prince DK, Morrison LJ, Atkins DL, Austin MA, Berg R, et al. Time on the scene and interventions are associated with improved survival in pediatric out-of-hospital cardiac arrest. Resuscitation. 2015;94:1–7.
21. Herlitz J, Svensson L, Engdahl J, Gelberg J, Silfverstolpe J, Wisten A, et al. Characteristics of cardiac arrest and resuscitation by age group: an analysis from the Swedish Cardiac Arrest Registry. Am J Emerg Med. 2007;25:1025–31.
22. Rajan S, Wissenberg M, Folke F, Hansen CM, Lippert FK, Weeke P, et al. Out-of-hospital cardiac arrests in children and adolescents: incidences, outcomes, and household socioeconomic status. Resuscitation. 2015;88:12–9.
23. Deasy C, Bernard SA, Cameron P, Jaison A, Smith K, Harriss L, et al. Epidemiology of paediatric out-of-hospital cardiac arrest in Melbourne, Australia. Resuscitation. 2010;81:1095–100.

24. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Nadkarni VM, et al. Conventional and chest-compression-only cardiopulmonary resuscitation by bystanders for children who have out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. Lancet. 2010;375:1347–54.
25. López-Herce J, García C, Domínguez P, Carrillo A, Rodríguez-Núñez A, Calvo C, et al. Characteristics and outcome of cardiorespiratory arrest in children. Resuscitation. 2004;63:311–20.
26. López-Herce J, García C, Rodríguez-Núñez A, Domínguez P, Carrillo A, Calvo C, et al. Long-term outcome of paediatric cardiorespiratory arrest in Spain. Resuscitation. 2005;64:79–85.
27. Rea TD, Eisenberg MS, Sinibaldi G, White RD. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. Resuscitation. 2004;63:17–24.
28. Johnson MA, Grahan BJH, Haukoos JS, McNally B, Campbell R, Sasson C, et al. Demographics, bystander CPR, and AED use in out-of-hospital pediatric arrests. Resuscitation. 2014;85:920–6.
29. Girotra S, Spertus JA, Li Y, Berg RA, Nadkarni VM, Chan PS, et al. Survival trends in pediatric in-hospital cardiac arrests: an analysis from Get With the Guidelines-Resuscitation. Circ Cardiovasc Qual Outcomes. 2013;6:42–9.
30. Atkins DL, Everson-Stewart S, Sears GK, Daya M, Osmond MH, Warden CR, et al. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. Circulation. 2009;119:1484–91.
31. Masterson S, McNally B, Cullinan J, Vellano K, Escutnaire J, Fitzpatrick D, et al. Out-of-hospital cardiac arrest survival in international airports. Resuscitation. 2018;127:58–62.
32. Gianotto-Oliveira R, Gonzalez MM, Vianna CB, Monteiro Alves M, Timerman S, Kalil Filho R, et al. Survival after ventricular fibrillation cardiac arrest in the Sao Paulo metropolitan subway system: first successful targeted automated external defibrillator (AED) program in Latin America. J Am Heart Assoc. 2015;4:e002185.
33. Berg MD, Schexnayder SM, Chameides L, Terry M, Donoghue A, Hickey RW, et al. Part 13: pediatric basic life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122:S862–875.
34. Topjian AA, Berg RA. Pediatric out-of-hospital cardiac arrest. Circulation. 2012;125:2374–8.
35. Forrest A, Butt WW, Namachivayam SP. Outcomes of children admitted to intensive care after out-of-hospital cardiac arrest in Victoria, Australia. Crit Care Resusc. 2017;19: 150–8.
36. Akahane M, Tanabe S, Ogawa T, Koike S, Horiguchi H, Yasunaga H, et al. Characteristics and outcomes of pediatric out-of-hospital cardiac arrest by scholastic age category. Pediatr Crit Care Med. 2013;14:130–6.
37. Rodríguez-Núñez A, López-Herce J, García C, Domínguez P, Carrillo A, Bellón JM, et al. Pediatric defibrillation after cardiac arrest: initial response and outcome. Crit Care Lond Engl. 2006;10:R113.
38. Chen N, Callaway CW, Guyette FX, Rittenberger JC, Doshi AA, Dezfulian C, et al. Arrest etiology among patients resuscitated from cardiac arrest. Resuscitation. 2018;130:33–40.
39. Gerein RB, Osmond MH, Stiell IG, Nesbitt LP, Burns S, OPALS Study Group. What are the etiology and epidemiology of out-of-hospital pediatric cardiopulmonary arrest in Ontario, Canada? Acad Emerg Med. 2006;13:653–8.
40. Heron M. Deaths: leading causes for 2016. Natl Vital Stat Rep. 2018;67:1–77.
41. Wilders R. Cardiac ion channel opathies and the sudden infant death syndrome. ISRN Cardiol. 2012;2012:846171.
42. Suominen P, Baillie C, Korpela R, Rautanen S, Ranta S, Olkkola KT. Impact of age, submersion time and water temperature on outcome in near-drowning. Resuscitation. 2002;52:247–54.
43. Goto Y, Maeda T, Goto Y. Impact of dispatcher-assisted bystander cardiopulmonary resuscitation on neurological outcomes in children with out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. J Am Heart Assoc. 2014;3:e000499.
44. Akahane M, Ogawa T, Tanabe S, Koike S, Horiguchi H, Yasunaga H, et al. Impact of telephone dispatcher assistance on the outcomes of pediatric out-of-hospital cardiac arrest. Crit Care Med. 2012;40:1410–6.
45. Sutton RM, Case E, Brown SP, Atkins DL, Nadkarni VM, Kaltman J, et al. A quantitative analysis of out-of-hospital pediatric and adolescent resuscitation quality—a report from the ROC epistry-cardiac arrest. Resuscitation. 2015;93:150–7.
46. Hickey RW, Cohen DM, Strausbaugh S, Dietrich AM. Pediatric patients requiring CPR in the prehospital setting. Ann Emerg Med. 1995;25:495–501.
47. de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF, et al. Part 12: Pediatric Advanced Life Support: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132:S526–42.
48. Part 12: Pediatric Advanced Life Support. Circulation. 2005;112 24_supplement. IV–167.
49. Christenson J, Andrusiek D, Everson-Stewart S, Kudenchuk P, Hostler D, Powell J, et al. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. Circulation. 2009;120:1241–7.
50. Idris AH, Guffey D, Aufderheide TP, Brown S, Morrison LJ, Nichols P, et al. Relationship between chest compression rates and outcomes from cardiac arrest. Circulation. 2012;125:3004–12.
51. Stiell IG, Brown SP, Nichol G, Cheskes S, Vaillancourt C, Callaway CW, et al. What is the optimal chest compression depth during out-of-hospital cardiac arrest resuscitation of adult patients? Circulation 25. 2014;130:1962–70.
52. Sutton RM, French B, Niles DE, Donoghue A, Topjian AA, Nishisaki A, et al. 2010 American Heart Association recommended compression depths during pediatric in-hospital resuscitations are associated with survival. Resuscitation. 2014;85:1179–84.
53. Aufderheide TP, Lurie KG. Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation. Crit Care Med. 2004;32:S345–51.
54. Aufderheide TP, Sigurdsson G, Pirrallo RG, Yannopoulos D, McKnite S, von Briesen C, et al. Hyperventilation-induced hypotension during cardiopulmonary resuscitation. Circulation. 2004;109:1960–5.
55. Ewy GA. Cardiocerebral resuscitation: the new cardiopulmonary resuscitation. Circulation. 2005;111:2134–42.
56. Yannopoulos D, McKnite S, Aufderheide TP, Sigurdsson G, Pirrallo RG, Benditt D, et al. Effects of incomplete chest wall decompression during cardiopulmonary resuscitation on coronary and cerebral perfusion pressures in a porcine model of cardiac arrest. Resuscitation. 2005;64:363–72.
57. Zaritsky A, Nadkarni V, Hazinski MF, Foltin G, Quan L, Wright J, et al. Recommended guidlines for uniform reporting of pediatric advanced life support: the pediatric Utstein Style. A statement for healthcare professionals from a task force of the American Academy of Pediatrics, the American Heart Association, and the European Resuscitation Council. Writing Group. Circulation. 1995;92:2006–20.
58. Peberdy MA, Kaye W, Ornato JP, Larkin GL, Nadkarni V, Mancini ME, et al. Cardiopulmonary resuscitation of adults in the hospital: a report of 14720 cardiac arrests from the

National Registry of Cardiopulmonary Resuscitation. Resuscitation. 2003;58:297–308.
59. Reis AG, Nadkarni V, Perondi MB, Grisi S, Berg RA. A prospective investigation into the epidemiology of in-hospital pediatric cardiopulmonary resuscitation using the international Utstein reporting style. Pediatrics. 2002;109:200–9.
60. Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, et al. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. JAMA. 2006;295:50–7.
61. Donoghue AJ, Abella BS, Merchant R, Praestgaard A, Topjian A, Berg R, et al. Cardiopulmonary resuscitation for in-hospital events in the emergency department: a comparison of adult and pediatric outcomes and care processes. Resuscitation. 2015;92:94–100.
62. Slonim AD, Patel KM, Ruttimann UE, Pollack MM. Cardiopulmonary resuscitation in pediatric intensive care units. Crit Care Med. 1997;25:1951–5.
63. Meaney PA, Nadkarni VM, Cook EF, Testa M, Helfaer M, Kaye W, et al. Higher survival rates among younger patients after pediatric intensive care unit cardiac arrests. Pediatrics. 2006;118:2424–33.
64. Sutton RM, Reeder RW, Landis W, Meert KL, Yates AR, Berger JT, et al. Chest compression rates and pediatric in-hospital cardiac arrest survival outcomes. Resuscitation. 2018;130:159–66.
65. Ahn JY, Lee MJ, Kim H, Yoon HD, Jang HY. Epidemiological and survival trends of pediatric cardiac arrests in emergency departments in Korea: a cross-sectional, nationwide report. J Korean Med Sci. 2015;30:1354–60.
66. Jayaram N, Spertus JA, Nadkarni V, Berg RA, Tang F, Raymond T, et al. Hospital variation in survival after pediatric in-hospital cardiac arrest. Circ Cardiovasc Qual Outcomes. 2014;7:517–23.
67. Del Castillo J, López-Herce J, Matamoros M, Cañadas S, Rodríguez-Calvo A, Cecchetti C, et al. Long-term evolution after in-hospital cardiac arrest in children: prospective multicenter multinational study. Resuscitation. 2015;96:126–34.
68. Rathore V, Bansal A, Singhi SC, Singhi P, Muralidharan J. Survival and neurological outcome following in-hospital paediatric cardiopulmonary resuscitation in North India. Paediatr Int Child Health. 2016;36:141–7.
69. Shimoda-Sakano TM, Paiva EF, Bello FPS, Schvartsman C, Reis AG. Análise descritiva da ressuscitação cardiopulmonar pediátrica em hospital terciário: estudo piloto.; 2018.
70. Edwards-Jackson N, North K, Chiume M, Nakanga W, Schubert C, Hathcock A, et al. Outcomes of in-hospital paediatric cardiac arrest from a tertiary hospital in a low-income African country. Paediatr Int Child Health. 2019:1–5.
71. Suominen P, Olkkola KT, Voipio V, Korpela R, Palo R, Räsänen J. Utstein style reporting of in-hospital paediatric cardiopulmonary resuscitation. Resuscitation. 2000;45:17–25.
72. Guay J, Lortie L. An evaluation of pediatric in-hospital advanced life support interventions using the pediatric Utstein guidelines: a review of 203 cardiorespiratory arrests. Can J Anaesth J Can Anesth. 2004;51:373–8.
73. Tibballs J, Kinney S. A prospective study of outcome of in-patient paediatric cardiopulmonary arrest. Resuscitation. 2006;71:310–8.
74. Zeng J, Qian S, Zheng M, Wang Y, Zhou G, Wang H. The epidemiology and resuscitation effects of cardiopulmonary arrest among hospitalized children and adolescents in Beijing: an observational study. Resuscitation. 2013;84:1685–90.
75. de Mos N, van Litsenburg RRL, McCrindle B, Bohn DJ, Parshuram CS. Pediatric in-intensive-care-unit cardiac arrest: incidence, survival, and predictive factors. Crit Care Med. 2006;34:1209–15.
76. Wu ET, Li MJ, Huang SC, Wang CC, Liu YP, Lu FL, et al. Survey of outcome of CPR in pediatric in-hospital cardiac arrest in a medical center in Taiwan. Resuscitation. 2009;80:443–8.
77. Meert KL, Donaldson A, Nadkarni V, Tieves KS, Schleien CL, Brilli RJ, et al. Multicenter cohort study of in-hospital pediatric cardiac arrest. Pediatr Crit Care Med. 2009;10:544–53.
78. Olotu A, Ndiritu M, Ismael M, Mohammed S, Mithwani S, Maitland K, et al. Characteristics and outcome of cardiopulmonary resuscitation in hospitalised African children. Resuscitation. 2009;80:69–72.
79. Berens RJ, Cassidy LD, Matchey J, Campbell D, Colpaert KD, Welch T, et al. Probability of survival based on etiology of cardiopulmonary arrest in pediatric patients. Paediatr Anaesth. 2011;21:834–40.
80. López-Herce J, del Castillo J, Cañadas S, Rodríguez-Núñez A, Carrillo A, Spanish Study Group of Cardiopulmonary Arrest in Children. In-hospital pediatric cardiac arrest in Spain. Rev Espanola Cardiol Engl Ed. 2014;67:189–95.
81. Berg RA, Sutton RM, Holubkov R, Nicholson CE, Dean JM, Harrison R, et al. Ratio of PICU versus ward cardiopulmonary resuscitation events is increasing. Crit Care Med. 2013;41:2292–7.
82. López-Herce J, Del Castillo J, Matamoros M, Cañadas S, Rodriguez-Calvo A, Cecchetti C, et al. Factors associated with mortality in pediatric in-hospital cardiac arrest: a prospective multicenter multinational observational study. Intensive Care Med. 2013;39:309–18.
83. Straney LD, Schlapbach LJ, Yong G, Bray JE, Millar J, Slater A, et al. Trends in PICU admission and survival rates in children in Australia and New Zealand following cardiac arrest. Pediatr Intensive Crit Care Soc. 2015;16:613–20.
84. Berg RA, Nadkarni VM, Clark AE, Moler F, Meert K, Harrison RE, et al. Incidence and outcomes of cardiopulmonary resuscitation in PICUs. Crit Care Med. 2016;44:798–808.
85. Gupta P, Wilcox A, Noel TR, Gossett JM, Rockett SR, Eble BK, et al. Characterizing cardiac arrest in children undergoing cardiac surgery: asingle-center study. J Thorac Cardiovasc Surg. 2017;153, 450-8.e1.
86. Andersen LW, Vognsen M, Topjian A, Brown L, Berg RA, Nadkarni VM, et al. Pediatric in-hospital acute respiratory compromise: a report from the American Heart Association's get with the Guidelines-Resuscitation Registry. Pediatr Intensive Crit Care Soc. 2017;18:838–49.
87. Meert K, Telford R, Holubkov R, Slomine BS, Christensen JR, Berger J, et al. Paediatric in-hospital cardiac arrest: factors associated with survival and neurobehavioural outcome one year later. Resuscitation. 2018;124:96–105.
88. Matos RI, Watson RS, Nadkarni VM, Huang HH, Berg RA, Meaney PA, et al. Duration of cardiopulmonary resuscitation and illness category impact survival and neurologic outcomes for in-hospital pediatric cardiac arrests. Circulation. 2013;127:442–51.
89. Rodríguez-Núñez A, López-Herce J, del Castillo J, Bellón JM. Iberian-American Paediatric Cardiac Arrest Study Network RIBEPCI. Shockable rhythms and defibrillation during in-hospital pediatric cardiac arrest. Resuscitation. 2014;85:387–91.
90. Peberdy MA, Ornato JP, Larkin GL, Braithwaite RS, Kashner TM, Carey SM, et al. Survival from in-hospital cardiac arrest during nights and weekends. JAMA. 2008;299:785–92.
91. Bhanji F, Topjian AA, Nadkarni VM, Praestgaard AH, Hunt EA, Cheng A, et al. Survival rates following pediatric in-hospital cardiac arrests during nights and weekends. JAMA Pediatr. 2017;171:39–45.
92. Finn J, Jacobs I, Williams TA, Gates S, Perkins GD. Adrenaline and vasopressin for cardiac arrest. Cochrane Database Syst Rev. 2019;1:CD003179.

93. Gough CJR, Nolan JP. The role of adrenaline in cardiopulmonary resuscitation. Crit Care Lond Engl. 2018;22:139.
94. Jacobs IG, Finn JC, Jelinek GA, Oxer HF, Thompson PL. Effect of adrenaline on survival in out-of-hospital cardiac arrest: a randomised double-blind placebo-controlled trial. Resuscitation. 2011;82:1138–43.
95. Perkins GD, Ji C, Deakin CD, Quinn T, Nolan JP, Scomparin C, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. N Engl J Med. 2018;379:711–21.
96. Perondi MBM, Reis AG, Paiva EF, Nadkarni VM, Berg RA. A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. N Engl J Med. 2004;350:1722–30.
97. Patterson MD, Boenning DA, Klein BL, Fuchs S, Smith KM, Hegenbarth MA, et al. The use of high-dose epinephrine for patients with out-of-hospital cardiopulmonary arrest refractory to prehospital interventions. Pediatr Emerg Care. 2005;21:227–37.
98. Donnino MW, Salciccioli JD, Howell MD, Cocchi MN, Giberson B, Berg K, et al. Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: retrospective analysis of large in-hospital data registry. BMJ. 2014;348:g3028.
99. Andersen LW, Berg KM, Saindon BZ, Massaro JM, Raymond TT, Berg RA, et al. Time to epinephrine and survival after pediatric in-hospital cardiac arrest. JAMA. 2015;314:802–10.
100. Hoyme DB, Patel SS, Samson RA, Raymond TT, Nadkarni VM, Gaies MG, et al. Epinephrine dosing interval and survival outcomes during pediatric in-hospital cardiac arrest. Resuscitation. 2017;117:18–23.
101. Kurosawa S, Shimizu N, Honma J, Marukawa S, Yonemoto N, Yokoyama H, et al. Abstract 155: International comparison of pediatric in-hospital cardiac arrest: impact of critical care settings for hospital safety and outcome. from the Japanese registry of CPR for in-hospital cardiac arrest. Circulation. 2011;124:155.
102. Meaney PA, Bobrow BJ, Mancini ME, Christenson J, de Caen AR, Bhanji F, et al. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association. Circulation. 2013;128:417–35.
103. Paiva EF, Paxton JH, O'Neil BJ. Data supporting the use of end-tidal carbon dioxide (ETCO2) measurement to guide management of cardiac arrest: asystematic review. Data Brief. 2018;18:1497–508.
104. Berg RA, Sutton RM, Reeder RW, Berger JT, Newth CJ, Carcillo JA, et al. Association between diastolic blood pressure during pediatric in-hospital cardiopulmonary resuscitation and survival. Circulation. 2018;137:1784–95.
105. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, et al. Part 7: Adult Advanced Cardiovascular Life Support: 2015 American Heart Association Guidelines Update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132:S444–64.
106. Sutton RM, French B, Nishisaki A, Niles DE, Maltese MR, Boyle L, et al. American Heart Association cardiopulmonary resuscitation quality targets are associated with improved arterial blood pressure during pediatric cardiac arrest. Resuscitation. 2013;84:168–72.
107. Abella BS, Alvarado JP, Myklebust H, Edelson DP, Barry A, O'Hearn N, et al. Quality of cardiopulmonary resuscitation during in-hospital cardiac arrest. JAMA. 2005;293:305–10.
108. Alten JA, Klugman D, Raymond TT, Cooper DS, Donohue JE, Zhang W, et al. Epidemiology and outcomes of cardiac arrest in pediatric cardiac ICUs. Pediatr Crit Care Med. 2017;18:935–43.