Chapter

Pediatric Cardiac Arrest

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Abstract

This chapter will focus on four important topics in pediatric cardiac arrest. We will highlight recent developments in pediatric CPR quality, medications used in cardiac arrest, ECPR, and post-cardiac arrest care (PCAC) and discuss the existing literature behind AHA guidelines and gaps in knowledge. Optimization of CPR quality is critical during cardiac arrest. We will summarize literature regarding current guidelines which target provider-centered goals and discuss evidence behind patient-centered goals. We will also discuss the evidence behind drugs used in the PALS guidelines. In cases of refractory cardiac arrest, ECMO can be lifesaving; however, there are still many gaps in our knowledge of this field. We will summarize the literature regarding determination of candidacy, cannulation strategies, resuscitation practices during ECPR, and outcomes. After a cardiac arrest, PCAC is crucial to minimize further injury from post-cardiac arrest syndrome (PCAS). The main goals of PCAC are to prevent further brain injury, treat myocardial dysfunction, and systemic ischemia/reperfusion injury. We will discuss AHA guidelines on oxygenation and ventilation goals, targeted temperature management, hemodynamic monitoring, and neuromonitoring.

Keywords: CPR quality, ECPR, extracorporeal cardiopulmonary resuscitation, pediatric cardiac arrest, post-cardiac arrest care

1. CPR quality

1.1 Introduction

There are distinct anatomic and physiologic differences between children and adults that influence not only the etiologies of cardiac arrest but also how we manage these two populations. Children are more at risk for the development of respiratory failure than adults. The discussion of the anatomic reasons behind this is outside the scope of this chapter. Given these anatomic differences between the respiratory systems of adults and children, it is not surprising that the etiology of cardiac arrest in children is usually hypoxia from respiratory failure. In contrast, in adults, the etiology of cardiac arrest is usually secondary to cardiac decompensation [1, 2].

The differences in chest wall compliance between children and adults can also affect their responses to closed chest compressions during CPR. Proposed mechanisms of blood flow during closed chest CPR include compression of the heart between the sternum and spine as well as chest compression (CC)-induced increases in intrathoracic pressure, resulting in pressure gradients from the right heart to the pulmonary vasculature to the left heart and into the systemic vasculature. Based on these mechanisms, it is thought that better chest wall compliance leads to better cardiac output during CPR. This may explain why infants have better outcomes from cardiac arrest after in-hospital cardiac arrest (IHCA) than older children [1]. There are also differences in their myocardial function. Younger children have a limited ability to increase their stroke volume in the face of demand compared to older children and adults and thus are more dependent on heart rate to maintain cardiac output. For these reasons, in the setting of bradycardia with poor perfusion in children, it is imperative to start CPR. In fact, Nadkarni et al. published a multicenter analysis of IHCA from the National Registry of Cardiopulmonary Resuscitation in 2006 and showed that the incidence of initial rhythm of bradycardia with poor perfusion was significantly higher in children than adults. Children receiving CPR for bradycardia who maintain pulses have much higher rates of survival to hospital discharge (SHD) than those who had pulseless cardiac arrest [2].

The AHA guidelines for CPR in children were last updated in 2015. This book chapter section will cover the most recent recommendations, the basis behind these recommendations, and the research that has accrued since the 2015 guidelines (as summarized in **Table 1**). Approximately 15,000 hospitalized children each year undergo CPR with outcomes improving over time [3]. An analysis of over 7000 pediatric pulseless IHCA events between 2000 and 2018 in the Get With the Guidelines-Resuscitation (GWTG-R) registry showed a 19% absolute increase in SHD over time [3]. Unfortunately, the etiology of these improved outcomes has yet to be elucidated. There are many factors that may have led to the increase in SHD in pediatric IHCA over time. One of the factors that may contribute to improved outcomes is improved CPR quality. The AHA guidelines focus on delivering five components of high- quality CPR, which are delivery of chest compressions of adequate rate and depth, ensuring full recoil between compressions, minimizing interruptions in chest compressions, and avoiding excessive ventilation [4]. Despite these guidelines, there have been multiple studies showing difficulty in achieving these targets during CPR. A single center prospective observational study sought to compare CPR quality before and after the institution of the 2010 AHA guidelines. The authors found that while there was an increase in CC depth, rate, and chest compression fraction (CCF) after the 2010 guidelines, it was difficult to achieve the target goals for rate and depth [5]. In 2018, the Pediatric Resuscitation Quality (pediRES-Q) Collaborative, a large multicenter international pediatric resuscitation quality improvement network, published a landscape study characterizing CPR metrics for children with IHCA. They analyzed 112 events and found that guideline compliance for rate and depth in children is poor, with the most difficulty achieving compliance in younger children [6].

There has been a shift from the "provider"-centric to a "patient"-centric approach to CPR. Instead of targeting a standard depth, rate, and ventilation rate (provider centric), the "patient"-centric approach involves incorporating physiologic monitoring and adjusting CPR to the patient's hemodynamic responses as assessed by more invasive monitors like arterial blood pressure and end tidal carbon dioxide ($ETCO_2$) level. This hemodynamic-directed CPR approach could explain the poor compliance with AHA guidelines (which are "provider" centric) that has been described in the literature.

1.1.1 Chest compression metrics

1.1.1.1 Chest compression rate

The 2015 update to the AHA guidelines continues to recommend a chest compression rate of 100–120/min. As stated in the 2015 evidence summary, there is

CPR quality marker	AHA pediatric recommendations	AHA adult recommendations	Most recent literature since AHA recommendations are released
Metric			
Rate	100–120 beats/min	100–120 beats/min	80–100 beats/min
Depth	1/3 AP diameter of the chest or about 4 cm in infants, >5 cm in children >1 year, and >5 cm but <6 cm in adolescents	>5 cm but <6 cm	No association between depth and outcomes
Pauses	No more than 10 s	No more than 10 s	No literature associated with outcomes
CCF	At least 60%	At least 60%	No literature associated with outcomes
Ventilation	No advanced airway: chest compression to ventilation ratio 15:2 Advanced airway: 10 breaths/min	No advanced airway: chest compression to ventilation ratio 30:2 Advanced airway: 10 breaths/min	Higher rates (≥30 breaths/min in children <1 year old and ≥25 breaths/min in older children) associated with improved outcomes compared to lower rates
Duty cycle	50%	50%	No association between duty cycle and outcomes
Chest recoil	Full	Full	
Physiologic markers			
$ETCO_2$	Reasonable to monitor, but no goals established	≥20 mm Hg	No association between $ETCO_2$ and outcomes
Arterial blood pressure	Reasonable to monitor, but no goals established	≥25 mm Hg	DBP ≥ 25 mm Hg in infants and DBP ≥ 30 mm Hg in children was associated with improved outcomes
Coronary perfusion pressure	Insufficient evidence to make a recommendation	≥20 mm Hg	No new evidence

Table 1.
AHA recommendations for various CPR quality markers in children vs. adults as well as the recent literature since guidelines are released.

insufficient data in children for a systematic review for CC rate, and therefore the recommendations are based on evidence for adults. Given simplicity in CPR training and insufficient pediatric evidence, the recommendation was that it is reasonable to use the adult basic life support (BLS) CC rate of 100–120 for children [4]. Since the 2015 update was published, there has been one pediatric study published on this subject. The Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) is a network of seven pediatric ICUs that conducts investigations related to pediatric critical care practice. Between 2013 and 2016, the CPCCRN conducted the Pediatric Intensive Care Unit Quality of CPR (PICqCPR) study, a multicenter prospective observational study to evaluate the association between invasive arterial blood pressures during CPR and outcomes. Using the dataset, the primary aim of the study was to evaluate the association between CC rates and blood pressure and survival outcomes. The results of the study showed that when compared to

AHA guidelines of 100 to <120, higher rate categories were associated with lower systolic (SBP); however, there was no correlation to survival. Also when compared to the AHA guidelines of 100 to <120, a CC rate of 80 to <100 was associated with a higher rate of SHD and survival with favorable neurological outcome (FNO) compared to CC rates within guidelines [7].

1.1.1.2 Chest compression depth

The 2015 update to AHA guidelines recommend to compress at least 1/3 of the anterior–posterior (AP) diameter of the chest, which is about 4 cm in infants, 5 cm in children, and greater than 5 cm but no more than 6 cm in adolescents [4]. Two single-center pediatric studies were reviewed for the 2015 update to the AHA guidelines. The first study was a case series of six infants after cardiac surgery who had CPR. In those infants, aged 0–7 months, attempting to compress the chest to ½ the AP diameter increased the SBP significantly compared to attempts to compress the chest to 1/3 the AP diameter [8]. The second study looked at 87 chest compression events in children >1 year and showed that AHA compliant guideline CC depths >51 mm were associated with improved 24-h survival compared to more shallow CC depths [9]. Since the 2015 update, there has been only one study published. This was a multicenter prospective observational study that looked at out-of-hospital cardiac arrests (OHCA). They looked at 153 pediatric events (children 1–19 years of age) with CPR metric data and found that there was no association with CC depth and return of spontaneous circulation (ROSC) [10].

1.1.1.3 Minimizing interruptions in chest compressions

The 2015 AHA guidelines continue to emphasize minimizing interruptions in chest compressions, in particular to less than 10 s. Ideally, these pauses should be coordinated so that a pulse check, rhythm check, and compressor switch occur at the same time and should only occur every 2 min. There should be a person assigned to the role of the pulse check, positioned with his/her finger on the pulse before the pause to minimize the pause duration. Chest compression fraction is defined as the time spent doing chest compressions during CPR. The 2013 AHA consensus statement on CPR quality recommended a CCF of at least 80% [11]; however, the 2015 AHA BLS guidelines recommend a CCF of at least 60% [12]. Observational studies of cardiac arrests often show that pauses can be more prolonged and more frequent than expected. In a single-center observational study in a pediatric emergency room, 33 cardiac arrests were analyzed. While the majority of pauses were <10 s in duration, 33% of pauses were >10 s. The number of coordinated pauses were rare, only 7% of the time [13]. A more recent observational study of CPR quality in two pediatric emergency departments analyzed 81 cardiac arrests. While median CCF was 91% with a median pause duration of 4 s, 22% of pauses were prolonged (>10 s). Again, the number of coordinated pauses were rare (6%) and prolonged with a median of 19 s [14]. Although the AHA guidelines recommend to switch providers performing CC every 2 min to prevent rescuer fatigue and therefore inadequate CPR quality, they also acknowledge that when a CPR feedback device is used, some individuals can go longer than 2 min [15]. A single-center observational study that sought to characterize causes for interruptions found that provider switch accounted for the majority of pauses. Individuals performing CC for at least 120 s compared to those switching earlier had less leaning, increased CC depth, and better compliance for depth with AHA guidelines [16]. While there is limited evidence in adults to support these guidelines on duration of pauses and CCF, these recommendations have been applied to children. There are no pediatric studies to date evaluating the association between CC interruptions and outcomes. In 2019, a single-center observational study was published that sought to evaluate the hemodynamic consequences of interruptions in CC. Thirty-two IHCA events were analyzed. The median duration of pauses was brief at 2.4 s; however, BPs before and after the pauses did not differ significantly [17].

1.1.1.4 Ventilation

For patients without an invasive airway at the time of cardiac arrest, BLS guidelines recommend a compression to ventilation ratio of 15:2 in children if there are two providers (in contrast to 30:2 for adults). Although there is no data to support the optimal compression to ventilation ratio in children, the recommended ventilation rate takes into account a higher baseline respiratory rate in children. For children without advanced airways in place at the time of arrest, there is often an emphasis on tracheal intubation during an IHCA given the most common etiology of IHCA is respiratory failure. The 2019 focused update on PALS reaffirms the 2010 recommendation that during a pediatric OHCA, the use of bag mask ventilation (BMV) is reasonable compared to an advanced airway. The update also specifies that no recommendation for or against an advanced airway could be made. These recommendations were made based on the review of 14 studies of airway interventions in children who had cardiac arrests [18].

In contrast to the recommendation for a higher ventilation rate without an advanced airway, when an advanced airway is in place, AHA guidelines recommend that ventilation rates of 10 breaths/min be applied to all age groups during CPR in order to simplify training. During CPR, cardiac output is usually about 25% of normal, and thus lower ventilation rates are recommended to match the lower output state, given the detrimental effects of positive pressure ventilation on venous return and right heart afterload. However, the etiology of cardiac arrest in children is usually asphyxia in nature compared to the primary cardiac origin of most adult cardiac arrests, and thus the recommendations of equal ventilation rates in children as to adults have been questioned. In 2019, the CCPCRN published the only study to date that has analyzed the association of ventilation rates in pediatric cardiac arrests and survival outcomes. As part of the PICqCPR study, the authors analyzed 52 events in patients with an invasive airway in place at the time of the cardiac arrest. No events were within the guideline ventilation rate (defined as 10 ± 2 breaths/min), and more than half of the events were considered high ventilation rates (defined as > or equal to 30 breath/min in infants <1 year and > or equal to 25 in children >1 year). In fact, higher ventilation rates were associated with higher odds of SHD [19].

1.1.1.5 Duty cycle

The term “duty cycle” refers to the amount of time spent in the compression phase of CPR. AHA guidelines for adult cardiac arrest recommend a duty cycle of 50% [20]. There have been no pediatric recommendations since 2005 on duty cycle. The only pediatric study to date on duty cycle was published in 2016. It was a single-center observational study that analyzed 97 pediatric events and found no association with duty cycle and survival [21].

1.1.1.6 Chest recoil

AHA guidelines recommend full chest recoil in between compressions, to avoid leaning. In 2009, a single-center prospective observational study sought to evaluate the prevalence of leaning and the effect of real-time feedback devices on leaning. They evaluated 20 pediatric cardiac arrests and found that leaning was common during pediatric CPR; however, leaning occurred significantly less when a feedback device was used [22]. In 2013, the same pediatric center published another prospective observational study looking at the quality of CPR in children 1–8 years of age with a real-time feedback device. In eight events, they found the percentage of CPR epochs (defined as 30-s periods of resuscitation) achieving the target goal of leaning <20% of compressions was 79%. In particular, the percent epochs achieving target leaning goals was better in the feedback group than in the no feedback device [23]. There are no studies to date evaluating the association with leaning and outcomes in children.

1.1.2 Physiologic monitoring

1.1.2.1 End tidal CO_2

The 2015 PALS guidelines state that it is reasonable to use $ETCO_2$ to guide the quality of CPR in children, although specific values to guide therapy in children have not been established [24]. These recommendations were made on extrapolation of adult and animal data since no pediatric literature at the time of these guidelines had been shown that $ETCO_2$ monitoring improves outcomes. For adults, AHA recommendations are to titrate to an $ETCO_2 \geq 20$ mm Hg [11]. In 2018, using the PICqCPR data, the CCPCRN published the only pediatric study to date that evaluates the association of ETCO2 values and survival outcomes. Contrary to adult literature, the authors found that there was no association between $ETCO_2 \geq 20$ mm Hg and SHD [25].

1.1.2.2 Arterial blood pressure

Similar to the recommendation for $ETCO_2$ monitoring, the 2015 PALS guidelines state that it is reasonable to use BP to guide CPR quality if an invasive arterial line is already in place; however, no specific values to guide therapy have been established [24]. At the time, these recommendations were based on animal data without any pediatric human literature. Since then, the CCPCRN has published three studies using PICqCPR data, evaluating the association of intra-arrest diastolic blood pressure (DBP) and post-arrest outcomes. The first study evaluated 164 events and showed that maintaining a mean DBP ≥ 25 mm Hg in infants and DBP ≥ 30 mm Hg in children was associated with SHD and survival with FNO. There was no association between SBP and outcomes [26]. The second study evaluated 77 survivors of the first study and sought to assess the association between intra-arrest BP and functional outcomes. Unlike the parent study which showed an association between DBP and FNO, there was no association between DBP and functional outcomes. Again, there was no association with SBP and functional outcomes [27]. The third study evaluated the subgroup of patients with cardiac disease. The authors analyzed the hemodynamic waveforms of 113 patients with cardiac disease and found an association with the same DBP goals and SHD in surgical patients but not medical patients. They also noted the majority of patients with single ventricles and open chest were able to attain the DBP goals. In patients who went on to have ECPR, approximately half were able to attain the DBP goals; however, there was no association between DBP goals and SHD [28].

1.1.2.3 Coronary perfusion pressure

Coronary perfusion pressure (CoPP) can be estimated by subtracting the right atrial (RA) pressure from the aortic DBP. While the 2013 AHA Consensus

Statement on CPR quality recommends titrating CoPP to >20 mm Hg in adults if invasive arterial line and central venous catheter is in place, they state that there is insufficient evidence to make a CoPP goal for infants and children [11]. While no pediatric studies exist, one pediatric animal study showed improvement in a hemodynamic-directed approach to CPR. In a study with 4-week-old piglets, hemodynamic-directed CPR with compression depth titrated to SBP > 90 mm Hg and vasopressor administration to maintain CPP ≥ 20 mm Hg resulted in higher survival rate than standard care of CC depth 1/3 AP diameter [29].

1.1.3 CPR devices

The 2015 AHA guidelines state that it is reasonable to use audiovisual feedback devices during CPR to optimize CPR quality. As mentioned before, there have been studies showing improvement in pediatric CPR quality with the addition of a real-time CPR feedback device [22, 23]. However, a systematic review and meta-analysis of studies using real-time feedback devices has not shown improvement in patient outcomes [30].

While mechanical chest compression devices such as Autopulse and LUCAS have been used in adults, both devices are not intended for use in children [31, 32].

1.1.4 Debriefing

There have been multiple adult studies showing that the implementation of a debriefing program can lead to improved CPR quality and outcomes [33]. There are generally two approaches to debriefing, hot debriefs and cold debriefs. Hot debriefs occur usually within hours after a cardiac arrest with team members involved in the cardiac arrest and involve mainly the members' recall of the events and their immediate reactions. Cold debriefs occur at a later time, within weeks of an event with a larger audience that includes the immediate team members but also other ICU staff. The cold debrief involves a more comprehensive review of the cardiac arrest and can include more objective measures such as defibrillator CPR data and physiologic monitor data [34]. Pediatric studies on debriefings have been limited. A study of the content and process of hot debriefs from the pediRES-Q collaborative revealed approximately half of all cardiac arrests are followed by hot debriefs. The content of the hot debriefs are usually about cooperation/coordination, communication, and clinical standards [35]. The association between hot debriefs and outcomes still needs to be determined. A single-center prospective interventional study sought to evaluate the effectiveness of the implementation of a cold debriefing program on survival outcomes in children. They found that implementation of their program was associated with improved CPR quality and survival with FNO [36].

1.1.5 CPR duration

Despite excellent quality CPR, many clinicians question whether continuing resuscitation is futile for prolonged cardiac arrests. An analysis of the GWTG registry aimed to examine the effect of CPR duration for pediatric IHCA on outcomes. The authors concluded that CPR duration was independently associated with SHD and survival with FNO. However, among survivors, survival with FNO was 70% in those arrests occurring <15 min and 60% for those patients with arrests >35 min. Compared to medical patients, surgical cardiac patients had the highest adjusted OR for SHD and survival with FNO [37].

1.2 Summary

The 2015 AHA guidelines on pediatric CPR are based on extrapolation of evidence from adult and animal studies. Since then there has been a growing amount of literature that supports transitioning CPR from a "provider"-centric to "patient"-centric CPR. Recent literature has shown no change or worse outcomes when providers follow "provider"-centric guidelines that use standardized targets. Chest compression rates lower than recommended have been associated with improved outcomes. There has been no association shown between CC depth and outcomes. Ventilation rates higher than 2015 AHA guidelines are associated with improved outcomes. More recent evidence is emerging that demonstrates targeting a patient's physiologic response to CPR may be more beneficial. Evidence has shown that DBP greater than 25 mm Hg in infants and 30 mm Hg in older children are associated with improved outcomes. There are many CPR quality metrics to choose from to guide CPR. These metrics can help improve the quality of CPR from a system-wide standpoint.

2. Medications used in cardiac arrest

The 2015 PALS guidelines discussed three drugs used during resuscitation in children: epinephrine, amiodarone, and lidocaine [24]. **Table 2** highlights these medications, comparing recommendations from the 2015 PALS update and most recent literature that has been published since then. The 2015 PALS guidelines state that it is reasonable to use epinephrine during cardiac arrest. This guideline was based on two pediatric observational studies that were inconclusive and one adult study showing increased ROSC and survival to admission but no change in SHD [24]. Since the 2015 guidelines, an analysis of nonshockable pediatric cardiac arrests in the GWTG registry showed a delay in epinephrine administration was associated with decreased likelihood of survival to admission, ROSC, SHD, and survival with FNO [38]. Another GWTG analysis looked at the intervals between epinephrine administration. Guidelines currently state to give epinephrine every 3–5 min during CPR. This study showed that compared to intervals of 1–5 min as the reference, longer intervals were associated with improved SHD [39]. For shock refractory VF or pulseless VT, the 2015 guidelines changed to state that either amiodarone or lidocaine was acceptable. Previous guidelines had recommended amiodarone as the preferred drug over lidocaine. This is based on pediatric retrospective data that shows lidocaine is associated with improved ROSC and 24-h survival; however, there is no change in SHD [24]. The 2018 update to the PALS guidelines continued

Medication	2015 PALS guidelines	Most recent literature
Epinephrine	It is reasonable to give epinephrine at intervals every 3–5 min	1. Delay in epinephrine administration associated with worse outcomes 2. Longer intervals between epinephrine are associated with better outcomes
Amiodarone/ lidocaine	Either amiodarone or lidocaine is equally acceptable for shock refractory VF or pulseless VT	2018 PALS update: no change

Table 2
Medications used during pediatric cardiac arrest: Current guidelines vs. most recent literature.

to reaffirm the 2015 guidelines. No new pediatric data was available for the updated review; however, the committee did not consider extrapolated adult data [40].

3. Pediatric ECPR

3.1 History and current use of extracorporeal cardiopulmonary resuscitation (ECPR) in pediatrics

Extracorporeal membrane oxygenation (ECMO) use for cardiopulmonary resuscitation (CPR) in children was first described in the literature by del Nido in 1992 [41]. Since then, utilization of extracorporeal cardiopulmonary resuscitation has expanded in all pediatric age groups. The current definition of ECPR according to the Extracorporeal Life Support Organization (ELSO) is "the application of rapid-deployment venoarterial ECMO, to provide circulatory support in patients in whom conventional CPR is unsuccessful in achieving sustained return of spontaneous circulation (ROSC). Sustained ROSC is deemed to have occurred when chest compressions are not required for 20 consecutive minutes and signs of circulation persist" [42]. This definition has been used since ELSO updated its data definitions in 2018. Pre-2018, the ELSO definition of ECPR was "ECMO used for initial resuscitation from cardiac arrest" and did not include patients who had achieved ROSC when they were being cannulated for ECMO [43]. Apart from the ELSO definitions, the definition of ECPR varies in clinical studies, and this presents challenges with medical communication and synthesis of research.

Based on ELSO registry data, there has been an increasing use of ECPR in pediatric patients over the years [44]. The overwhelming majority of pediatric ECPR use reported in the literature is for in-hospital cardiac arrest (IHCA) [44]. There are only few reports of ECPR deployed in pediatric patients for out-of-hospital cardiac arrest (OHCA); 2% of pediatric ECPR cases reported to ELSO were for OHCA according to the 2016 pediatric ELSO registry report [44, 45]. There is one case report of out-of-hospital ECMO deployment in a child ("pre-hospital ECPR") [46].

From reported literature, the incidence of ECPR use varies from 5 to 27% of all pediatric IHCA cases between 2000 and 2016 [37, 47–49]. Of pediatric IHCA cases reported to the American Heart Association (AHA) Get With the Guidelines®-Resuscitation registry between the years 2000 and 2008, the incidence of ECPR use was 5–7% overall and 19–21% in patients with a cardiac diagnosis [37, 47]. More recently, the incidence of ECPR use was 27.2% in cardiac arrest patients reported to the Pediatric Cardiac Critical Care Consortium (PC4) registry between 2014 and 2016 [49].

The AHA had not included ECPR in Pediatric Advanced Life Support (PALS) guidelines until 2005 when guidelines were updated to include a consideration of ECPR in patients with a reversible cause of arrest or whose underlying condition could be treated by heart transplantation and who were located at an institution that could rapidly deploy ECMO, where effective conventional CPR had been started promptly [50]. Subsequent PALS updates have included this cautious recommendation to consider ECPR, particularly for cardiac patients with IHCA [18, 24, 51].

3.2 Cannulation procedure during CPR

Determination of a patient's ECPR candidacy and feasibility of cannulation should preferably be done prior to cardiac arrest. Criteria for determination of candidacy may vary from center to center, and there are no universal guidelines for this. Though the AHA recommends considering ECMO for pediatric IHCA, there are no specific guidelines for the actual implementation of ECMO during CPR.

Site of cannulation varies in pediatrics and could be central or peripheral. Central (transthoracic) cannulation is more frequently performed in cardiac surgical patients, some of whom may already have an open sternum [52–54] . Peripheral cannulation could be via right neck vessels (internal jugular vein and carotid artery) or femoral vessels. Data is conflicting on the presence of a correlation between cannulation site and outcomes in pediatric ECPR [55–62].

Questions also remain surrounding (i) the appropriate timing of initiating a request for ECMO implementation during CPR, (ii) the use of timed cycled interruptions of chest compressions to allow for cannulation, and (iii) the ongoing administration of epinephrine (adrenaline) during ECPR cannulation. From a review of the literature, clinical practice varies in regard to how long after the initiation of chest compressions that ECMO is requested for pediatric IHCA [57, 60, 63–66]. A cross-sectional survey of pediatric cardiac intensive care practitioners published in 2018 showed that 38% of respondents reported activating ECMO after just one dose of epinephrine, while more than 80% called for ECMO after the second dose [67]. The timing of initiation of ECMO cannulation during CPR is important because it contributes to total CPR duration. Based on this, it would seem prudent to request ECMO early into the resuscitation effort. But caution must also be taken to avoid deployment prematurely, for example, if return of spontaneous circulation (ROSC) could have been achieved without ECMO. The effect of total CPR duration on survival and neurological outcomes after pediatric ECPR is unclear. In a recent large study using data from both ELSO and GWTG-R registries, a linear relationship was demonstrated between CPR duration and odds of death before hospital discharge [68]. Multiple single-center studies have also shown worse outcomes from pediatric ECPR if duration of CPR is longer [52, 60, 63, 64, 66, 69–72]. However, still other studies have shown no correlation between ECPR duration and outcomes [37, 53, 57, 73–79]. The patient population possibly dictates the effect of ECPR duration on outcome. Compared to other illness categories, pediatric cardiac surgical patients have been shown to have a higher probability of favorable neurologic outcomes despite ECPR of prolonged duration [37].

The use of timed cycled interruptions of chest compressions to facilitate cannulation during ECPR is practiced in some centers, but there is no literature to show how widespread this practice is or whether it has positive effects on outcomes. Without timed cycled interruptions, chest compressions are paused randomly, usually at the discretion of the cannulating surgeon, and they are paused for varying amounts of time. With timed cycled interruptions, pauses in chest compressions are on a cycle—compressions are not paused unless a minimum time has passed (e.g., 2 min), and they are only paused for a maximum amount of time (e.g., 30–45 s). With the cycled method, the cannulating surgeon is only able to work in short bursts of time, and it is possible that overall CPR duration is therefore longer. However, it is also likely that CPR "no-flow" time is less. This is an area that needs to be studied.

Epinephrine administration for CPR during ECMO cannulation is also an area of research interest. Proponents of the cessation of epinephrine administration during ECMO cannulation for CPR argue that ongoing administration would only increase systemic vascular resistance (which would impede ECMO flow subsequently and hamper myocardial recovery) and is futile for ROSC since the decision would have already been made to cannulate. However, the 2009 study of 199 pediatric ECPR recipients from GWTG-R registry demonstrated no statistically significant difference between survivors and non-survivors in cumulative dose of epinephrine received during ECPR [73]. Also, in the cross-sectional survey of pediatric cardiac critical care clinicians published in 2018, only 19% of respondents reported limiting epinephrine to 1–3 doses during CPR before ECMO cannulation [67].

3.3 Elements of an ECPR program

Deployment of ECPR requires that a well-coordinated, streamlined, and efficient sequence of activities takes place. For success of an ECPR program, it is essential that clinical teams are always ready since time is of the essence. Important elements to a successful ECPR program include (i) prior identification of patients that would be offered ECMO in the case of cardiac arrest, (ii) prior establishment of a system of emergently notifying all required parties in the event of cardiac arrest (e.g., through paging), (iii) ready availability of primed ECMO circuits and blood products, and (iv) effectively trained and prepared team members [80, 81].

Some ECPR programs have crystalloid-primed or non-blood colloid-primed circuits always on standby [57, 76, 81, 82]. Sixty-five percent of 1828 pediatric ECPR cases reported to ELSO from 2011 to 2015 had an ECMO circuit primed with blood products [44]. Different considerations go into the choice of prime solution for rapid deployment. Blood-primed circuits are dependent on the rapid availability of blood products and cannot be stored long-term. Some programs do not keep pre-primed circuits if blood can be obtained quickly [83]. Crystalloid-primed circuits may be stored for up to 30 days but may require adjustment of pH and addition of blood prior to use [57, 76, 81]. Cost must also be considered in the decision to have pre-primed circuits on standby. For example, as published in 2017 by Erek et al., their pediatric ECPR program in Turkey avoids pre-primed ECMO circuits due to cost. Instead they emergently deploy cardiopulmonary bypass circuits for ECPR then transition to ECMO circuits later in the course [52].

Teams must be effectively trained and prepared. Simulation has proven to be an effective method for ECPR team training and has been used in many programs around the world with good results [84–86].

3.4 Pediatric ECPR outcomes

Survival after ECPR in pediatrics is around 43% in all age groups, according to ELSO [44]. Only a few pediatric studies have compared conventional CPR (CCPR) with ECPR [48, 87, 88]. In an analysis published in 2016 of almost 600 pediatric IHCA patients from the GWTG-R registry, there were increased odds of survival to hospital discharge for patients who received ECPR compared to CCPR only (adjusted OR 2.76; 95% CI 2.08–3.65; $p < 0.0001$) [87]. An earlier study published in 2013 did not demonstrate an association between ECPR and improved survival to discharge compared to CCPR, but that study had a small ECPR subgroup and was unable to match controls [48].

Taeb et al. compared CPR quality between ECPR and CCPR in pediatric cardiac intensive care patients. They found that CPR duration was significantly longer for patients who received ECPR than those who received CCPR [30 min (9.5–33 min) vs. 5.5 min (4–12.5 min); $p = 0.016$]. Rate of ROSC, intensive care unit length of stay, and hospital length of stay were not different between the groups [88].

Neurological outcomes after ECPR are important metrics, but there is a general paucity of data on this topic. Multiple single-center and registry studies have reported on neurologic status at hospital discharge using the Pediatric Cerebral Performance Category (PCPC) scale [37, 57, 61, 64, 73, 81, 87, 89–91]. However, many of those studies have incomplete data, and designation of a patient's PCPC is also subjective. In addition, the definition of favorable neurologic outcome scores using PCPC varies. All these make interpretation of the data somewhat difficult. In the 2019 study of merged ELSO and GWTG-R data, discharge PCPC was only available in 48% of 241 pediatric ECPR survivors; 93% of those had a PCPC ≤2 which was considered favorable [68].

There is limited data on functional and neurobehavioral status in pediatric ECPR patients beyond hospital discharge [60, 63, 92–95]. Torres-Andres et al. assessed health-related quality of life after pediatric ECPR. Children with normal brain imaging at the time of ECMO decannulation had statistically higher quality of life scores compared to other children, and those with ischemic changes on brain imaging at decannulation had higher quality of life scores than those with hemorrhagic changes [96].

3.5 Transportation of pediatric cardiac arrest patients to ECMO centers

The decision to transport pediatric cardiac arrest patients with active chest compressions to a hospital that performs ECPR must be considered carefully. Literature on this subject is minimal. Prolonged CPR before ECMO cannulation has been shown in some studies to not result in worse mortality, especially in patients with cardiac diagnoses [77, 97, 98]. However, Eich et al. describe the outcomes of 12 pediatric patients who suffered near-drowning episodes between 1987 and 2005 and who were transported to a tertiary center in Germany for emergent cardiopulmonary bypass [45]. Only 5 of the 12 survived to hospital discharge, of which 3 were in a persistent vegetative state.

In deciding to transport pediatric patients receiving CPR, one must consider the following: etiology of cardiac arrest, origin of transport (i.e., out-of-hospital transport vs. interhospital transfer), the duration of "no-flow" time, the anticipated total duration of CPR, the physical distance to the ECMO center, effectiveness of CPR during transport, and safety of medical personnel performing compressions during transport. Safety and effectiveness of CPR during transport of children has not been studied [99].

3.6 Summary

In summary, ECPR use in pediatrics is on the rise. There is evidence of its positive impact, and it has been included in resuscitation guidelines for pediatric in-hospital cardiac arrest, in specific patients and where existing programs are available. It is important that hospitals establishing and running ECPR programs have detailed protocols and repeated training and rehearsing for ECPR.

4. Pediatric post-arrest care

4.1 Introduction

In 1966, the National Academy of Sciences published a consensus statement on CPR describing the ABCDs of resuscitation. In this document A denoted airway opened; B denoted breathing restored; C denoted circulation restored; and D denoted definitive therapy. Definitive therapy was described as therapy for the management of the cause(s) of the arrest and management of resulting pathology from the arrest [100]. Successful return of spontaneous circulation (ROSC) that is sustained often results in post-cardiac arrest syndrome (PCAS). PCAS is described in phases defined by time. The immediate post-arrest phase is described as the first 20 min after ROSC. This is followed by the early post-arrest phase which is described as between 20 min through 6–12 h after ROSC. The intermediate phase follows lasting up to 72 h following ROSC. Afterwards the recovery phase starts and lasts until disposition when the rehabilitation phase begins. These last two phases vary in duration [101].

Post-cardiac arrest syndrome encompasses (1) post-cardiac arrest brain injury, (2) post-cardiac arrest myocardial dysfunction, (3) systemic ischemia/reperfusion response, and (4) persistent precipitating pathology. The severity of illness from this pathology varies based on the extent of the ischemic insult, the cause of the cardiac arrest, and patient's prearrest state of health. The mechanism of post-cardiac arrest brain injury is complex and includes excitotoxicity, disrupted calcium homeostasis, free radical formation, protease cascades, and activation of cell death signaling pathways. Post-cardiac arrest brain injury is also influenced by what is often hyperemic reperfusion and frequent failure to achieve adequate cerebral reperfusion. Post-cardiac arrest myocardial dysfunction describes the transient global dysfunction that is seen immediately after ROSC. The systemic ischemia/reperfusion response describes the whole-body ischemia/reperfusion that occurs with hypoxia-induced activation of immunologic and coagulation pathways that is seen with cardiac arrest. Clinically this appears as intravascular volume depletion, impaired vasoregulation, impaired oxygen delivery, and increased susceptibility to infection. The persistence of the precipitating cause of the cardiac arrest often complicates the pathology of post-cardiac arrest syndrome. Specific treatment of the cause must be aligned with treatment of the PCAS [101]. In 2019, the AHA scientific statement estimated that more than 1800 children and infants were at risk for PCAS annually [102]. The individual components of PCAS are potentially treatable, and this has led to an emphasis on post-cardiac arrest care (PCAC).

PCAC varies depending on the phase of post-cardiac arrest syndrome and the setting in which care is being delivered. PCAC requires multisystem support and must begin promptly after ROSC. The goal of the treatment is to support end-organ function, treat PCAS, and correct the causal factor for the arrest. PCAC begins with the initiation of monitoring as soon after ROSC as feasible. This monitoring includes continuous cardiac telemetry, pulse oximetry, continuous capnography, continuous temperature monitoring, blood pressure measurement, and monitoring of urine output. Laboratory analysis is also important and includes blood gases, serum electrolytes, serum glucose, and calcium. Other monitoring to consider includes arterial lactate, central venous oxygen saturation, chest x-ray, renal function, hemoglobin concentration, coagulation function, and monitoring for signs of inflammation. Neurologic monitoring is useful in a comatose post-cardiac arrest patient. The goal of neurologic monitoring is to prevent secondary neurological injury and aid in prognostication. This monitoring could include serial exams and electroencephalogram [103]. Appendix Figure A1 shows an example of a post-arrest care checklist.

4.2 Hemodynamics

There is no high-quality evidence to support a single strategy for providing optimal hemodynamic support in pediatric patients post-cardiac arrest. Post-cardiac arrest myocardial dysfunction treatment can be aided by monitoring arterial lactate and central venous oxygen saturation. Parenteral fluids, inotropes, and vasoactive medications are to be used as needed to provide hemodynamic support. Optimal use of parenteral fluids vs. vasopressors/inotropes has not yet been determined. At times hemodynamic stability will include management of arrhythmias. Medications to treat arrhythmias are dependent on the underlying cardiac pathology. Hemodynamic treatment should be adjusted to account for the patient's PCAS and prearrest characteristics. At times extracorporeal membrane oxygenation is initiated during CPR as described earlier in the chapter. The efficacy of ECMO for hemodynamic support after ROSC is unclear [104].

4.3 Oxygenation and ventilation

Optimizing oxygenation and ventilation after ROSC is essential and may be hindered by the cause of the arrest and the ongoing PCAS. Providing oxygen is a common therapy in critically ill children. There is no consistent data on the usefulness of hyperoxia after cardiac arrest in children. Treatment with a goal of providing normal paO2 using the lowest possible fraction of inspired oxygen to maintain an oxygen saturation of 94–99% is the current strategy [102]. It is important to manage ventilation as both hypercarbia and hypocarbia have deleterious effects on cerebral perfusion. Current data suggest that it is appropriate to target normocapnia or a PaCO2 specific for the patient's condition while minimizing hypercapnia and hypocapnia [24, 105]. While providing strategies to optimize oxygenation and ventilation, we must be mindful that therapeutic hypothermia can alter the arterial oxygen saturation and affect carbon dioxide production which will be reflected in the minute ventilation [106].

4.4 Targeted temperature management (TTM)

The 2019 American Heart Association update for Pediatric Advanced Life Support included endorsement of post-cardiac arrest continuous maintenance of patient temperature, also referred to as TTM. In 2019 ILCOR pediatric CoSTR summarized evidence supporting the use of TTM (32–34°C) in infants and children after cardiac arrest [107]. Referring to their work, the American Heart Association recommends continuous measurement of core temperature during TTM. Additionally, for infants and children between 24 h of age and 18 years of age who remain comatose after out of hospital cardiac arrest or IHCA, it is reasonable to use TTM at 32–34°C followed by TTM at 36–37.5°C. Initiating hypothermia can be achieve in many ways including cooling blankets, surface cooling with ice packets, or gastric lavage. Electrolyte derangements including hyperglycemia, hypokalemia, hypophosphatemia, hypomagnesaemia, and hypocalcemia can occur during induction of hypothermia. This electrolyte instability can lead to arrhythmias. While maintaining hypothermia, careful monitoring is required. The ideal strategy for rewarming has not yet been identified. In children, the rewarming is usually done at a rate no faster than 0.5°C every 2 h. This reduces the risk of cerebral hyperperfusion, vasogenic edema, and acute systemic hypotension [102]. During PCAC, a temperature >37.5°C should be avoided and aggressively treated [108].

There was data suggesting that earlier timing of hypothermia was associated with better outcomes. Moler and colleagues developed a trial to investigate if shorter time to goal temperature was associated with improved outcomes at 1 year. Using data from the Therapeutic Hypothermia After Pediatric Cardiac Arrest Out-of-Hosptial Trial (ThAPCA –OH), critically ill children from 38 pediatric intensive care units in the United States and Canada were randomized to therapeutic hypothermia or normothermia [109]. Median time to goal temperature in group 1 was 5.8 h and in group 2 was 8.8 h. However, outcomes between the groups did not differ. They concluded that earlier time to goal temperature was not associated with better outcomes [110].

4.5 Sedation

Similarly, to other critically ill children, children with PCAS will likely require treatment with sedatives, analgesics, and possibly neuromuscular blockade. There is insufficient data to describe optimal management of sedation and analgesia for pediatric patients with PCAS. With the use of TTM sedation, analgesia and neuromuscular blockade may be used to facilitate cooling and prevent shivering. Caution is advised when using neuromuscular blockade as this will hinder the clinical neurologic exam and will mask seizures.

4.6 Neurologic monitoring

Continuous EEG monitoring for pediatric patients who are encephalopathic following cardiac arrest and ROSC is recommended. This recommendation came forth from the recent consensus statement from the American Clinical Neurophysiology Society Critical Care Continuous EEG Guidelines Committee [111]. It is recommended that EEG monitoring be initiated as soon as possible and continue for 24–48 h. The recommendation also advises to continue monitoring for 24 h after patients treated with hypothermia are rewarmed to normothermia. There have not been studies to evaluate the effect of treatment of seizures in the post-cardiac arrest period on patient outcomes. Generally, most clinicians treat seizures as they can increase metabolic demand and contribute to secondary brain injury.

4.7 AKI and glucose control

The impact of the management of AKI and glucose control during PCAC is unclear. Data evaluating pediatric post-cardiac arrest AKI and glucose control management is scarce. AKI in critically ill children is associated with increased mortality and morbidity [112, 113]. It is important to monitor kidney function during PCAC as these patients are at risk to develop AKI. During PCAC, it is important to monitor for and treat hypoglycemia and hyperglycemia in post-cardiac arrest patients. Both hypoglycemia and hyperglycemia have been associated with poor outcomes in children [114]. There is no data that evaluates interventional studies of glucose control on PCAC pediatric patients.

4.8 Rehabilitation

Rehabilitation following cardiac arrest is vital. Children surviving cardiac arrest are at risk for alterations in their quality of life from physical, cognitive, and emotional disabilities. They are at risk for significant declines in neurobehavioral function across multiple functional domains [115]. There is also evidence that post-cardiac arrest patients are at risk for developing delirium [116]. There is little data on specific interventions during PCAC that will improve functional outcomes in children after cardiac arrest. More information is needed to identify specific rehabilitation interventions that can be used in PCAC that will improve outcomes for pediatric post-cardiac arrest patients [102].

4.9 Summary

To summarize, how we care for pediatric patients post successful ROSC after cardiac arrest critically influences their outcomes. Each component of post-cardiac arrest care requires focused management. This care is highly complex and time sensitive. Despite knowing how crucial this management is to the outcomes of patients post-cardiac arrest, significant gaps in knowledge remain. More work is needed to identify the most efficient approaches to provide this care for pediatric patients.

5. Conclusions

Many of the recommendations regarding CPR quality metrics in children are based on extrapolation of adult and animal data, given the scarcity of pediatric literature. Although current AHA guidelines focus on “provider”-centric CPR, the evidence for transitioning to a “patient”-centric guided CPR is growing. Along with

CPR quality, the choice of the right medications and dosing intervals is critical during a pediatric cardiac arrest and is also a field of pediatric resuscitation that is lacking evidence. Despite good-quality CPR, there are many times when ROSC does not occur. Although PALS guidelines state that ECPR can be considered in certain circumstances, there are still gaps in the literature regarding cannulation strategies and resuscitation practices during ECPR. After successful ROSC or return of circulation after ECPR, the medical management of a child is critical to ameliorate the effects of PCAS and prevent further injury to vital organs, in particular the brain.

Appendix

Post Arrest Care Checklist

1. **Optimize Ventilation and Oxygenation**
   - Maintain advanced airway
   - Maintain normoxia (SpO_2 94-98%)
   - Maintain normocapnia (maintain continuous $ETCO_2$)

2. **Circulation**
   - Maintain reliable IV access
   - Maintain invasive BP monitoring
   - Optimize hemodynamic status
     - Aim for age specific BP target
     - Monitor MAP, CVP, lactate, $ScvO_2$, urine output
   - Assess for and treat persistent shock
     - Identify and treat possible contributing factors
3. **Active temperature management**
   - Constant core temperature monitoring
   - Can choose either pathway
     - *Hypo*thermic: 32°C-34°C
     - *Normo*thermic: 35°C-37°C
   - Prevent and treat fever for 96 hours
4. **Monitor and Treat:**
   - Neurological status
     - Neuro checks q1 hour
     - Need for Sedation/Paralysis
       - Continuous EEG monitoring with paralysis
     - Seizures
       - Obtain EEG for clinical seizure
     - Hyperosmolar therapy to target Na >140
   - Glucose Control
   - Serial Laboratory Sampling:
     - Arterial blood gas
     - Venous blood gas
     - Lactate
     - Chemistry
     - Glucose
     - Liver Function
     - Coagulation Labs

Figure A1.
Post arrest care checklist.

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