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Chapter

# Extracorporeal Cardiopulmonary Resuscitation

*Abdelaziz Farhat, Cindy Darnell Bowens, Ravi Thiagarajan and Lakshmi Raman*

## Abstract

ECMO, or extracorporeal membrane oxygenation, is an advanced life support technique that provides cardiac and pulmonary support similar to cardiopulmonary bypass. ECPR (extracorporeal cardiopulmonary resuscitation) is the rapid deployment of VA-ECMO when conventional cardiopulmonary resuscitation fails to provide return of spontaneous circulation. Evidence in the literature is sparse, but with expanding reported applications, ECPR has shown promise to improve outcomes of cardiac arrest. ECPR is superior to conventional CPR for both survival and neurologic outcomes. ECPR has been successfully used to manage arrests secondary to cardiac and non-cardiac causes. Arrests secondary to primary cardiac causes have the best overall outcome. Other determinants of outcomes of ECPR include duration of low flow state and on-ECMO complications. A narrow list of ECPR contraindications exists, and includes severe neurologic injury and irreversible primary disease process. Various complications can occur with ECPR, and include mechanical, cardiovascular, pulmonary, hematologic, renal, and neurologic complications. Neurologic complications are the most serious, and significantly affect mortality or quality of life. ECPR is a nascent field, and substantial work remains to be done to optimize its application. Given the small number of patients at each institutional level, this is a field ripe for collaborative work and rewarding results.

**Keywords:** extracorporeal membrane oxygenation, cardiopulmonary resuscitation, ECPR, cardiac arrest

## 1. Background

ECMO, or extracorporeal membrane oxygenation, is an advanced life support technique that provides cardiac and pulmonary support similar to cardiopulmonary bypass. Venous blood is drained and pumped through a membrane where gas exchange occurs. Oxygenated blood is returned back to the patient either through venous circulation in VV-ECMO (venovenous ECMO) or arterial circulation in VA-ECMO (venoarterial ECMO).

ECPR (extracorporeal cardiopulmonary resuscitation) is the rapid deployment of VA-ECMO during cardiopulmonary resuscitation (CPR) when conventional CPR fails to provide return of spontaneous circulation (ROSC) [1]. The first reported use of ECMO in CPR was in 1976. Since then, the use of ECPR has become well-described in adults and children, with a continuously expanding list of diagnoses.

ECPR literature is limited, more so for pediatrics. Reports are mainly single center experiences, registry retrospective analyses, and a few meta-analyses. Small sample sizes and lack of standardization impede drawing conclusions on utilization and care processes for ECPR. Regardless, utilization of ECPR continues to expand. The Extracorporeal Life Support Organization (ELSO) reports more than a total of 10,000 ECPR patients since 1990, of which more than 5000 are pediatric or neonatal runs [2]. ECPR cases make up approximately 10% of all ECMO runs recorded over this time frame. Most ECPR cases originate in the intensive care unit, but there is growing literature demonstrating widening the use to emergency room arrests and out-of-hospital arrests [3, 4].

With expanding application, ECPR has shown promise to improve outcomes of cardiac arrest. ELSO recognizes that ECMO can be considered for select patients in cardiac arrest. In 2015, the American Heart Association (AHA) cautiously pointed out that while the evidence is still lacking, ECPR may reasonably be considered in potentially reversible situations [5].

This chapter explores the current utility of ECPR, and provides a literature summary of its indications and limitations. The chapter will also describe current use and outcomes in adults and children. Finally, complications of ECPR will be reviewed. A special focus will highlight neurologic complications and their influence on meaningful outcomes after ECPR.

## 2. ECPR is superior to conventional CPR

ECPR use for victims of cardiac arrest consistently demonstrates a survival benefit over conventional CPR [5–8]. This survival benefit is more pronounced as the duration of CPR increases. In contrast to arrest survivors who only receive conventional CPR, patients rescued with ECPR have higher survival rates at discharge and at 6-12 months post discharge [9]. Arrest victims rescued with ECPR are also more likely to have better neurologic outcome, when compared to patients rescued with conventional CPR [10].

## 3. Indications

The goal of ECPR is to augment cardiac output during the low flow phase of CPR, restoring oxygenation and perfusion in the setting of cardiac arrest. In some cases ECPR alone may be therapeutic, and in other cases it allows maintenance of perfusion while further treatment is explored.

At this time, no universal criteria exist for the deployment of ECPR. AHA recommendations are limited to heart disease amenable to either recovery or transplantation, in a setting where the arrest occurs in a highly supervised environment [11]. Their only other recommendation is for use in out of hospital cardiac arrest in the setting of severe hypothermia if appropriate expertise, equipment, and protocols are available. ELSO recommends ECPR in arrest victims "with an easily reversible event and have had excellent CPR" [12]. The UK Resuscitation Council considers ECPR as a "rescue therapy for patients in whom initial ALS measures are unsuccessful to facilitate specific interventions" such as coronary interventions or thrombectomies [13].

Centers that offer ECPR use center-specific processes, based on experience and availability of resources. ECPR is most commonly available to in-hospital cardiac arrest. Arrests in the emergency department can also be managed with ECPR. In some settings with appropriate resources, experience, and planning, out-of-hospital cardiac arrest has been managed with out-of-hospital ECPR [4, 14].

## 4. Contraindications

Contraindications to ECPR vary between institutions, and a unified consensus does not exist. ECMO-related prognostic factors in the current literature are unreliable with regards to ECPR outcomes. On their own, most of these factors do not provide sufficient evidence to support denial of life-saving ECPR to a victim of arrest. The only absolute contraindications to ECPR are the presence of a valid "Do Not Resuscitate" order and the absence of appropriate staff/equipment to initiate ECPR. All contraindications to ECMO use, such as extreme prematurity, also apply.

Otherwise, a range of situations can be proposed as relative contraindications for ECPR:

1. Severe neurological impairment prior to cardiac arrest: Exact definitions of impairment will vary between providers and institutions. In a similar vein, conditions that place a patient at high risk for severe neurologic injury despite good CPR (such as severe primary pulmonary hypertension or patients with cavopulmonary circulation) may be a reason to not offer ECPR. Determinations to preclude a child from ECMO candidacy may involve a discussion with family, and should contain an understanding the perceived and expected quality of the child's life.

2. Known irreversible disease process: When cardiac arrest occurs in the setting of a known irreversible and untreatable disease process, ECPR will only prolong suffering. Providers must work with the appropriate subspecialists to understand primary disease prognosis in order to determine if ECPR is an appropriate choice should the patient arrest.

3. Severe immunosuppressed state: While literature is limited, certain groups of severely immunocompromised patients tend to do worse on ECMO. Patients with immunosuppression in the setting of solid organ transplantation or high-dose steroid regimens may have outcomes comparable to the general population. In contrast, patients with solid tumors, hematological malignancies, or acquired immunodeficiency syndrome (AIDS) do much worse on ECMO. In one study, survival to discharge was 7–20% [15]. This highlights the need to understand primary disease prognosis, and determine ECMO candidacy prior to arrest.

4. Severe coagulopathy: Management of ECMO post-resuscitation requires use of anticoagulation to maintain appropriate circuit function. In cases of severe coagulopathy, the physician must balance the management of the coagulopathy and the circuit anticoagulation. If the coagulopathy is difficult to treat, devastating and fatal hemorrhagic side effects may occur [16].

5. Prolonged total arrest time: There is no consensus on a cut-off time, but as shown in **Figure 1**, prolonged low-flow states are associated with lower survival [17]. Neurologic outcomes are also worse. The impact is magnified if combined with failure to initiate chest compressions in a timely fashion after arrest. While a prolonged resuscitation may be not futile, each institution must consider its capabilities and available resources before establishing a cutoff time. This decision will also likely be patient-dependent.

6. Lack of access for cannulation: Anatomic or other vascular anomalies that preclude successful cannulation render a patient a non-candidate for ECPR.

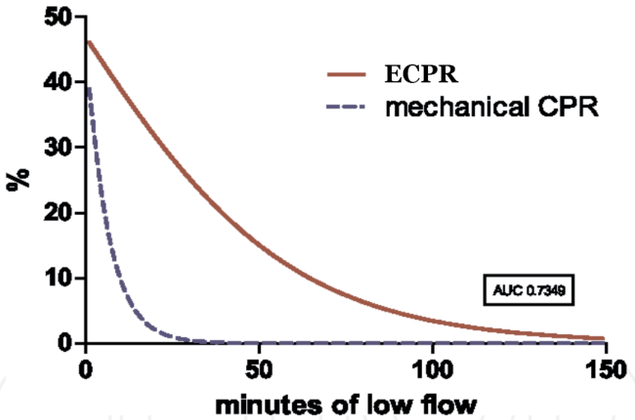



**Figure 1.**
*Estimated survival rates for extracorporeal membrane oxygenation (ECPR) patients after every given low-flow time (red line). Survival with conventional CPR (dashes) is demonstrated as a comparison. Wengenmayer T, et al. Influence of low-flow time on survival after extracorporeal cardiopulmonary resuscitation Crit Care. 2017;21(1):157. Published under terms of the Creative Commons Attribution 4.0 International License.*

## 5. The ECPR experience

According to recent reviews of the ELSO registry, ECPR is currently most commonly used in patients who suffer cardiac arrest secondary to a primary cardiac cause [7]. This is independent from patients who fail to wean off cardiopulmonary bypass. These patients include arrests post cardiac surgery, such as surgery for congenital heart disease (CHD). CHD patients rescued with ECPR include both single and two-ventricle patients. This cardiac cohort also includes patients with structurally normal hearts but develop heart failure in the setting of myocarditis, cardiomyopathy, arrhythmias, pulmonary arterial hypertension, and heart transplant graft failures.

A variety of non-cardiac causes of arrest have also been supported by ECPR. These include arrests in the setting of septic and other forms of non-cardiogenic shock. Arrests that occur in the setting of pneumonia, ARDS, acute airway compromise, toxic ingestions, severe hypothermia, and trauma have also been supported with ECPR.

In some situations where the cause of arrest is unclear, ECPR allows for preserving the patient while the diagnosis can be clarified. For example, ECMO support allows for time to perform head imaging or other diagnostic testing that helps with clarifying treatment or prognostication. If a negative prognosis is uncovered, there is time to involve palliative care, if desired, and allows family another opportunity for closure.

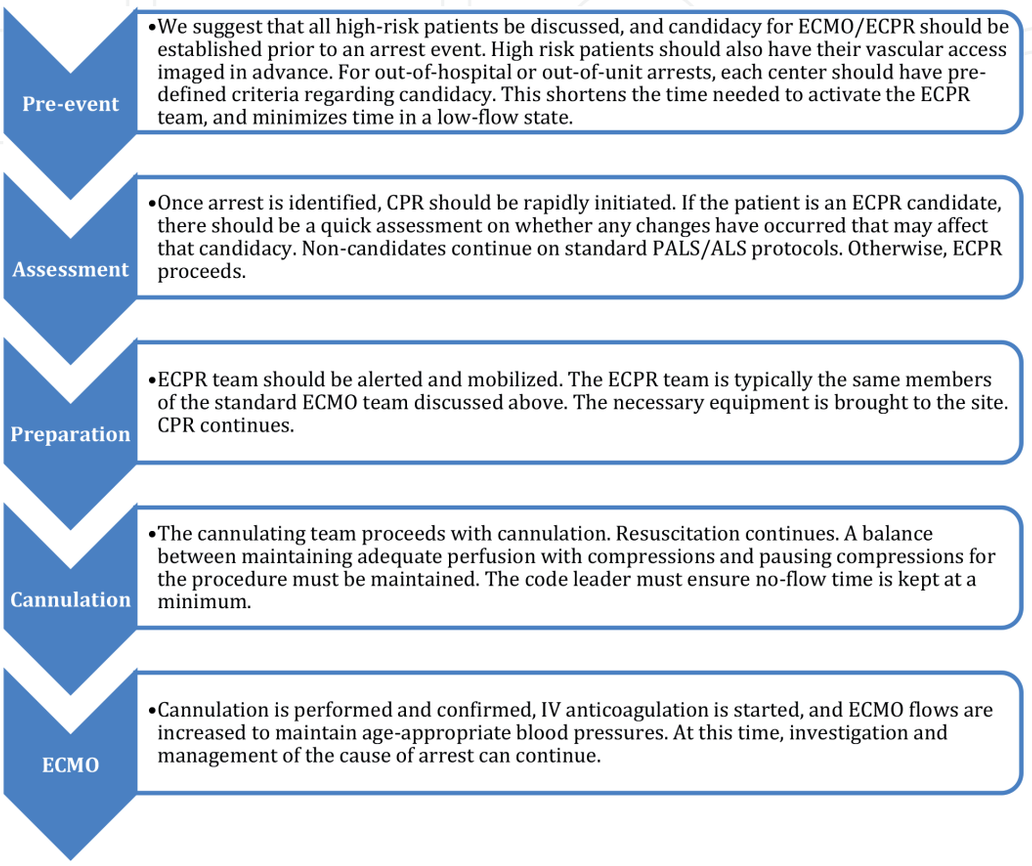
Some institutions have reported ECPR use as a temporary measure for organ perfusion while organ procurement organizations work to facilitate organ placement [18, 19]. This is usually in situations where brain death is quickly identified after placement on ECMO. Viability of the organs is preserved, and the transplanted organs have a high rate of good functional recovery [20].

## 6. Application of ECPR

### 6.1 Process

The real-life application of ECPR varies between centers [21]. At a minimum, a core group that consists of a code team, a cannulation team (surgeon

or interventionalist to cannulate), and an ECMO specialist must be available. Support staff including additional nursing, pharmacy, and OR staff may be needed. Location of the cannulation procedure will depend on center experience and appropriateness of available space. For example, the procedure can happen in the intensive care unit, in the catheterization lab, or in the operating room. Some centers have reported experience with cannulating in other locations, such as in the emergency department, in the IR suite, or on regular hospital wards. Most reported experiences follow a similar algorithm.




## 6.2 ECMO cannulation

Cannulation technique for ECPR depends on anatomy, experience and training of the cannulating provider, and circumstances necessitating support [22]. In almost all cases, ECPR patients require VA cannulation. If the patient has an open sternum, central cannulation is the easiest approach. In smaller children, the right carotid artery and internal jugular vein are the most common choice. In adults and adult-sized children, femoral cannulation is technically feasible. Femoral cannulation can limit the no-flow time due to minimal or no interruptions in compressions. Placed cannulas should support at least 120-150 mL/kg/min flow in order to provide an appropriate cardiac index in smaller children. In larger children and adults, the cannulas should support 3.5 to 5 L/min depending on the underlying etiology of cardiac arrest. If cannula sizes are deemed to be insufficient for flow, additional venous drainage can be added.

## 6.3 Initial management: post arrest care

The goal of post arrest care is to safeguard neurologic function and prevent secondary organ injury, while working towards the diagnosis and management of

| Management goal | Reasoning |
|---|---|
| Maintain normal oxygenation | Elevated PO2 contributes to oxidative stress, and adult studies associate hyperoxia with decreased survival [24]. Hypoxia is associated with worse neurologic and overall outcomes. |
| Maintain normocarbia | Hypocapnia has been associated with worse outcomes in adults, and hypercapnia has been associated with decreased survival in pediatrics [24]. |
| Maintain normotension | Post-ROSC hypotension is associated with decreased survival to discharge and worse neurologic outcomes [25]. Severe hypertension may adversely affect cardiac output, and has also been associated with neurologic injury [26]. |
| Targeted temperature management | Aggressively avoid hyperthermia, which is associated with poor outcomes [27]. At this time, there is insufficient evidence to recommend hypothermia over goal-directed normothermia. |

**Table 1.**
*Post arrest care.*

| Continuous telemetry | Assists with close monitoring of rhythm status |
|---|---|
| Exhaled $CO_2$ monitor | Allows for capturing $CO_2$ changes early |
| Continuous pulse oximetry | Assists with maintaining normoxia |
| Cerebral NIRS (near-infrared spectrometry) monitor | May be useful in identifying periods of increased vulnerability to developing neurologic injury [28] |
| Electroencephalogram (EEG) | Discontinuous or isoelectric tracings are associated with worse neurologic outcome. EEG data in this setting is limited but may be useful in prognostication in consort with other criteria. |
| Arterial blood pressure monitor | Assists with close monitoring of hemodynamics thus avoiding hypotension |
| Central venous pressure monitor | Assists with assessment of volume status |
| Continuous temperature monitor | Rectal or bladder monitor: may allow for capturing temperature changes early |

**Table 2.**
*Monitoring modalities.*

the cause of arrest. The AHA recommends adopting a systems-based, protocolized, goal-directed approach to the management of post-arrest patients [23]. This includes ECPR patients.

**Table 1** highlights the most important care recommendations from the AHA, and **Table 2** includes monitoring modalities to be considered. These are based on the best available evidence, which may be limited to expert opinion in some cases. All recommendations are continuously reviewed and updated by the AHA as more evidence becomes available.

### 6.4 Initial management: A systems approach

Critical care management of post-ECPR ECMO patients should involve a multidisciplinary team that includes ECMO nurse/therapist, bedside staff, intensivists, and surgeons. Post arrest management should be implemented per local protocols. Like all ECMO patients, sedation, ventilation, anticoagulation, nutrition, and infection control should be cautiously monitored:

1. Neurological/Sedation: Soon after resuscitation, it is imperative to determine the patient's neurologic status, as this will guide further decision making

and management. Close monitoring of the neurologic exam is imperative. Evaluate for signs of seizures, and EEG should be obtained if there is any suspicion. Near-infrared spectroscopy (NIRS) monitors can be used to follow cerebral oxygenation, possibly serving as an indicator of neurological activity and overall perfusion. In infants, routine bedside head ultrasounds should be considered, since these are simple and inexpensive assessments that can provide important information about development of neurologic injury. For all patients, head imaging such as with computed topography should be considered as indicated by exam and other clinical findings. Analgesia and sedation should be appropriately used to provide comfort; muscle relaxants use should be minimized to cases of safety or medical concerns.

2. Cardiovascular: Continuous cardiac and hemodynamic monitoring is important. Peripheral perfusion should be monitored, especially in patients with femoral cannulation. Volume must be judiciously used to maintain cardiac preload. Systemic vascular resistance should be balanced to the patient's needs, with judicious use of inotropy if cardiac contractility needs augmentation. All patients should be monitored for need for LV decompression as discussed below. In patients with absent pulsatility, the LV must be monitored for clot formation.

3. Pulmonary: Maintain functional residual capacity to facilitate oxygenation of pulmonary blood flow, balancing that with allowing for lung rest. Gentle pulmonary toilet is warranted, balancing secretion clearance with avoiding trauma and bleeding.

4. Gastrointestinal/Renal: Nutrition should be considered as indicated; we promote early enteral feeding if able. Gastric drainage and stool output must be monitored for bleeding. Urine output should be monitored closely, with promotion of diuresis as needed. In case of renal failure, hemofiltration or dialysis must be considered.

5. Infection: Routine indicators of infection are unreliable: vital signs are influenced or controlled by the circuit, and lab parameters can be affected by the circuit. Assessment of the patient must include diligent monitoring of all sites of cannula or line insertion, as well as all wounds. Routine monitoring of CBC with differential is recommended. Surveillance cultures, as well as antibiotic prophylaxis, should be done per institutional protocol.

### 6.5 Initial management: Anticoagulation

Most ECMO centers have their own institutional protocols for ECMO anticoagulation, usually an amalgam of center experience, ELSO guidelines, and published literature. We suggest utilizing an anticoagulation expert when setting up such a protocol, and recommend reviewing institutional practices regularly with the goal of keeping up-to-date with the literature.

Anticoagulation in this patient population starts with the cannulation procedure. A bolus of unfractionated heparin (typically 50–100 units per kg) is given directly to the patient prior to cannula placement. Afterwards, an unfractionated heparin infusion is started, usually 28–30 units/kg/hr. in neonates and infants, and 20 units/kg/hr. in larger children. Of note, neonates may need higher doses of unfractionated heparin secondary to naturally lower antithrombin III (ATIII) plasma concentrations. Less heparin may be required in patients who have a coagulopathy.

Anticoagulation monitoring differs between centers [29, 30]. Labs can include partial thromboplastin time (PTT), anti-Xa, and thromboelastography (TEG). ATIII levels may be monitored dependent on the clinical situation. Platelets, fibrinogen, and plasma free hemoglobin are adjunct values that can be monitored, and can help with management of a circuit's anticoagulation. The patient's coagulable state must be taken into consideration, and this may alter dosing and target lab values. **Table 3** lists the most common parameters used in monitoring anticoagulation.

Some centers report the use of direct thrombin inhibitors, such as bivalirudin, as an alternative to unfractionated heparin infusions [31]. Direct thrombin inhibitors (DTI) have the advantage of not requiring ATIII for action and can inhibit clot-bound thrombin. However, DTIs do not act on the contact pathway, which may be an issue in low-flow parts of a circuit (such as a bridge or a pigtail for lab draws). DTIs are titrated to a PTT of 1.5–2 times normal, and so it is important to establish a baseline value prior to use.

### 6.6 Special consideration: left heart decompression

Patients managed with ECMO, more so in the setting of cardiac disease or ECPR, can develop myocardial dysfunction and left heart failure [32]. In ECMO patients who develop poor left heart function, the team must work to offload the heart [33]. This is necessary to prevent complications such as worsening cardiac function or pulmonary edema [34].

Management of ECMO-related LV distension should start with exclusion of poor cannula positioning and eliminating mechanical issues with the ECMO circuit [35]. Pump function should be adjusted to maintain appropriate flows. LV distension can be secondary to volume overload, and so volume status should be addressed accordingly. In case of poor cardiac muscle function, inotropes to improve contractility and vasodilators to decrease LV afterload can be utilized.

If offloading the left heart cannot be achieved medically, and cardiac output remains compromised, the institution of an interventional approach may be required. Several interventional decompression strategies have been described and are listed in **Table 4**. Evidence-based guidelines are lacking with regards of absolute indications, timing of intervention, and management method. The following is a non-comprehensive list of indications from the literature:

1. Elevated LA pressure and LVEDP despite maximal medical management
2. Severe distension of LA or LV (can include LV thrombus in setting of stasis)
3. Poor left outflow tract ejection/closed aortic valve
4. Refractory pulmonary edema or pulmonary hemorrhage
5. Aortic valve regurgitation
6. Elevated LV wall stress
7. LV or RV dysfunction

### 6.7 ECPR program

Several authors have discussed the essential components of an ECMO program, which are needed before ECPR can be offered as a treatment option [21, 47]. With

| Lab parameter | Description | Goals |
|---|---|---|
| Activated Clotting Time (ACT) | Assesses whole blood clotting | Normal: 80–160 sec<br>ECMO target:<br>180–240 seconds |
| Activated Partial Thromboplastin Time (aPTT) | Assesses the intrinsic pathway | Normal: 30–40 sec ECMO target: 1.5x normal |
| Anti-Xa level | Assesses clotting activity | ECMO target:<br>0.35–0.70 units/ml |
| Thromboelastography (TEG) | Assessment of whole blood clotting, fibrinolysis and platelet activity | |

**Table 3.**
*Monitoring anticoagulation.*

| Strategy | Reference |
|---|---|
| Intra-aortic balloon pump | Aso et al. [36] |
| Pulmonary artery vent | Fouilloux et al. [37] |
| Percutaneous trans-septal LA decompression | Aiyagari et al. [38], O'Byrne et al. [39] |
| Trans-septal LA decompression with BAS and LA vent insertion | Eastaugh et al. [40] |
| Transaortic vent | Hong et al. [41] |
| Static over-the-wire balloon dilation | Baruteau et al. [42], Eastaugh et al. [40] |
| Blade balloon septostomy | Johnston et al. [43] |
| Atrial stenting | Haynes et al. [44] |
| Direct surgical LA or LV venting | Guirgis et al. [45], Sandrio et al. [46] |

**Table 4.**
*Interventional decompression strategies for ECMO-related left heart dysfunction.*

ECPR, time is of the essence. In order to successfully offer ECPR, a well-established protocol needs to be in-place and needs to be followed each time. There are several reported characteristics of a successful ECPR program, independent of the quality and capability of the ECMO team. An ideal team should be able to respond to situations in a consistent manner while maintaining that quality despite negative situations or hardship.

Consistency is maintained by continued training of all members of the team. Ongoing training must be both theoretical and hands-on. Simulation is a unique, effective way to incorporate the necessary training and dispense it to all members of the team in a way that can model real-life situations [48–52]. Leaders of the team must be able to keep up with the most up-to-date literature in ECMO and ECPR. Continued improvement of team performance is also assisted with maintaining quality improvement projects focused on outcomes-based factors related to each institution. On-the-spot debriefing after each event is a good way to identify concerns that need to be addressed.

## 7. Complications

ECPR, like all other forms of extracorporeal life support, is associated with a host of mechanical and non-mechanical complications. Frequency and severity

for most ECPR-specific complications are not reported in the literature at this time –reports generally include all ECMO patients as a single group. The ELSO website has a comprehensive list of reported ECMO and ECPR complications, including mechanical, neurologic, cardiovascular, infectious, immunologic, hematologic, metabolic, pulmonary, and renal [53].

Here we will highlight some of the better studied complications.

### 7.1 Neurologic complications

Neurologic complications on ECMO have been extensively documented due to their significant burden and influence on outcomes. In pediatric patients treated with ECMO, there is a 7% prevalence of intracranial hemorrhages and a 6% prevalence of cerebral infarctions. Overall ECMO survival drops by half in patients who develop neurological injury. Survivors have multiple long-term morbidities, including seizures and global developmental delay.

ECPR specific neurologic injuries are more prevalent and more significant than with routine ECMO. The ELSO database reports 12% incidence of seizures, 11.8% incidence of hemorrhage or infarct, and 11% incidence of brain death. Hemorrhages and infarcts were associated with lower survival. Severe acidosis, non-cardiac arrest etiology, and on ECMO CPR were risk factors for the neurologic injuries. Unfortunately, registry datasets are not granular and more specific associations are difficult to identify.

Literature reporting of neurodevelopmental outcomes post ECMO and ECPR is limited, and there is a varied approach to assessment and documentation [54]. However, overall trends appear encouraging. Favorable neurologic outcomes have been shown in up-to 65% of ECPR survivors. Favorable outcomes in these reports are defined as normal function or mild cerebral disability, showing that a good quality of life is attainable for arrest patients treated with ECPR. Further work is needed to uncover determinants of good outcomes.

### 7.2 Acute kidney injury and renal replacement therapy

Acute kidney injury (AKI) is common in critically ill patients, and patients treated with ECMO are especially prone to developing AKI. ECMO patients with AKI and subsequent fluid overload have a higher risk of longer ECMO runs and greater mortality [7]. Fluid overload management differs between centers, and includes fluid restriction, diuresis, slow continuous ultrafiltration (SCUF). None of these methods are efficient in removing solutes, and so continuous renal replacement therapy may be needed when fluid overload coincides with AKI. It should be noted that aggressive early CRRT may be associated with worse outcome [55], and indicates that judicious fluid management must always be an ongoing balance tailored to each patient.

## 8. Outcomes

ECPR is superior to conventional CPR. Overall survival to discharge in pediatric patients treated with ECPR in the ELSO registry is approximately 40%; **Table 5** shows a breakdown of this data. Other reports of ECPR survival vary across the literature, and the quoted numbers range between 23%-55%. In contrast, overall reported survival rates for conventional CPR in pediatrics range between 16 to 30%. The large range of variability is due to differences between institutional experience, expertise, and reporting on these patients. Superior survival rates persist with longer term follow-up and have been demonstrated up-to 12 months after discharge.

A major indicator of quality of life in survivors of ECPR is neurologic outcome. While work is limited, there is indication that these outcomes may be positive, and perhaps better than in patients rescued by conventional CPR. Several reviews have shown that survival with minimal neurologic damage was more frequent in patients rescued with ECPR. This trend remained true even after performing propensity score matching for patients across these groups.

### 8.1 Determining outcomes

Several pre-ECMO factors have been identified as important to determining outcomes of ECPR. Disease process leading to arrest is one such factor. Post-cardiac surgery patients, or patients who arrest in the setting of another primary cardiac process, have consistently demonstrated the best survival when rescued with ECPR versus conventional CPR. Patients who arrest in the setting of neonatal respiratory disease also have favorable outcomes. Patients who arrest in the setting of sepsis have higher mortality rates than patients with a pure cardiac process, but have better survival than if managed with CPR alone [57]. Patients with arrest in the setting of a respiratory illness also do well [58]. Patients with gastrointestinal conditions, who are usually patients with complex multiorgan disorders, tend to have worse outcomes. Patients with oncologic disease and other immunosuppressed processes also do worse [15].

Time to full support is another important predictor of survival of patients rescued with ECPR [17]. Longer time spent in a low flow state is associated with drastic drops on survival to hospital discharge. Post-discharge, patients with longer low flow times have worse neurologic outcomes and higher post-discharge mortality. Duration in a low flow state is a highly modifiable factor, and should be minimized in order to achieve the best outcomes. It is important to establish ECMO candidacy for all high risk patients, so that ECMO can be deployed quickly in the setting of an arrest. In centers that offer ECPR, a rapid response team must be available at all times, in order to minimize the time needed to establish ECMO flow. This team must be highly trained and very adaptable, highlighting the need for an ongoing development program for any center that offers ECPR. In addition to the presence of a rapid response team, ECMO equipment must be readily available for utilization at all times. During the resuscitation, pauses in compressions are needed to allow for cannula insertion. Duration and frequency of such pauses must be limited as much as possible, since any no-flow time dramatically decreases survival as well.

It is important to note that prolonged resuscitation may not be futile if ECPR is utilized, highlighting the importance of choosing the right patients for ECPR therapy [59].

Location of arrest can influence survival. Arrests that occur in the intensive care unit, have the best outcomes post management with ECPR. Outside the intensive care unit, outcomes worsen, perhaps related to the quality of resuscitation provided and the duration it may take to establish access for ECMO. Locations where ECPR can be offered will be dependent on institutional logistics and resource availability. Regardless, there should be advance coordination to ensure the equipment and

| | Total runs | Survive ECLS | Survival to discharge |
|---|---|---|---|
| Neonatal ECPR | 1718 | 1140 (66%) | 708 (41%) |
| Pediatric ECPR | 3946 | 2262 (57%) | 1675 (42%) |
| Total | 5664 | 3402 (60%) | 2383 (42%) |

**Table 5.**
*ECPR runs per the ELSO database, 1990–2018 [56].*

personnel needed can be deployed smoothly. Literature has shown that it is possible to successfully offer ECPR in the emergency department with such arrangements.

On-ECMO complications also influence survival, regardless whether it is a planned run or ECPR [57]. Neurologic complications are associated with high mortality post-ECPR. Inability to achieve and maintain adequate perfusion while on ECMO, noted by metabolic and lactic acidosis, has been tied to worse outcomes [60, 61]. Similarly, cardiac arrest during the ECMO run is also associated with poor outcomes. Renal failure and the need for renal replacement therapy have an association with inferior outcomes [58]. Severe coagulopathy and DIC also worsen survival – maintaining anticoagulation for the circuit and avoidance of fatal hemorrhage is a fine balance, and coagulopathy raises the risk of fatal hemorrhages [16, 62].

## 9. Special mention: out-of-hospital ECPR

Out of hospital cardiac arrests (OHCA) have very high mortality rates and very poor neurologic outcomes for both pediatric and adult patients [63, 64]. As a result, there has been growing interest in applying ECPR to OHCA. Overall survival rates vary for OHCA ECPR. Reported survival rates range from 12 to 30%, but patient numbers are very limited and there is extreme selection bias in this cohort [4]. ELSO reports that about half of all OHCA ECPR were reported in Europe, followed by the Asia-Pacific region, and lastly North America [65]. Almost all published experience is exclusively adult experience [66].

Application of ECPR for OHCA varies across different centers. Some institutions provide a "scoop and run" strategy, with quick transport to the emergency department for cannulation in select patients with OHCA [67]. Other centers have a different approach, with the ability to "stay and treat" by initiating ECPR on the scene of the OHCA [68]. The different styles of application are dependent on availability of resources, feasibility, and local experience.

Provision of ECPR to OHCA presents challenges with cost-effectiveness, optimal candidacy, and timing of deployment. However, if done in settings with the appropriate resources utilizing an aggressive strategy with optimum patient selection, survival can possibly be favorable [14]. However, evidence remains inconclusive and requires further study [66].

## 10. Conclusion and future directions

ECPR has emerged as an exciting rescue therapy, promising to improve outcomes of cardiac arrest. It has shown superiority over conventional CPR, with better survival to discharge and better longer-term survival. It has also shown better neurologic outcomes. As overall experience grows, we expect to see increased uses and even better outcomes.

Nonetheless, this is an emerging field and there is a lot left to learn. Especially in pediatrics, knowledge gaps include:

1. Ideal ECPR candidacy

    a. Definition of refractory arrest, i.e. how long should conventional CPR continue before ECPR should be considered

    b. Inclusion and exclusion criteria for higher risk populations, including immunosuppressed patients and trauma patients

c. Inclusion and exclusion criteria for out-of-hospital cardiac arrest

d. Assessment of futility in possible ECPR candidates

2. Team preparedness: specific nature of training to maintain ECPR team competency to decrease low flow time

3. Optimal approach to comprehensive post arrest care for ECPR patients

4. Approach to neuroprotection and neuroprognostication post-ECPR

5. Functional and neurodevelopmental post-discharge status of patients rescued with ECPR, and how to improve such outcomes

At this time, most ECMO and ECPR research is observational in nature. Generalization of pediatric data is hindered by the heterogeneity of patient ages and diagnosis, as well as variability of practice between different institutions. Because of the small numbers of patients overall and per institution, the field is ripe with opportunity for collaborative work. International registries and large research collaboratives may be able to provide enough patients to power larger investigations. More data will help empower decisions to treat children with ECPR, refine the caliber of care they receive, and improve their future quality of life.

## Author details

Abdelaziz Farhat[1*], Cindy Darnell Bowens[1], Ravi Thiagarajan[2] and Lakshmi Raman[1]

1 Children's Medical Center and University of Texas Southwestern Medical Center, Dallas, TX, USA

2 Children's Hospital Boston and the Harvard Medical School, Boston, MA, USA

*Address all correspondence to: abdelaziz.farhat@utsouthwestern.edu

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