post–cardiac arrest care (PCAC)

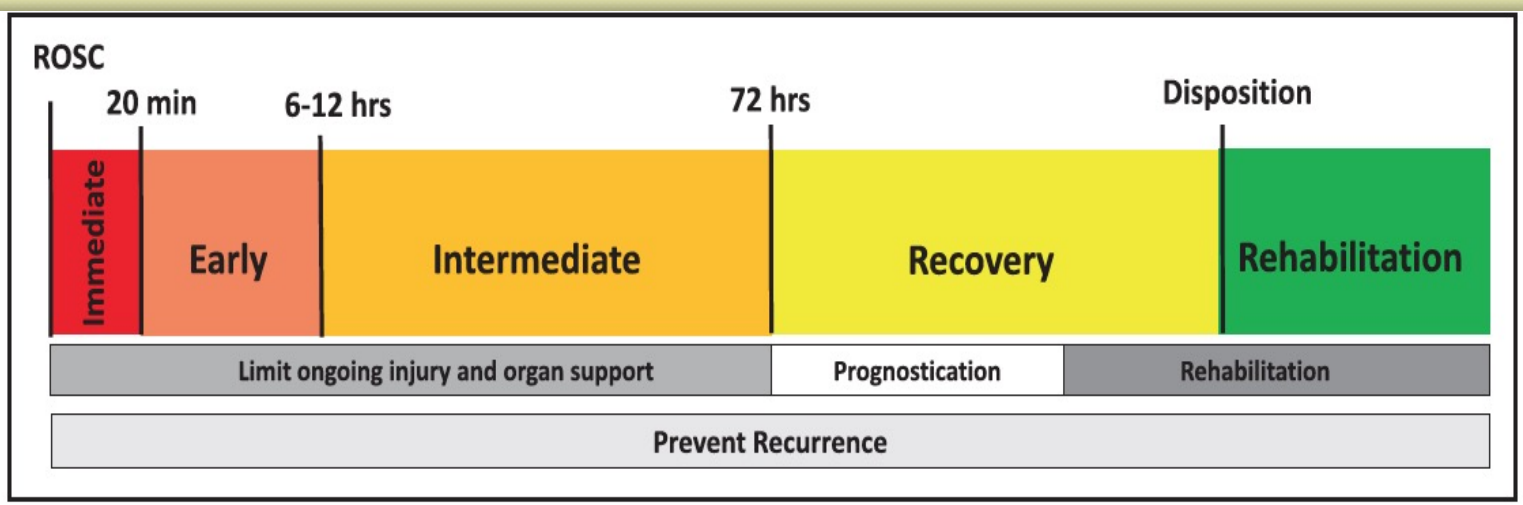

Figure 1. Phases of post–cardiac arrest syndrome.
ROSC indicates return of sustained circulation. Adapted from Neumar et al.[4] Copyright © 2008, American Heart Association, Inc.

- The immediate phase: the first 0 to 20 min after ROSC
- The early phase: from 20 min up to 6 to 12 hours
- The intermediate phase: 12 to 72 hours
- The recovery phase: approximately 72 hours to day 7
- The rehabilitation phase

The goal of PCAC is to increase not only survival to hospital discharge but also survival with favorable neurological outcome.

- ongoing assessment of the resuscitation,
- determining and managing the etiology of the arrest
- maintain and or minimize brain injury with TTM,
- consideration of vasoactive drugs,
- preventing decompensation,
- managing the patient in the emergency department, setting, and/or while transporting to PICU.

AHA SCIENTIFIC STATEMENT
Pediatric Post–Cardiac Arrest Care

TTM: targeted T management

PCAS: post–cardiac arrest syndrome

It was determined that all resuscitations from CA result in predictable sequelae in the days to weeks following the arrest now accepted as 4 key components of PCAS:

- **post–cardiac arrest brain injury,**
- **post–cardiac arrest myocardial dysfunction,**
- **systemic ischemia/reperfusion response,**
- **persistent precipitating pathophysiology**

AHA SCIENTIFIC STATEMENT
Pediatric Post–Cardiac Arrest Care

- Post-CA brain injury remains a leading cause of morbidity and mortality in adults and children due to limited tolerance of ischemia, hyperemia, or edema.

- **The first *3* phases of PCAS involve hypoxemic-hypotensive perfusion with energy deprivation.**

- With ROSC, there is a burst of reactive oxygen species, and oxidative stress may ensue in tissue that is depleted of antioxidants.

- As a result, **reperfusion** is associated with **excitotoxicity**, **calcium accumulation**, and **free radical–mediated cell injury or death.**
- Both neuronal cellular necrosis and apoptosis result from this cascading injury and can continue in the days to weeks after ROSC.

- A variety of post–CA clinical conditions, including hyperoxia, hypoxemia, and hypotension, can exacerbate the neuronal injury.

Oxygenation and Ventilation

- All intubated children require continued assessment to ensure **proper ETT positioning**, including continuous monitoring of oxygenation (pulse oximetry), and
- **ongoing monitoring of ventilation (continuous EtCO2 monitoring, &/or intermittent ABG assessment).**
- Insertion of a gastric tube reduces gastric distension and prevents vomiting.

- **D**: Dislodged or displaced ETT(right mainstem or esophageal location)
- **O**: Obstructed endotracheal tube (mucous plug, kinked ET)
- **P**: Pneumothorax
- **E**: Equipment failure (ventilator malfunction, O2 disconnection)

Avoid low and high arterial oxygen

- **Once ROSC has been achieved,** The **lowest possible FiO2** should be used to maintain an **O2 sat of 94%-99%** to avoid hypo or hyperoxemia.

- **Small observational studies have failed to show an association between arterial oxygenation and mortality in resuscitated children.**

- One large, retrospective, multicenter observational pediatric study of 1875 infants and children who survived to PICU admission, analysis showed that:
- **hypoxemia** (PaO_2 <60 mmHg) &
- **hyperoxemia** (PaO_2 ≥300 mmHg)

  independently & significantly increased the ERD by 90 & 25 %, respectively.

ERD: estimated risk of death

Monitor ventilation

- $PaCO_2$ after ROSC must be targeted and severe **hypocapnia ($PaCO_2$ <30 mmHg)** or **hypercapnia ($PaCO_2$ >50 mmHg)** should be limited.

- In one study **hypo and hypercapnia was associated with a mortality of 50 & 59 %, respectively,** compared with 33% mortality if $PaCO_2$ was 30-50 mmHg.

Arterial CO_2 tension influences cerebral perfusion in both children and adults.

- Hyperventilation decreases coronary perfusion and survival rate after CA.
- Hyperventilation decrease CBF through cerebral vasoconstriction, thereby potentially exacerbating cerebral ischemia.
- Hypercapnia causes increased CBF through cerebral vasodilation.

- **Global myocardial dysfunction** occurs even in the absence of a cardiac cause of the arrest, and the severity may be related to the duration of no-flow time during cardiac arrest.

- It has been associated with early mortality despite successful initial resuscitation in children and adults.

- The onset of PCA **myocardial dysfunction** begins within hours of the arrest, peaks at ≈8 hours, begins to improve at 24 h, and typically resolves within 48 to 72 hours.

    - cardiovascular ischemia/ reperfusion injury
    - cytokine-mediated cardiovascular dysfunction,
    - induced myocardial injury secondary to catecholamines or electric shocks

Clinical manifestations of myocardial dysfunction

- **Hypotension,**
- **LV and RV systolic or diastolic dysfunction**
  - **reduced CO,**
  - **arrhythmias, and**
  - **pulmonary edema, leading to recurrent CA**

- No support for routine administration of prophylactic antiarrhythmics after ROSC, but rhythm disturbances during this period may warrant therapy.
- No therapy for PACs and PVCs other than maintenance of adequate perfusion and NL fluid and electrolyte balance.
- Ventricular arrhythmias may signify more serious myocardial dysfunction.
- Echo is a beneficial noninvasive tool for identifying myocardial dysfunction and congenital and acquired cardiac abnormalities, although no optimal timing or frequency of PCA echo.
- A 12-lead ECG is helpful in establishing the cause of arrest.

Systemic Ischemia/Reperfusion

- The combination of systemic ischemia/reperfusion produces a state similar to the sepsis syndrome, with elevated cytokines, the presence of endotoxin in plasma, activation of coagulation pathways, and inhibition of anticoagulant pathways.

- Clinical manifestations of systemic ischemia/reperfusion include capillary leak with intravascular hypovolemia, vasoplegia, coagulopathy, hyperglycemia, adrenal insufficiency, and impaired O2 utilization and delivery, contributing to multisystem organ dysfunction.

Persistent Precipitating Pathophysiology

- Management of the child after cardiac arrest includes DX and treatment of the precipitating cause.
- Failure to identify and correct the original cause of CA leaves the patient at risk for secondary injury and even recurrence of CA.

Hemodynamic Monitoring

- Approximately 95% of pediatric IHCA occurs in an ICU, and almost 50% of these patients will have arterial catheters in place before the CA.
- If possible, an arterial catheter should be placed for continuous intra-arterial pressure monitoring to facilitate the identification and treatment of hypotension.
- Central venous catheters may be useful to monitor central venous o2 sat and to provide a route for the administration of fluids and medications.

Hypoperfusion and Hypotension

- Perfusion is compromised after CA, and patients are often hypotensive. Of note, **cardiogenic shock** occurs frequently in survivors of CA.

- **After ROSC in a child, circulatory instability may be the result of:**
  - **Ongoing fluid loss,**
  - **Decreased cardiac function, and/or**
  - **Harmful alterations in SVR**

- **Hypotension after ROSC is associated with:**
  - * decreased survival to hospital discharge
  - * decreased survival W favorable neurologic outcome

- Based on data poor perfusion is associated with increased morbidity and mortality. Thus, vasoactive drug therapy is recommended, and should be tailored to each patient.

- The 2015 international guidelines recommend that parenteral fluids, inotropes and vasoactive medications be used to maintain the **SBP>5th percentile for age**.
- If hypovolemia is suspected in a patient with cardiogenic shock, the clinician should carefully infuse 5-10cc/kg of isotonic fluids over 10-20 min followed by reevaluation of endpoints.

Septic Shock

Fluid Boluses

2020 (Updated): In patients with septic shock, it is reasonable to administer fluid in 10 mL/kg or 20 mL/kg aliquots with frequent reassessment.

2015 (Old): Administration of an initial fluid bolus of 20 mL/kg to infants and children with shock is reasonable, including those with conditions such as severe sepsis, severe malaria, and dengue.

Choice of Vasopressor

2020 (New): In infants and children with fluid-refractory septic shock, it is reasonable to use either epinephrine or norepinephrine as an initial vasoactive infusion.

2020 (New): In infants and children with fluid-refractory septic shock, if epinephrine or norepinephrine are unavailable, dopamine may be considered.

Early and continuous epinephrine infusion for post-arrest hypotension is the preferred agent in pediatric patients.

One study suggested that early EPI (within 15 min of arrest):

- decreased the time to ROSC,
- higher survival rate and
- better neurologic outcomes in non-shockable OHCA.
- Epinephrine a peripheral vasoconstrictor, **improves BP, also a potent ino** and **chronotropic agent.**

Dopamine, norepinephrine, and dobutamine recommended as 2nd line therapies, or in specific pre-existing conditions such as renal failure or cardiogenic shock.

Analgesia & sedation

- should be used to ensure comfort and prevent shivering.
- shivering can occur at different goal temperatures during TTM, including both therapeutic hypothermia and therapeutic normothermia
- Combinations of opioids and benzodiazepines are commonly used in adults, although sedative-anesthetic agents such as propofol & dexmedetomidine are also good options.
- must be balanced against the risk of complications:
    - infection and pneumonia,
    - hypotension, and
    - prolonged mechanical ventilation

Sedation and Neuromuscular Blockade

- The 2010 AHA PALS guidelines recommended controlling pain and discomfort with analgesics (eg, morphine, fentanyl) and sedatives (eg, lorazepam or midazolam).

- Neuromuscular blocking agents (eg, vecuronium or pancuronium) with analgesia or sedation (or both) may improve oxygenation and ventilation in case of patient-ventilator dys synchrony or severely compromised pulmonary function.

- The use of NMB potentially lead to over or undersedation, or masking of worsening neurological examination findings. In addition, NMB will mask seizures.

BS Monitoring

Prevent & treat hypoglycemia (≤45 mg/dL in the newborn and ≤60 mg/dL in the child) to avoid further neurologic insult.

- Severe hyperglycemia can lead causes osmotic diuresis, which can exacerbate volume depletion and hemodynamic instability.
- Sustained hyperglycemia (2 consecutive BS≥150mg/dL) is associated with higher mortality in critically ill children and should be avoided.

Seizures occur in 10%-50% of children who remain encephalopathic after achieving ROSC.

- About half of children with post-ROSC seizures experience exclusively nonconvulsive (subclinical, EEG only) seizures.

- Seizures can not be predicted from any clinical or resuscitation variables.
- Seizures were associated with unfavorable gross neurological outcomes at discharge but not with higher mortality.

Seizures can cause:

- increased metabolic demand,
- worsened metabolic dysfunction,
- increased ICP
- secondary brain injury

For these reasons, many clinicians aim to treat seizures, although the approach is generally guided by the child's overall medical condition and other prognostic indicators.

Continuous EEG monitoring is recommended as soon as feasible for adult and pediatric patients who remain encephalopathic after CA to identify electrographic seizures.

for 24-48 hours in most patients, but continuing until after 24 hours of normothermia in patients treated with hypothermia.

Effect of treatment of clinical or EEG seizure on patient outcome ?

what are optimal methods to manage seizures after CA?

- Acute, electrographic seizures are treated with benzodiazepines, levetiracetam, or phenytoin. myoclonic seizures may be refractory to treatment.

- Potential adverse effects of anticonvulsants:
- cardiac arrhythmias,
- hypotension, and
- respiratory depression

- It must be taken into into consideration that sedation induced by these medications may complicate the neurological examination.

TTM

- To treat the child who remains comatose after OHCA, the 2015 AHA PALS guidelines update recommended that it is reasonable either to maintain
  - continuous normothermia (36–37.5°C) for 5 days

or

  - 2 days of continuous hypothermia (32–34°C) followed by 3 days of continuous normothermia (36–37.5°C)
- Because of increased mortality was associated with T<32°C, meticulous care must be provided to prevent T<32°C.

T management

- TTM to 32-34°C can be divided into 3 phases: induction, maintenance, and rewarming.

- **surface-cooling methods**
  - positioning cooling blankets under or above the patient
  - use of ice packs around the body,
  - core-cooling methods (IV catheters circulating cold saline) or
  - combination approach

core T should be continuously monitored.

- Hypokalemia,
- hypophosphatemia,
- hypomagnesemia, → may precipitate arrhythmias
- Hypocalcemia
- decreases insulin sensitivity

- The maintenance phase requires careful monitoring to avoid fluctuations in T.

In children, rewarming is generally accomplished at a rate 0.5°C/2h to reduce the risk of:

- cerebral hyperperfusion,
- vasogenic edema, and
- acute systemic hypotension documented during rewarming in TBI

- For children who are comatose after OHCA and IHCA, TTM to 32-34°C for 24-48 hours is relatively safe.

TBI: traumatic brain injury

In two recent multicenter multinational randomized controlled trials children comatose within 6 hours of ROSC were randomly assigned to 2 groups.

- Those on lower T range were cooled to 32-34°C for 48 hours, rewarmed over 16-24 hours, and maintained at 36-37.5°C until 5 days after the initiation of TTM.
- Another group were actively maintained at 36-37.5°C for 5D.

the percentage of survivors with favorable neurological outcomes at 1 year did not significantly differ between 2 groups.

Fever is common in children after resuscitation from CA

- **During PCAC, T≥ 38°C should be aggressively treated.**
- **Remember that once TTM is initiated, the TT should be maintained consistently for 12-24 h, W/O intermittent rewarming, as unintentional or early re-warming has been associated with poor neurologic outcomes compared to patients who did not undergo TTM at all.**
- **Despite contradicting evidence, current guidelines recommend the use of TTM in both OHCA and IHCA, as well as in CA due to shockable or non-shockable rhythms.**

Identification and Treatment of Adrenal Dysfunction

- Approximately 30% of critically ill children have relative adrenal insufficiency, but this has not been evaluated in children resuscitated from CA.
  - A recent meta-analysis did not demonstrate a difference in outcomes between those who did and those who did not receive exogenous steroids. Insufficient evidence to support the routine use of corticosteroids after CA.
  - Based on guidelines for the management of pediatric and neonatal sepsis consider steroid administration if the patient is at risk for adrenal insufficiency with refractory shock.

prognosis

- Overall survival rates from 2005 to 2013 data collection range from only 6.4% to 10.2%.
- survival to hospital discharge after OHCA has not significantly changed over the past 10 years.
- Risk-adjusted rates of ROSC in IHCA increased from 42.9% in 2000 to 81.2% in 2009, and risk-adjusted rates of survival to discharge improved from 14.3% in 2000 to 43.4% in 2009 W/O an increase in unfavorable neurological outcome.

Factors for all ages with a better prognosis:

- short duration of arrest,
- early initiation of CPR,
- hypothermia as the cause, and
- IHCA

prognosis

Factors associated with unfavorable neurologic outcomes from OHCA:

- decreased age,
- sudden infant death syndrome, and
- blunt trauma

Factors associated with decreased survival after IHCA:

- older age,
- pre-existing conditions,
- Interventions (ETT, mechanical ventilation),
- use of vasopressors at the time of arrest, &
- arrests occurring during night and weekend shifts

For both OHCA and IHCA:

- pre-arrest rhythms of bradycardia and VF/VT were associated with the highest survival, and PEA was associated with higher survival than asystole.

- Post–cardiac arrest brain injury and myocardial dysfunction are the leading causes of morbidity and mortality in children.

Phase of Injury	Pre-Event	Cardiopulmonary Arrest
Prognostic Factors	• Age > 1 yr • Preexisting condition • Interventions in place • Cause of arrest • Night / weekends • Congenital heart disease • Pulmonary artery hypertension	• CPR duration • Witnessed • Bystander CPR • EMS response time • Calcium & Bicarbonate administration • Shorter time to epinephrine • Non-shockable rhythm • Intubation • CPR quality • ECPR

ECPR: extracorporeal resuscitation

Post-Cardiac Arrest Syndrome

- Lack of pupillary responsiveness
- Abnormal motor response to pain
- Seizures
- Early hypotension
- Substantially abnormal EEG background
- Elevated blood glucose
- Elevated blood lactate
- Neuron-specific enolase, S100B

- Neuron-specific enolase (NSE) is **an acidic protease unique to neurons and neuroendocrine cells**. It is a sensitive indicator for assessing the severity of nerve cell damage and prognosis. High serum levels of neuron-specific enolase (NSE) and S-100B protein are known to be associated with **ischemic brain injury and poor outcome after cardiac arrest**.
- S100B is a useful neurobiochemical marker of **brain damage such as in circulatory arrest, stroke and traumatic brain injury**. In histopathology, S100 is widely accepted as **the marker of choice for immunohistochemical identification of malignant melanoma**.

S100 proteins are low-molecular-weight calcium-binding proteins and appear to play an important role in various cellular processes such as cell division and differentiation. In histopathology, S100 is widely accepted as **the marker of choice for immunohistochemical identification of malignant melanoma**.