Cardiopulmonary resuscitation in children
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Introduction

Approximately 16,000 American children (8–20/100,000 children/year) suffer an out-of-hospital cardiac arrest each year, and approximately 2% of children admitted to a pediatric intensive care unit (PICU) have a sudden cardiac arrest during that PICU admission [1**,2]. Although once deemed a rare event with dismal survival rates, the past 25 years have heralded improved discharge survival rates following both in-hospital and out-of-hospital pediatric cardiac arrests. Among children treated for their cardiac arrests, approximately 8% survive to discharge following an out-of-hospital arrest and 27% following an in-hospital arrest [3]. Critical factors that influence survival outcomes include the environment in which the arrest occurs, the preexisting condition of the child, the duration of no flow prior to resuscitation, the initial ECG rhythm detected and the quality of the basic and advanced life support interventions provided. We review 21st century epidemiology and new periarrest interventions that are promising to change the future of pediatric cardiac resuscitation.

Purpose of review

To summarize recent advances in pediatric cardiopulmonary resuscitation prevention, resuscitation and postresuscitation management.

Recent findings

Pediatric cardiac arrest has traditionally been considered a futile medical condition with dismal outcomes. Data in the 21st century indicate that more than 25% of children treated for in-hospital cardiac arrests survive to hospital discharge and more than 10% of children older than 1 year treated for out-of-hospital cardiac arrests survive to hospital discharge. These data establish that children are more likely to survive to hospital discharge than adults after both in-hospital and out-of-hospital cardiac arrests. Before arrest, exciting new studies demonstrate that the implementation of in-hospital pediatric medical emergency teams is associated with significant decreases in cardiac arrest incidence and overall pediatric hospital mortality. During arrest, ventricular fibrillation or ventricular tachycardia, once thought to be rare in children, occurs during 25% of in-hospital pediatric cardiac arrests and at least 7% of out-of-hospital pediatric cardiac arrests. Survival to hospital discharge is much more likely after arrests with a first documented rhythm of ventricular fibrillation or ventricular tachycardia than after pulseless electric activity and asystole. However, ventricular fibrillation or ventricular tachycardia is not always a favorable rhythm, as survival to discharge is much less likely when ventricular fibrillation or ventricular tachycardia occurs during resuscitation from an arrest with the first documented rhythm of pulseless electric activity or asystole. Further, extracorporeal membrane oxygenation cardiopulmonary resuscitation appears promising under special resuscitation circumstances to improve outcome from highly selected in-hospital pediatric cardiac arrest victims. Further, postresuscitation interventions such as goal-directed therapies and therapeutic hypothermia have been demonstrated in adults and infants to improve outcome for selected cardiac arrest victims and are promising candidate targets for study in children.

Summary

Pediatric cardiac arrest is not a futile condition; many children are successfully resuscitated each year. The implementation of new prearrest, intraarrest and postresuscitative therapies has the potential to further improve survival rates following pediatric cardiac arrest.

Keywords

cardiac arrest, cardiopulmonary resuscitation, extracorporeal membrane oxygenation, pediatric, ventricular fibrillation
In-hospital cardiac arrest

Almost two-thirds of in-hospital pediatric cardiac arrest patients can be successfully resuscitated, that is, attain sustained return of spontaneous circulation (ROSC) [3–10] Table 1 [11–15]. Approximately 25–50% of initial survivors survive to hospital discharge and almost three-quarters of survivors to discharge have good neurological outcomes. Nadkarni et al. [3] published an Utstein style report of in-hospital pediatric cardiac arrests from the American Heart Association’s multicenter National Registry of Cardiopulmonary Resuscitation (NRCPR). 95% of arrests were witnessed or monitored or both, and only 14% occurred in a general pediatric ward, 52% attained sustained ROSC, 36% survived for 24 h and 27% survived to hospital discharge. Outcomes for these children were substantially superior to outcomes for adults in this registry [27% survival to discharge versus 18%, respectively; adjusted odds ratio, 2.3 (95% confidence interval, 2.0–2.7)]. Importantly, 65% of these children had a favorable neurological outcome [3].

Out-of-hospital cardiac arrest

Outcomes following pediatric out-of-hospital arrests are much worse than in-hospital arrests [5,13,14,16] Table 1. Survival to hospital discharge typically occurs in less than 10% of these children, and many have severe neurological sequelae. These poor outcomes are in part because of prolonged periods of ‘no flow’ and in part because of specific diseases (e.g. traumatic cardiac arrest and sudden infant death syndrome). Many pediatric out-of-hospital cardiac arrests are not witnessed, and in most settings, less than 30% of children are provided with bystander cardiopulmonary resuscitation (CPR) [2].

This previous paradigm of survival is now being challenged by the first pediatric results from the National Heart, Lung, and Blood Institute (NHLBI)-funded multicenter Resuscitation Outcomes Consortium (ROC) evaluating all out-of-hospital cardiac arrests from 1 March 2006 to 28 February 2007 among 21.4 million persons in 11 US and Canadian ROC sites [1**]. Atkins et al. [1**] recently described epidemiological characteristics and outcomes of the out-of-hospital pediatric cardiac arrests in this cohort by age group (<1 year, infants; 1–11 years, children and 12–19 years, adolescents) [1**]. Survival to hospital discharge for all nontraumatic pediatric cardiac arrests was 6.4 versus 4.5% in adults (P = 0.03). Importantly, the hospital discharge survival rate was 7.8% for all emergency medical services treated pediatric cardiac arrests, yet, only 3.5% of infants compared with 10.4% of children and 12.6% of adolescents. Notably, children and adolescents were twice as likely to survive compared with infants and adults.

Pediatric ventricular fibrillation

Ventricular fibrillation arrests in children, once thought to be rare, are, in fact, not uncommon. The incidence of ventricular fibrillation varies by setting and age [17]. Out-of-hospital ventricular fibrillation cardiac arrest is uncommon in infants and children (4–5%) but occurs more frequently in adolescents (15%) [1**]. Survival to discharge in these populations increases with age. Approximately 25% of children suffering in-hospital cardiac arrest suffer from ventricular tachycardia or fibrillation [9]. Approximately 10% have initial ventricular fibrillation or ventricular tachycardia, whereas 15% have a secondary rhythm of ventricular fibrillation or ventricular tachycardia, that is, during resuscitation from asystole or pulseless electric activity (PEA). Survival to hospital discharge is much more likely after arrests with a first documented rhythm of ventricular fibrillation or ventricular tachycardia than after PEA and asystole [1**;9]; however, survival to discharge is much less likely when ventricular fibrillation or ventricular tachycardia occurs during resuscitation from an arrest with the first documented rhythm of PEA or asystole [9]. These data support the old paradigm that ‘initial’ ventricular fibrillation or ventricular tachycardia...
are ‘good’ arrest rhythms with better outcomes, but add a new wrinkle that ‘subsequent’ ventricular fibrillation or ventricular tachycardia are ‘bad’ arrest rhythms especially with poor outcomes [9].

Defibrillation (defined as termination of ventricular fibrillation) is necessary for successful resuscitation from ventricular fibrillation cardiac arrest. The termination of fibrillation can result in asystole, PEA or a perfusing rhythm. The goal of defibrillation is return of an organized electrical rhythm with pulse. When prompt defibrillation is provided soon after the induction of ventricular fibrillation in a cardiac catheterization laboratory, the rates of successful defibrillation and survival approach 100% [18]. When automated external defibrillators are used within 3 min of adult-witnessed ventricular fibrillation, long-term survival can occur in more than 70% [19,20]. In general, mortality increases by 7–10% per minute of delay to defibrillation. Early and effective, near-continuous chest compressions can attenuate the incremental increase in mortality with delayed defibrillation [21]. Because pediatric cardiac arrests are commonly due to progressive asphyxia or shock or both, the initial treatment of choice is prompt CPR. Therefore, rhythm recognition is relatively less emphasized than adult cardiac arrests. The earlier that ventricular fibrillation can be diagnosed, the more successfully we can treat it.

**Phases of resuscitation: prearrest, no flow, cardiopulmonary resuscitation low flow and postreturn of spontaneous circulation**

Interventions to improve outcome from pediatric cardiac arrest should be targeted to optimize therapies according to the cause, timing, duration, intensity and ‘phase’ of resuscitation. There are at least four ‘phases’ of cardiac arrest: prearrest, no flow (untreated cardiac arrest), low flow (CPR) and postresuscitation.

**Interventions during the prearrest phase: medical emergency teams**

The prearrest phase is the ideal phase to decrease mortality and morbidity from cardiac arrest by decreasing the incidence of cardiac arrest events. Patients suffering from in-hospital cardiac arrest often have abnormal physiologic parameters in the hours prior to their event [22,23]. Moreover, the precipitating causes of most pediatric cardiac arrests are acute respiratory insufficiency and circulatory shock [3]. Medical emergency teams (METs) are designed to respond to patients in imminent danger of decompensation, thereby preventing progression to cardiac arrest. Brilli et al. [24] revealed a nonsignificant trend toward decrease in in-hospital cardiac arrests with MET implementation when compared with historic controls. The landmark study of pediatric MET implementation by Sharek et al. [25] demonstrated a marked reduction in the mean monthly mortality rate by 18% (1.01 to 0.83 deaths per 100 discharges, \(P = 0.007\)) and the mean monthly code rate by more than 70% at a large children’s hospital. Most recently, Tibballs and Kinney [26*] also reported that implementation of a pediatric MET at The Royal Children’s Hospital in Melbourne was associated with a 33% decrease in hospital mortality, a 67% decrease in unexpected hospital ward deaths, a 56% decrease in hospital ward preventable cardiac arrests and a 91% decrease in deaths from preventable hospital ward cardiac arrests. Although these data are inherently limited by their before–after study designs (i.e., comparisons with historical controls), one implication of this new paradigm is that perhaps any cardiac arrest that is not in a monitored unit should be considered a potentially avoidable event.

**Interventions during cardiac arrest (no flow) and cardiopulmonary resuscitation (low flow)**

Interventions during the no-flow phase of pulseless cardiac arrest focus on early recognition of cardiac arrest and prompt initiation of basic life support. The goal of effective CPR is to optimize coronary and cerebral perfusion and blood flow to critical organs during the low-flow phase. Unfortunately, bystander CPR is only provided for approximately one out of three pediatric out-of-hospital arrests [1**]. The most critical elements of CPR are ‘push hard, push fast, minimize interruptions, allow full chest recoil and don’t overventilate’. Overventilation and interruptions in compressions during adult and pediatric CPR are common and can substantially compromise venous return and cardiac output, contributing to worse survival [27,28*,29*,30–32].

Bystander hands-only CPR (i.e., chest compression-only CPR) is now recommended for adult sudden collapse cardiac arrests [29*]. In addition, implementation of minimally interrupted cardiac resuscitation by emergency medical service providers (including initial avoidance of endotracheal intubation and frequently avoidance of active rescue breathing) significantly improved survival from out-of-hospital adult cardiac arrest [33**,**34**]. In contrast, animal studies of asphyxia-precipitated cardiac arrests have established that rescue breathing is a critical component of successful CPR [35,36]. A larger percentage of pediatric arrests are asphyxial in nature, and therefore, children who suffer from cardiac arrest should receive chest compressions and rescue breathing.

Medication use during CPR is recommended and taught for both pediatric and adult advanced life support. Although animal studies indicate that epinephrine can improve initial ROSC resuscitation success after both asphyxial and ventricular fibrillation cardiac arrests, no single medication has been shown to improve survival outcome from pediatric cardiac arrest. Vasopressin during
prolonged pediatric cardiac arrest may result in ROSC when standard medications have failed [37] but has not yet been subjected to rigorous clinical trials with appropriate controls. Contrary to common belief, nonselective use of calcium is associated with worse survival outcomes [38], and it should be reserved for select circumstances such as hyperkalemia. Medications commonly used for pediatric cardiac arrests are summarized in Table 2.

**Interventions during the postresuscitation phase**

The postresuscitation phase is a high-risk period for brain injury, ventricular arrhythmias and extension of reperfusion injuries. The reintroduction of blood flow can lead to inflammation and oxidative stress and can cause secondary injury. Interventions during the immediate postresuscitation phase strive to minimize reperfusion injury and support cellular recovery. Two seminal articles [39,40] established that induced hypothermia (32–34°C) could improve outcome for comatose adults after resuscitation from ventricular fibrillation cardiac arrest. Interpretation and extrapolation of these studies to children is difficult. Hyperthermia following pediatric brain injury is common and is associated with poor neurological outcome [41]. Neonatal trials of selective brain cooling and systemic cooling show promise in neonatal hypoxic–ischemic encephalopathy, suggesting that induced hypothermia may improve outcomes [42,43].

Although no explicit postarrest methodology for improving survival outcome from pediatric cardiac arrest has yet been elucidated, a defined goal-directed protocol improved outcomes following adult cardiac arrest [44]. Improvements in postresuscitation care are a promising strategy to improve resuscitation survival outcomes.

**Prognosis**

Prediction of neurologic outcome following pediatric cardiac arrest is a complex task without clearly delineated prognosticators for individual recovery. Emerging data suggest that burst-suppression pattern on postarrest electroencephalogram is sensitive and specific for poor neurologic outcome [45]. Elevated plasma neuron-specific enolase biomarker concentrations are associated with poor neurologic outcomes when measured 48 h after ROSC in children suffering from cardiac arrest, and elevated serum S100B biomarker concentrations are associated with increased mortality [46]. However, no single test can stand
alone, and thus far, no summary physiologic or biomarker score has been validated to predict outcome with a high level of sensitivity and specificity.

**Extracorporeal membrane oxygenation**
Multiple retrospective series have reported extraordinary results with the use of extracorporeal membrane oxygenation (ECMO) as a rescue therapy for pediatric cardiac arrests, especially from potentially reversible acute postoperative myocardial dysfunction or arrhythmias [47–50]. Morris et al. [51] reported on 66 children placed on ECMO during CPR. The median duration of CPR prior to establishment of ECMO was 50 min, yet, 35% (23/66) of these children survived to hospital discharge. Over one-third of patients in another recent retrospective study of 682 pediatric patients receiving ECMO–CPR also survived to discharge [11]. Although there are more patients receiving ECMO–CPR, the proportion of those treated with ECMO–CPR who survive has not improved, potentially implicating the importance of selecting patients with reversible disease causes. It is important to emphasize that the children who survived with ECMO–CPR despite prolonged CPR had brief periods of ‘no flow,’ excellent CPR during the ‘low-flow’ period and a well controlled postresuscitation phase.

**Conclusion**
Exciting new epidemiological studies such as the NRCPR for in-hospital cardiac arrests and the large-scale, multicenter out-of-hospital Resuscitation Outcome Consortium funded by NHLBI are providing new data to guide our resuscitation practices and generate hypotheses for new approaches to improve outcomes. It is increasingly clear that excellent basic life support is often not provided in either out-of-hospital or in-hospital settings. Attention to ‘push hard, push fast, minimize interruptions, allow full chest recoil and don’t overventilat’ may have impact on the ability to achieve ROSC. System-based approaches of prevention, such as METs, may be an answer to decrease the incidence of in-hospital cardiac arrests. Mechanical interventions, such as ECMO or other cardiopulmonary bypass systems, are already commonplace interventions for prolonged in-hospital cardiac arrests. Technical advances are likely to further improve our ability to provide such mechanical support.

Outcomes from pediatric cardiac arrest and CPR appear to be improving. The evolution of clinical practice to integrate the pathophysiology and timing, intensity, duration and variability of the hypoxic–ischemic insult may lead to more patient-specific and time-specific goal-directed therapy and better outcomes. By strategically focusing therapies to specific phases of cardiac arrest and resuscitation and to evolving pathophysiology, there is great promise that critical care interventions will lead the way to more successful cardiopulmonary and cerebral resuscitation in children.

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**References and recommended reading**
Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 267–268).


Cardiopulmonary resuscitation


This study reviews the animal and human literature supporting bystander hands-only CPR.


Demonstration that a new approach to out-of-hospital CPR improved outcomes.


This study shows how implementation of minimally interrupted chest compressions can improve survival to discharge.


This study examines potential harm of calcium use during CPR.


This study describes the landscape of biomarkers in survivors of pediatric cardiac arrest.


