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Pediatric In-Hospital Cardiac Arrest and Cardiopulmonary Resuscitation in the United States
A Review

Ryan W. Morgan, MD, MTR; Matthew P. Kirschen, MD, PhD; Todd J. Kilbaugh, MD; Robert M. Sutton, MD, MSCE; Alexis A. Topjian, MD, MSCE

IMPORTANCE Pediatric in-hospital cardiac arrest (IHCA) occurs frequently and is associated with high morbidity and mortality. The objective of this narrative review is to summarize the current knowledge and recommendations regarding pediatric IHCA and cardiopulmonary resuscitation (CPR).

OBSERVATIONS Each year, more than 15 000 children receive CPR for cardiac arrest during hospitalization in the United States. As many as 80% to 90% survive the event, but most patients do not survive to hospital discharge. Most IHCAs occur in intensive care units and other monitored settings and are associated with respiratory failure or shock. Bradycardia with poor perfusion is the initial rhythm in half of CPR events, and only about 10% of events have an initial shockable rhythm. Pre–cardiac arrest systems focus on identifying at-risk patients and ensuring that they are in monitored settings. Important components of CPR include high-quality chest compressions, timely defibrillation when indicated, appropriate ventilation and airway management, administration of epinephrine to increase coronary perfusion pressure, and treatment of the underlying cause of cardiac arrest. Extracorporeal CPR and measurement of physiological parameters are evolving areas in improving outcomes. Structured post–cardiac arrest care focused on targeted temperature management, optimization of hemodynamics, and careful intensive care unit management is associated with improved survival and neurological outcomes.

CONCLUSIONS AND RELEVANCE Pediatric IHCA occurs frequently and has a high mortality rate. Early identification of risk, prevention, delivery of high-quality CPR, and post–cardiac arrest care can maximize the chances of achieving favorable outcomes. More research in this field is warranted.

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Author Affiliations: Department of Anesthesiology and Critical Care Medicine, Division of Critical Care Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Morgan, Kirschen, Kilbaugh, Sutton, Topjian); Department of Anesthesiology and Critical Care Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia (Morgan, Kirschen, Kilbaugh, Sutton, Topjian).

Corresponding Author: Ryan W. Morgan, MD, MTR, Division of Critical Care Medicine, Children's Hospital of Philadelphia, 3401 Civic Center Blvd, 6 Wood-6104, Philadelphia, PA 19104 (morganr1@email.chop.edu).

An estimated 15 200 children receive cardiopulmonary resuscitation (CPR) for in-hospital cardiac arrest (IHCA) annually in the United States.[1] Pediatric IHCA outcomes improved during the first decade of the 21st century,[2,3] likely owing to a widespread recognition of the need for high-quality resuscitation and a focus on recognizing and transferring the deteriorating pediatric inpatient to an intensive care unit (ICU). However, survival rates have plateaued and more than half of children with IHCA do not survive to hospital discharge.[3]

Compared with adults with IHCA, children with IHCA differ in demographic characteristics, location within the hospital, cause of cardiac arrest, initial cardiac arrest rhythm, and type of monitoring in place.[4-7] **Table 1** shows a comparison of these variables between pediatric and adult patients.[3-8] However, prospective pediatric IHCA studies are limited, and most pediatric resuscitation guidelines are extrapolated from adult guidelines.[9,10] Substantial differences also exist between pediatric IHCA and pediatric out-of-hospital cardiac arrest (OHCA). Although IHCA occurrence is frequently associated with the progression of underlying disease processes, such as shock and respiratory failure, common causes of pediatric OHCA include drowning, sudden infant death syndrome, and sudden cardiac death from arrhythmias.[11] Compared with IHCA, OHCA survival outcomes are worse,[12] and OHCA systems of care are focused on encouraging bystander CPR and optimizing basic life support measures in the prehospital state.[13]

Pediatric IHCA is a modifiable disease process. Efforts to prevent its occurrence, treat it with high-quality CPR, and deliver successful post–cardiac arrest care can demonstrably improve outcomes. In this narrative review, we discuss pediatric IHCA, including incidence, causes, prevention, treatment, and post–cardiac arrest therapies.

Methods

This narrative review was based on several informal searches of PubMed for peer-reviewed English-language articles related to pediatric IHCA. The searches were conducted between January 4,

Table 1. Characteristics of Pediatric vs Adult In-Hospital Cardiac Arrest

Characteristic	Pediatric patients[3-5,7]	Adult patients[4,6,7]
Incidence	Approximately 15 200/y in United States	Approximately 292 000/y in United States
Age	Median: 1-2 y; mean: 3-5 y[a]	Mean: 66 y
Male sex	50%-55%	60%
Hospital location	85%-90% In monitored settings[b]	50% In monitored settings[b]
Airway in place	Approximately 80%	Approximately 30%-35%
Cause of cardiac arrest	Most with respiratory failure and/or progressive shock	50%-60% Cardiac; 15%-40% respiratory
Initial cardiac arrest rhythm	50% Bradycardia with poor perfusion; 40% other nonshockable rhythms	80% Nonshockable rhythms (pulseless electrical activity or asystole)
Survival to discharge	45%-50% (40% Among those with pulseless events)	25%
Neurological outcome	Favorable in 80%-90% of survivors[c]	Good functional status in 80% of survivors[d]

[a] Age depends on inclusion criteria of studies.

[b] Monitored settings include intensive care units, emergency departments, and operating rooms.

[c] Pediatric Cerebral Performance Category scale (range: 1-6, with 1 indicating normal function and 6 indicating brain death[8]): 1 to 3 or unchanged from baseline.

[d] Cerebral Performance Category scale: 1 or 2.

2020, and April 15, 2020. Searches were limited to studies that included children younger than 18 years. Search terms were as follows: in-hospital cardiac arrest, cardiac arrest, cardiopulmonary resuscitation, resuscitation, rapid response, medical emergency team, post-arrest, and post-resuscitation. We placed no limit on the date ranges of reviewed articles. Because of the small number of prospective randomized trials in pediatric resuscitation, we did not perform a systematic review. Our objective was to review the current knowledge and recommendations regarding pediatric IHCA and CPR.

Discussion

Epidemiological Characteristics of Pediatric IHCA

Incidence and Location

Because of the lack of a central reporting process, the actual incidence of pediatric IHCA in the United States remains unknown. Currently accepted estimates are based on data from the American Heart Association (AHA) Get With The Guidelines—Resuscitation (GWTG-R) registry. Given the voluntary nature of this prospective quality improvement registry, data from participating hospitals may not be entirely representative of other hospitals. Regardless, every year, an estimated 15 200 children have IHCAs in the United States.[1] This number includes 7100 pulseless IHCAs and 8100 cases of CPR provided for bradycardia with poor perfusion.[1] Including recurrent events, the total annual number of pediatric IHCA cases is approximately 19 900.[1] In accordance with Utstein CPR reporting guidelines,[14] we refer to all CPR events (pulseless rhythms or bradycardia with poor perfusion) as IHCA.

As opposed to adult IHCAs, which are generally divided between monitored and unmonitored in-hospital settings,[7] 85% to 90% of pediatric IHCAs have occurred in monitored settings, most commonly the ICU.[15] This proportion has increased over time,[15] likely because of widespread implementation of rapid response systems and the recognition and timely transfer of deteriorating patients.[16-19] The incidence of IHCA among children admitted to pediatric ICUs is approximately 1.8%.[5] Children with heart disease have a substantially higher risk of IHCA,[20] and 3.1% of pediatric patients in cardiac ICUs receive CPR during their admission.[21]

Causes and Rhythms

Pediatric IHCA most often occurs in the setting of progressive respiratory failure or shock.[4,5,22] Interventions in place at the onset of CPR include invasive mechanical ventilation in 59% to 82% of children and vasopressor infusions in 29% to 78% of children.[23,24]

Most initial cardiac arrest rhythms are nonshockable (ie, asystole, pulseless electrical activity [PEA], or bradycardia with poor perfusion). Bradycardia with poor perfusion is the initial CPR rhythm in more than half of IHCA events. Children with bradycardia with poor perfusion have superior survival outcomes vs survival outcomes in those with pulselessness at CPR onset.[24,25] However, between 31% and 51% of patients with bradycardia and poor perfusion become pulseless during CPR, and these patients have worse outcomes than either those who were initially pulseless or those who were never pulseless.[24,26]

Ventricular fibrillation (VF) and pulseless ventricular tachycardia (PVT) account for approximately 10% of CPR events.[2,4,27] Primary VF and PVT are associated with more favorable outcomes than PEA and asystole. However, when they occur as secondary rhythms during CPR (after initial PEA or asystole), the outcomes are worse than in those with either primary VF or PVT or in those without VF or PVT at any time.[4,27] This observation may reflect that secondary VF and PVT occur because of worsening myocardial injury over the course of CPR or that secondary VF and PVT are not immediately recognized and thus defibrillated.[27]

Outcomes

Survival outcomes are associated with the patient's underlying diagnoses and the cause of the event,[4] the initial cardiac arrest rhythm,[4,27] the quality of CPR delivered and hemodynamics achieved,[23,28,29] the duration of CPR,[5,22] and the quality of post–cardiac arrest care.[30] Although the incidence of IHCA in children with heart disease is relatively high, the survival rates among these patients, particularly those undergoing surgical cardiac treatment during their hospitalization, are higher than among patients without heart disease.[22]

In ICUs, rates of acute IHCA event survival (return of spontaneous circulation [ROSC] or return of circulation with extracorporeal support) are 78% to 90% in recent multicenter observational studies.[5,23] These rates have doubled over the past 2 decades; however, many children with event survival die before hospital discharge.[2,3] According to a recent GWTG-R study, 32% of children with pulseless cardiac arrests from 2000 to 2018 survived to hospital discharge, increasing from 19% in 2000 to 40% in 2011 and then remaining relatively stable through the subsequent 7 years.[3] Among patients with bradycardia with poor perfusion who never became pulseless during their CPR event, 66% survived to hospital discharge in 2018.[3]

Of those patients who survive to discharge, approximately 90% have grossly favorable neurological outcomes,[5,23] as ascertained with the Pediatric Cerebral Performance Category scale (range: 1-6, with 1 indicating normal function and 6 indicating brain death).[8] How-

ever, this scale, typically extrapolated retrospectively from medical record review, lacks sensitivity for more granular neurological dysfunction, and many IHCA event survivors have subtle and sustained neurological impairment.[5,31] Moreover, postresuscitation death is commonly attributed to declaration of death by neurological criteria or poor neurological outcome, which prompts the withdrawal of life-sustaining therapies.[32] Further studies are necessary to better characterize neurocognitive and neurobehavioral outcomes among survivors.

Prevention of Pediatric IHCA

Rapid response teams and medical emergency teams have become a nearly universal presence in pediatric hospitals over the past 2 decades. Although their composition and characteristics vary,[17] their implementation has been temporally associated with decreases in cardiac arrest frequency and improvements in mortality.[18,33,34] In addition, severity-of-illness scoring systems have been used to identify patients at risk for clinical deterioration but have not consistently been associated with decreased hospital mortality.[35]

Among children in the ICU, previous work has sought to identify those at risk for IHCA to provide situational awareness and facilitate focused treatment to prevent deterioration.[36,37] Across 15 cardiac ICUs, implementation of an IHCA prevention bundle was associated with a decreased incidence of IHCA.[38] In addition, evidence showed that specific ICU staffing models, such as 24 hours per day for 7 days per week in-hospital attending-intensivist coverage, were associated with IHCA prevention.[39]

Treatment of Cardiac Arrest

The cornerstone of cardiac arrest therapy is the delivery of high-quality CPR that temporarily supports organ perfusion while optimizing the probability of attaining ROSC. The components of CPR and other therapies delivered during IHCA are discussed in this section.

Chest Compressions

High-quality CPR consists of chest compressions delivered at an appropriate rate with adequate depth, full chest wall recoil, and minimal interruptions. Compliance with the AHA pediatric basic and advanced life support guidelines recommendations for chest compressions[9,10] is associated with higher rates of survival.[28,29] Table 2 shows the AHA guidelines target for each metric of high-quality CPR.[9,10] Widespread technology is now available, largely in the form of CPR quality–monitoring defibrillators, that measures chest compression mechanics and provides feedback to clinicians in real time. Systematic use of such technology coupled with resuscitation debriefing programs focused on CPR quality is associated with improved outcomes.[40]

Training and equipping clinicians to deliver high-quality CPR according to these metrics has likely been associated with improvement in IHCA outcomes.[2] However, specific targets for pediatric chest compression rates and depths are largely based on expert consensus and extrapolation from adult studies.[10] Rates outside of those recommended by the AHA guidelines have recently been associated with improved outcomes.[41] Moreover, depths within the target range are frequently difficult to achieve, even in high-performing centers that largely achieve other CPR metrics.[42] These data highlight the need for further studies to refine the specific targets for chest compression mechanics.

Table 2. Guideline Targets for Pediatric Cardiopulmonary Resuscitation Quality

Metric	Target[9,10]
Rate	100-120 Compressions/min
Depth	Adolescents[a]: 5-6 cm
	Children[b]: approximately 5 cm (≥one-third anterior-posterior chest depth)
	Infants[c]: approximately 4 cm (≥one-third anterior-posterior chest depth)
Chest compression fraction	Chest compressions for ≥80% of time of arrest
Chest recoil	Allow full recoil between compressions; avoid leaning
Ventilations	Advanced airway: 10 breaths/min
	No advanced airway (adolescents[a]): 30:2 compression to ventilation ratio
	No advanced airway (children[b] and infants[c]): 15:2 compression to ventilation ratio

[a] Adolescents are those showing signs of puberty (eg, breast development in girls; axillary hair in boys).

[b] Children are those 1 year or older without signs of puberty.

[c] Infants are those younger than 1 year.

Defibrillation

Prompt defibrillation is a critical component in the treatment of VF or PVT. In adults, delays in time to defibrillation are associated with a relatively linear increase in the risk of mortality of 7% to 10% per minute.[43] However, in a 2018 GWTG-R registry study of hospitalized children with VF or PVT IHCAs, no association between time to defibrillation and survival was found.[44] The reasons for this finding are likely multifactorial. Most notably, the median time to the first defibrillation attempt was just 1 minute, which presumably limited the ability to detect timing-driven outcome differences. Moreover, given that 78% of cardiac arrests occurred in the ICU,[44] these children likely received more immediate CPR than adult patients in unmonitored settings. High-quality CPR optimizes myocardial blood flow to the fibrillating myocardium and enhances the likelihood of defibrillation success,[45] so this process likely decreased the implications of modest delays in defibrillation. Nonetheless, being prepared for defibrillation is imperative throughout pediatric CPR events, especially given that many children develop shockable rhythms as a secondary rhythm during CPR.[27]

Ventilation and Airway Management

Assisted ventilation is a key component of pediatric CPR, but resuscitation guidelines recommend relatively low ventilation rates during CPR for several reasons.[9,10] First, because of the lower cardiac output and pulmonary blood flow during CPR, less minute ventilation is necessary to balance ventilation and perfusion.[46,47] Second, the delivery of positive-pressure breaths can have deleterious hemodynamic results, most directly through the reduction of systemic venous return.[48] Third, in patients without an invasive airway in place, interruptions in CPR to deliver rescue breaths decrease the chest compression fraction and therefore compromise organ perfusion.[49]

Although based on sound physiological principles, ventilation rates for children that match those recommended for adults do not

take into account that children have higher ventilation rates at baseline or that most pediatric IHCAs occur in the setting of respiratory failure.[23,24] A recent observational cohort study of children with IHCA in the ICU found that higher ventilation rates during CPR were associated with improved outcomes.[50] None of the 52 CPR events had AHA guideline–compliant ventilation rates; the median ventilation rate delivered to these children was 30.1 breaths per minute.[50] This finding represents a substantial gap between consensus guidelines and clinical practice, highlighting the need for prospective studies.

Similarly, a clear consensus on optimal pediatric airway management during CPR is needed. As many as 82% of hospitalized children have an invasive airway in place at the time of CPR initiation.[23] A large retrospective study of children without an advanced airway in place during IHCA found an association between the performance of tracheal intubation during cardiac arrest and lower rates of survival.[51] These findings are similar to those of a pediatric OHCA study that demonstrated worse outcomes with endotracheal intubation than with bag-mask ventilation.[52] This association of intubation with worse outcomes may be attributed to interruptions in CPR to facilitate intubation, diverted focus from maintaining CPR quality, unrecognized esophageal intubation and other intubation-associated adverse events, or other unmeasured confounders. When assessing the risk of intubation, pediatric clinicians must consider patient-specific factors as well as their setting and clinical capabilities. The cause of the cardiac arrest and the likelihood of achieving ROSC without invasive ventilation should be considered along with the detrimental implications of interrupting compressions to deliver ventilations.[49] Given the limitations in the quality of data available, the authors of the 2019 AHA guidelines were unable "to make any recommendation about advanced airway management for IHCA."[53(pe907)]

Medications

Epinephrine is recommended during pediatric IHCA because of its α-adrenergic function of increasing systemic vascular resistance, which increases coronary and cerebral perfusion pressures.[9] No prospective pediatric trial has established the efficacy of epinephrine in improving survival outcomes, but delays in epinephrine administration are associated with worse outcomes in children.[54] Observational findings are mixed regarding the appropriate dosing intervals. The recommended dosing interval of 3 to 5 minutes was associated with improved outcomes in one study,[55] whereas more frequent[56] and less frequent[57] intervals have each been independently associated with superior outcomes in other studies.

Vasopressin, which was previously recommended as an alternative vasopressor for adult cardiac arrest, has not been shown to have a gross survival advantage over epinephrine alone in either adult[58] or pediatric[59] studies. Given that vasopressin induces vasoconstriction through the activation of V1a receptors rather than as an adrenergic agonist, vasopressin could hypothetically be advantageous in specific scenarios in which epinephrine is not efficacious or deleterious.[60] For example, in cardiac arrest associated with catecholamine-refractory vasodilatory shock, vasopressin offers an alternative mechanism of increasing systemic vascular resistance.[61] Similarly, in patients with pulmonary hypertension, the potentially harmful increase in pulmonary vascular resistance associated with epinephrine[62] may be avoided by using a vasoactive drug that largely spares the pulmonary vasculature from its effects. Regardless, dedicated studies are needed to characterize potential indications for vasopressin in pediatric resuscitation.

Antiarrhythmic agents are provided during pediatric IHCA for defibrillation-refractory VF or PVT. A GWTG-R registry study that compared lidocaine with amiodarone hydrochloride revealed increased rates of ROSC with lidocaine,[63] but a more recent propensity-matched cohort study found no difference in clinical outcomes between these 2 medications.[64] Given the lack of definitive evidence supporting one antiarrhythmic over another, consensus guidelines conclude that use of either lidocaine or amiodarone is reasonable for shock-refractory VF or PVT.[65]

Other medications commonly used during pediatric IHCA include calcium (eg, calcium gluconate, calcium chloride) and sodium bicarbonate. Despite frequent use, routine administration of either of these medications is associated with decreased rates of survival.[66,67] Each is recommended only for specific indications, such as hyperkalemia and sodium channel overdose.[9]

Personalizing CPR

Resuscitation techniques and standards have been developed primarily for adult OHCA, with algorithms and guidelines recommending a uniform approach to account for the wide variation in rescuer experience and knowledge base. However, pediatric IHCA is associated with the progression of many disease processes, the pathophysiological characteristics of which persist during CPR. Recognizing and treating the underlying cause of cardiac arrest is imperative for resuscitation success. The immediate cause of cardiac arrest can generally be attributed to one or more of the classic *Hs and Ts* (eg, hypovolemia, hyperkalemia, and tension pneumothorax) and should be promptly addressed. In addition, common underlying pediatric ICU diagnoses, such as congenital heart disease, septic shock, and pulmonary hypertension, may warrant alternative therapies during resuscitation.[9,61,68]

Given that most pediatric in-hospital CPR is performed by trained teams in highly monitored and well-resourced settings,[15] clinicians frequently have the ability to monitor an individual patient's physiological response to CPR and titrate therapies accordingly. The most well-established physiological monitors during resuscitation are invasively measured blood pressure and end-tidal carbon dioxide ($EtCO_2$).[9,69] A growing body of literature recognizes that measurement of these physiological parameters can be used to gauge CPR quality, identify likely outcomes, and help guide therapies during resuscitation.[69,70]

Coronary perfusion pressure is the driving force for myocardial blood flow, and higher values during CPR are associated with increased likelihood of ROSC in adult IHCA.[71] Because nearly half of the children with IHCAs have an arterial catheter in place,[15] hemodynamic monitoring during CPR is often possible. Diastolic blood pressure is recommended as a feasible surrogate for coronary perfusion pressure,[69] and in a prospective observational trial, intra-arrest diastolic blood pressure of 25 mm Hg or higher in infants and 30 mm Hg or higher in older children was associated with increased rates of survival to discharge and survival with favorable neurological outcome.[23] The ideal methods of optimizing hemodynamics during CPR have not been prospectively studied in humans, but in large animal models of pediatric IHCA, titration of vasopressor drugs according to coronary perfusion pressure during CPR has led

Table 3. Post–Cardiac Arrest Syndrome[9,30,53,83-96]

Key component	Clinical manifestations	Monitoring	Therapies
Brain injury	• Encephalopathy • Cerebral edema • Seizures • Myoclonus • Coma	• EEG • Clinical neurological examination • Brain CT • Brain MRI • Near-infrared spectroscopy; transcranial Doppler	• Antiseizure medications • TTM: 32-34 °C or 36-37.5 °C • Sedation • Oxygen saturation 94%-99%
Myocardial dysfunction	• Left and right ventricular systolic and diastolic dysfunction • Hypotension • Arrhythmias • Low cardiac output • Pulmonary edema	• Arterial line • Echocardiogram • Cardiac monitoring	• Inotropic medications • Antiarrhythmic medications • Electrolyte repletion • Mechanical ventilation
Systemic ischemia-reperfusion response	• Hypotension • Vasoplegia • Hypovolemia • Hyperglycemia/hypoglycemia • Adrenal insufficiency • Coagulopathy • Multisystem organ dysfunction • Pyrexia	• Pulse oximetry • Temperature • Urine output • Laboratory studies (pH; lactate; end-organ perfusion; coagulation; oxygenation/ventilation) • Chest radiograph	• Vasoactive medications • Insulin/dextrose • Corticosteroids • Product replacement • TTM/antipyretic medications • Renal replacement therapy
Persistent precipitating pathophysiological condition	• Ongoing underlying disease process (eg, respiratory failure, sepsis, and pulmonary hypertension)	• Observation/monitoring in ICU setting • Ongoing assessment of progression of underlying illnesses	• Specific to individual pathophysiological processes

Abbreviations: CT, computed tomography; EEG, electroencephalogram; ICU, intensive care unit; MRI, magnetic resonance imaging; TTM, targeted temperature management.

to superior survival outcomes.[72,73] Given the diverse phenotypes of children with IHCA and the known differences in catecholamine responsiveness in humans, vasopressor doses that are titrated to an individual's physiological response may be advantageous.

In the low-flow state of CPR, $EtCO_2$ largely reflects pulmonary blood flow and is thereby an indirect marker of cardiac output.[46] Particularly low $EtCO_2$ values during CPR (ie, <10 mm Hg) are associated with mortality in observational adult studies.[74,75] As with hemodynamics, preclinical studies have demonstrated efficacy in targeting $EtCO_2$ during CPR.[76] A recent observational study in children did not find an association between $EtCO_2$ and outcomes.[77] Although limited by statistical power, these findings highlight the need to understand potential confounders in the interpretation of $EtCO_2$ values, including decrements associated with epinephrine administration and elevated values associated with alveolar hypercapnia in the setting of asphyxial cardiac arrest.[62,78]

CPR Duration and Extracorporeal Support

Children who require prolonged CPR have worse outcomes than those with brief cardiac arrests.[22] However, a multicenter cohort study demonstrated a 28% rate of survival to discharge among children who received 30 minutes or more of CPR,[5] and a GWTG-R registry publication reported that 16% of children who received 35 minutes or more of CPR survived to hospital discharge.[22] In each of these studies, most survivors had favorable gross neurological outcomes, suggesting that decisions regarding CPR duration and futility are complex and should not be based on CPR duration alone.

These findings are, in part, attributed to the increased use of extracorporeal CPR (ECPR) as a rescue therapy during cardiac arrest. No prospective trial has compared pediatric ECPR with conventional CPR, but a number of observational studies have identified a survival advantage in children, especially those with congenital cardiac disease, who received ECPR compared with children who received conventional CPR.[79-81] Based on these data, the AHA offered a Class 2b recommendation for ECPR to be considered in children with IHCA and underlying cardiac diagnoses in settings with "existing ECMO [extracorporeal membrane oxygenation] protocols, expertise, and equipment."[53(pe908)] Although ECPR is also being used for patients without heart disease, evidence of its effectiveness in this group is insufficient.[53]

Post–Cardiac Arrest Syndrome and Care

Post–cardiac arrest syndrome (PCAS) is a complex cascade that begins immediately after ROSC and continues for days to weeks. The 4 key components are brain injury, myocardial dysfunction, systemic ischemia-reperfusion injury, and persistent precipitating pathophysiological condition.[30,82]

Clinical manifestations of PCAS range in severity and are summarized in **Table 3**.[30] Hypoxic-ischemic brain injury can present as encephalopathy or seizures, progress in the days after ROSC, and result in long-term neurodevelopmental deficits in survivors.[30,97] Myocardial dysfunction occurs early after ROSC and, in many patients, peaks at approximately 24 hours before normalizing within 48 to 72 hours after ROSC.[98] Not surprisingly, children with more severe left ventricular dysfunction and those who require a higher vasoactive infusion dose have lower rates of survival to discharge.[83,84] The systemic ischemia-reperfusion response resembles a sepsislike syndrome and can exacerbate myocardial dysfunction and brain injury.[98] The combination of these 3 key components is superimposed on the initial precipitating pathophysiological condition that may persist after ROSC. Identifying and treating the underlying disease process associated with the cardiac arrest can reduce the risk of rearrest.[30,82] Understanding the pathophysiological process allows the clinician to initiate prompt post–cardiac arrest care with the goal of minimizing secondary injury.

Therapeutics

Prompt initiation of treatment after IHCA is important to prevent secondary multisystem organ injury (Table 3).[9,30,53,83-96] Initial treatment should focus on normalizing systemic derangements such as

hypotension and hypoxemia. Although patients may be hypertensive immediately after cardiac arrest, hypotension occurs in more than half of children in the first 6 hours after ROSC.[85] At least 1 blood pressure measure below the 5th percentile for age in the first 12 hours after ROSC and longer durations of hypotension during the first 24 hours after ROSC are associated with lower rates of survival to discharge.[86,87] Despite this finding, at least 25% of patients with hypotension do not receive vasoactive infusions.[85] Fluids, inotropes, and vasoactive medications should be administered with the goal of avoiding hypotension by treating cardiac dysfunction and vasoplegia.[9,30]

Post–cardiac arrest hypoxemia is commonly attributed to precipitating lung disease, aspiration, or pulmonary edema and should be anticipated and immediately addressed.[30] Research findings regarding the implications of post–cardiac arrest hyperoxia for outcomes are mixed,[88-90] but it is recommended that clinicians avoid hyperoxia and target normoxia with a goal oxygen saturation of 94% to 99%.[9,30] Studies are similarly in conflict regarding the clinical significance of hypercapnia or hypocapnia after cardiac arrest.[88,91] Guidelines advocate targeting normocapnia or "a $PaCO_2$ specific for the patient's condition" in the post-ROSC period.[30(p203)] This recommendation is based, in part, on the physiological rationale that hypercapnia may result in cerebral vasodilation and hyperemia and that hypocapnia may cause cerebral vasoconstriction and ischemia.[30,92]

Fever is common after cardiac arrest and is associated with worse outcomes through increasing metabolic demand, promoting free radical production, and other detrimental consequences.[93] Targeted temperature management (TTM) using active temperature regulation devices and antipyretics should be initiated early after ROSC, but therapeutic hypothermia has not been found to offer an advantage over normothermia.[94] The AHA guidelines recommend targeting a temperature of either 32 to 34 °C or 36 to 37.5 °C for 48 hours, followed by 36 to 37.5 °C for an additional 3 days.[30,53]

Seizures are common after cardiac arrest and are often nonconvulsive.[95] Electrographic status epilepticus is associated with worse outcomes.[96] Therefore, continuous electroencephalogram monitoring is recommended for detection and guiding therapy.[30] Antiseizure medications are routinely used to treat seizures and status epilepticus, but it is unclear whether treatment is associated with improved outcomes.

Although most care is supportive, clinicians should consider antibiotics for infection, blood products for coagulopathy-induced bleeding, and corticosteroids for adrenal insufficiency. Close monitoring for organ dysfunction such as acute kidney injury is important to minimize the toxic effects of therapies as patients recover from PCAS.[30] Active areas of investigation for post–cardiac arrest care include advanced neuroimaging, continuous optical measurements of cerebral blood flow and oxygenation, and peripheral biosignatures of neurological injury.[99]

Identification of Risk and Probable Outcomes

After ROSC, only half of patients survive to discharge, and many survivors are left with substantial neurological morbidities.[3,31] Accurate and timely identification of at-risk patients and probable outcomes enables families and clinicians to make informed decisions regarding goals of care. However, this identification should not be done too early because it can result in incorrect conclusions, and post–cardiac arrest care may lead to improved outcomes.[30] The optimal timing for identification of risk and probable outcomes in children has not been established,[30] but adult guidelines recommend waiting for 72 hours after ROSC in patients who were not treated with TTM and 72 hours after return to normothermia in patients who were treated with TTM.[100] In addition, the neurological examination can be confounded by sedative medications often used during post–cardiac arrest care, and medication clearance may be delayed in the setting of hepatic injury, kidney injury, or therapeutic hypothermia.[101]

Post–cardiac arrest neuroprognostication requires the integration of a patient's pre–cardiac arrest functional status and comorbid medical conditions; IHCA characteristics; and post–cardiac arrest neurological examination, cerebral physiological functions, neuroimaging, and electroencephalogram. Many of these factors have been associated with outcomes, but no single factor has had sufficient accuracy in early identification of risks and probable outcomes after ROSC.[9,30] Serum biomarkers of hypoxic-ischemic brain injury have demonstrated an association with neurological outcomes,[102-104] although further prospective study at serial time points after cardiac arrest is needed before these biomarkers can be incorporated into prognostic algorithms. Patients with catastrophic, irreversible brain injury who do not demonstrate neurological recovery may be evaluated for death by neurological criteria. To undergo such evaluation, patients must be normothermic, have been observed for sufficient time for clearance of any sedating medications, and have no confounding conditions.[105]

Conclusions

Despite improvements in care and survival in the United States, more than half of children with IHCA die before hospital discharge. Recognition and timely identification of at-risk patients as well as delivery of high-quality CPR and post–cardiac arrest care are imperative to maximize the chances of achieving favorable outcomes. Substantial knowledge gaps remain in how to best care for these vulnerable patients, highlighting the ongoing need for research in this field.

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