Extracorporeal membrane oxygenation cardiopulmonary resuscitation, a luxury we cannot afford missing: a narrative review

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Extracorporeal membrane oxygenation (ECMO) was introduced into practice since more than four decades to support patients with advanced yet potentially reversible cardiopulmonary failure. Following several prospective clinical trials, ECMO is considered a widely accepted support modality in severe neonatal respiratory failure and in pediatric cardiac failure, particularly in the perioperative environment. Compared with conventional CPR, ECPR provides higher level of cardiac output support and several potential advantages including a higher rate of successful ROSC, support of post-resuscitation cardiogenic shock while arranging and performing coronary interventions and maintaining organ perfusion during recovery of native cardiac output.

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Introduction

Extracorporeal membrane oxygenation (ECMO) was introduced into practice since more than four decades to support patients with advanced yet potentially reversible cardiopulmonary failure. Following several prospective clinical trials, ECMO is considered a widely accepted support modality in severe neonatal respiratory failure and in pediatric cardiac failure, particularly in the perioperative environment [1–3]. ECMO subsequently became increasingly adopted in pediatric respiratory failure and adult cardiac support with apparent success, albeit without prospective studies [4]. Following the publication of the CESAR trial and reports from the H1N1 epidemic suggesting a survival benefit use in adults for respiratory failure, ECMO became widely adopted [5,6]. At the present time, the most rapidly growing application of ECMO is to provide circulatory support to patients in cardiac arrest following failure of conventional cardiopulmonary resuscitation (CPR) [extracorporeal cardiopulmonary resuscitation (ECPR)] to provide a return of spontaneous circulation (ROSC) [7].

Compared with conventional CPR, ECPR provides higher level of cardiac output support and several potential advantages including a higher rate of successful ROSC, support of post-resuscitation cardiogenic shock while arranging and performing coronary interventions, and maintaining organ perfusion during recovery of native cardiac output. The Extracorporeal Life Support Organization (ELSO) maintains a registry of extracorporeal life support (ECLS) cases reported by its member of healthcare organizations. The number of actual cases worldwide is likely much higher, as the ELSO participation is optional, and the registry does not include all cases where ECLS was performed [8]. ELSO defines ECPR as the use of ECLS in sustained cardiac arrest without ROSC, or in patients in ROSC may be transient but not sustained.

Rationale for extracorporeal cardiopulmonary resuscitation

Survival is low for both in-hospital (15–20%) and out-of-hospital (10%) cardiac arrest managed with conventional CPR [9]. A properly performed CPR maintains only a fraction of normal cardiac output as well as cerebral and myocardial blood flow [10]. An initial rhythm of ventricular fibrillation (VF) or ventricular tachycardia (shockable rhythm) is associated with better outcome [11], representing a rhythm disturbance in a previously almost healthy myocardium as opposed to diseased myocardium from underlying chronic heart disease. Pre-existing comorbidities even with VF as a presenting rhythm decrease the chance of survival. Witnessed cardiac arrest with immediate CPR is associated with improved outcomes [11,12]. The longer the time to initial defibrillation in a shockable rhythm or administration of epinephrine in a nonshockable rhythm, the lesser the chances of survival, suggesting that an enough duration of ischemia results in diminished response to resuscitation efforts or the irreversible loss of cellular energetics. Properly performed CPR results in improved cardiac output and appears to increase the time before irreversibility sets in, increasing the chance of survival [13–15].

ECPR plays the role of ROSC in the provision of vital organ perfusion. Upon cannulation and initiation of extracorporeal flow, perfusion of the brain, myocardium (in unobstructed coronary arteries), and splanchnic organs is immediately restored, and the post-resuscitation low-flow state is eliminated. Improvement in myocardial blood flow enhances the chance of myocardial recovery and return of a spontaneous rhythm or a shockable rhythm more responsive to defibrillation. Introduction of interventions becomes easier. With earlier achievement of adequate systemic perfusion, the risk of neurologic injury may be reduced despite delayed return of spontaneous rhythm. Moreover, therapeutic hypothermia can be promptly achieved and sustained. Coronary interventions are facilitated even if the patient remains in VF as stable perfusion has been achieved. Restoration of coronary perfusion may permit defibrillation or cardioversion of otherwise refractory VF or ventricular tachycardia. The success of ECPR relies on early initiation in a patient with the potential for myocardial recovery [8].

When to extracorporeal membrane oxygenation cardiopulmonary resuscitation?

As there are no prospective studies of ECPR, and no clearly identified selection and initiation criteria for its use in cardiac arrest, the American Heart Association recognizes that, at the present time, there is insufficient evidence to recommend the routine use of ECPR in cardiac arrest. ECPR may be considered when it is readily available, blood flow interruption is brief, and the underlying condition leading to arrest is believed to be potentially reversible [16,17].

A major determinant of outcome following cardiac arrest is the time to return of adequate perfusion. In conventional CPR, it is the time to ROSC, and in ECPR it is the time to initiation of ECLS flow. There are observational studies on the effect of the time to ROSC on survival following CPR but none following time to ECPR. In in-hospital cardiac arrest, nearly half of patients who had ROSC did so within 10 min of CPR and ~75% within 20 min, with 81% of those having ROSC within 15 min had good functional recovery [18]. In out-of-hospital cardiac arrest, ROSC occurred within 16 min in nearly 90% of those patients with good functional recovery. After 15 min, good functional recovery was only 2%. These data suggest that CPR should be considered refractory at 15 min. Implementation of ECPR should take place as soon as possible after this time. The target to complete the transition to ECPR is 30 min when possible and no more than 60 min [8].

The reversibility is more challenging. Although having a witnessed arrest is important in identifying the exact time of arrest and documentation of time to CPR, which should be within 5 min, a no-flow period of 10 min or more disfavors ECPR. Once CPR has been initiated, it should have been continuous and of good quality, preferably with a mechanical compression device. The etiology of arrest is a clear determinant of reversibility. In out-of-hospital cardiac arrest, the etiology and comorbidities are often unknown. A shockable rhythm suggests an ischemic event with retained myocardial viability and provides strong support for ECPR. A patient in pulseless electrical activity poses the most challenge. Patients with known major comorbidity are generally not candidates. Younger patients with a respiratory etiology for arrest and patients with suspected massive pulmonary embolism may be considered. Inpatients usually have a well-characterized diagnosis and known comorbidities. Patients experiencing in-hospital cardiac arrest with known or suspected acute coronary syndrome, suspected pulmonary embolism, or arrhythmia associated with acute ventricular failure who may be ventricular assist device or transplant candidates are candidates [8].

Technique and application of extracorporeal life support

The mode of support for ECPR is venoarterial to provide both circulatory support and gas exchange. Venoarterial support involves cannulation of the right atrium for venous drainage and the aorta or a large artery (femoral or carotid) for return to the arterial system. The heart and lungs are bypassed during ECPR, and the extracorporeal circuit, just like a heart lung machine, provides full cardiopulmonary support. Upon ROSC, systemic blood flow is the product of patient's native cardiac output and the extracorporeal flow.

Cannulation

Several cannulation approaches are available, with the choice dictated by the circumstances surrounding cardiac arrest. Cannulation can be central or peripheral. Peripheral cannulation is usually performed through the femoral vessels in adults and adolescents. The femoral approach is easily accessible during CPR. Cannulation of both the common femoral artery and femoral vein on the same side can be performed by a single operator, though for faster cannulation, two operators can cannulate one vessel on each side [8].

Either percutaneous or surgical cannulation can be performed. Experience and preferences of the operator dictate the choice between percutaneous or surgical approaches for femoral access, bearing in mind that a percutaneous access in the absence of pulses renders a percutaneous approach prone to complications. On the flip side, vascular ultrasound allows the identification of vessel anatomy and size to ensure success with percutaneous access. As a result, percutaneous access seems to be the preferred approach as it is faster, is associated with less bleeding complications, can be performed by non-surgeons (intensivists, emergency physicians, interventional cardiologists, and interventional radiologists), and does not require ligation of the artery [19,20]. A two-stage technique can be employed that may facilitate decision-making and cannulation. If there is no response to conventional resuscitation within 10 min, then cannulation of the femoral vessels using small vascular catheters can be initially performed. If further resuscitation attempts remain unsuccessful and ECPR is elected, then cannulation is facilitated by placing guide wires in the existing catheters [20].

Cannulas used in ECPR must be capable of the provision of enough flow to provide full circulatory support ($\geq$4 l/min in the adult). For percutaneous femoral venous cannulation, a 24–28-Fr cannula is long enough to reach the right atrium from the femoral insertion site. Adult femoral arterial cannulas are short and range from 16 to 18 Fr. Surgical cannulation of the femoral artery in all cases and percutaneous in many cases will result in distal limb ischemia, necessitating placement of an antegrade cannula into the superficial femoral artery that can support over 200 ml/min, usually 6–8 Fr in size. When surgical placement is chosen, the cannula size is often chosen based on the directly observed vessel size [8].

Extracorporeal life support decannulation

ECLS decannulation following successful return of adequate circulation depends on the cannulation approach. Surgically placed cannulas are removed by surgical cutdown and repair of the vessels. Percutaneous venous cannulas are simply withdrawn, with a horizontal mattress suture straddling the cannula to provide hemostasis. Percutaneous arterial cannula usually requires vessel repair, but withdrawal and manual pressure or a vascular occlusion device used for sizes up to 16 Fr. If the patient is cannulated centrally, decannulation requires an operative approach with closure of the sternotomy incision. Conversion to peripheral cannulation can be considered to reduce risk of infection and bleeding associated with central cannulation if long-term support is needed [8].

The extracorporeal circuit

The most widely adopted design for extracorporeal support, including ECPR, incorporates a centrifugal pump and hollow-fiber membrane lung. The circuit can be primed rapidly, and the centrifugal pump can provide a controlled negative inlet pressure enhancing venous drainage. Being afterload dependent, these pumps will not generate very high pressure in the event of an occlusion. Hollow-fiber membrane lungs have low transmembrane pressure drop with highly efficient gas exchange, supporting up to 400 ml/min or more of oxygen transfer. Adult hollow-fiber membrane lungs have rated flows on the order of 7 l/min, more than adequate for most applications. Pediatric membrane lungs have rated flows on the order of 3 l/min.

The extracorporeal circuit is primed with isotonic-balanced electrolyte solution for adults and pediatric patients in whom the extracorporeal circuit volume is no more than 30% of the patient's blood volume. Albumin is added by some centers to reduce osmotic shifts on initiation of support. Pediatric patients have higher extracorporeal circuit volumes relative to their blood volume and may require a blood prime owing to hemodilution or immediate transfusion to restore hematocrit. Circuits pre-primed with crystalloid solution only (no albumin or blood products) may be prepared ahead of time and stored for ready availability for ECPR [21].

Complications of extracorporeal life support

Bleeding is the most common complication associated with all forms of ECLS, including ECPR with the cannulation site being the most common and is greater following surgical cannulation placement. Cannulation site bleeding can usually be managed with topical thrombotic agents but may require surgical exploration. Systemic anticoagulation increases the risk of bleeding at other sites, including intracranial and gastrointestinal. In addition, ECPR involves the exposure to systemic anticoagulation. The risk of intracranial hemorrhage in ECPR is higher than in patients with ECMO support. Multiple factors may be responsible for this difference, for example, altered neurovascular unit, anticoagulation practices, cannulation strategies, microemboli, or inflammation [22].

During percutaneous insertion, vascular injury can result in failure to cannulate, vascular injury, loss of distal flow, arteriovenous fistulas, and retroperitoneal hematomas. ECPR is deployed under time-sensitive circumstances, and it could be expected to have a higher rate of complications. Several conditions can lead to failure to achieve adequate extracorporeal flow such as inadequate intravascular volume, inadequately sized cannulas (especially the venous cannula), or if the cannulas are incorrectly positioned. Ultrasound guidance during percutaneous insertion helps ensure proper intravascular placement. Fluoroscopic imaging is helpful for ensuring proper positioning but is generally not available during ECPR initiation but may be helpful once ECPR is initiated [8].

Outcomes following extracorporeal cardiopulmonary resuscitation

A finding in a recent ELSO report was that therapeutic hypothermia was used after about 60% of ECPR events [7]. Although the THAPCA trial denies additional benefit for targeted temperature control with hypothermia after a cardiac arrest over normothermia [23,24], there are no data yet for the benefit or risk of hypothermia induced during the resuscitation or ECPR. Some centers initiate ECPR at 34° centigrade and either maintain targeted temperature at 34°C or rewarm at 36–37.5°C based on the individual patient characteristics [22].

Once ECMO flow has been established, target flow rate and perfusion pressure should be discussed depending on patient's age and diagnosis. Cerebral and myocardial reperfusion may be associated with altered cerebral autoregulation and myocardial stunning; therefore, careful attention is required to maintain adequate cerebral perfusion. The ECMO specialists are trained to carefully increase circuit blood flow to target perfusion pressures, and to carefully titrate gas flow to avoid hypocapnia and hypercapnia, all in an effort to minimize secondary ischemia [22]. It is common for the myocardium to have electrical activity but with limited ejection after ECPR, and up to 48 h may elapse before effective ejection and pulse width on the arterial waveform ensue. It is also vital that the heart not to over distend, as this will lead to further myocardial injury from the elevated wall stress. The assessment of need for left ventricle decompression, either transcatheter or surgical, can be made clinically at the bedside and with echocardiography [22].

Getting started

Starting an ECLS program can be daunting. The first step is to achieve a concept at a senior administrative level that an ECPR program is a requirement and a fundamental safety net for select patient populations. Given the wealth of data available, there should be no need to prove 'value' nor to present data around a 'return on investment'. The equipment, resources, and training are expensive, but the value is in lives saved and in the fundamental support required to develop a contemporary resuscitation program, particularly in children undergoing cardiac surgery. The next step is to identify key stakeholders and their contributions to the ECPR program. Leaders should be chosen who have the responsibility and authority to direct all phases of the program. At a minimum, this includes the surgeons who will perform the cannulation, critical care clinicians, and perfusion or ECPR specialists who will manage the circuit. Settling on equipment and resources to provide ECPR is the next step. It may take 6 months to be prepared, and it is highly recommended that new programs contact and partner with established programs to help navigate all the steps required to establish an ECPR program. These partnerships are critical for sharing information and ideas, and for benchmarking outcomes. In addition, joining established registries, such as the ELSO, is recommended, as this will also provide important benchmarks against which success is measured [22].

Conclusion

ECPR is an emerging technology for the management of patients with cardiac arrest refractory to conventional CPR and resuscitative approaches.

Observational studies suggest that survival with good neurologic recovery may be better with ECPR than with conventional CPR. Consideration for ECPR is given to individuals with in-hospital or out-of-hospital witnessed cardiac arrest receiving good-quality sustained external chest compressions within 5 min of arrest, and in whom ROSC does not return within 15–30 min. Cannulation for ECPR should ideally occur within 30 min of arrest, with up to 60 min considered. A potentially reversible cause of cardiac arrest should be identified, such as a shockable rhythm for out-of-hospital cardiac arrest or a known reversible cause for in-hospital arrest. Both children and adults are candidates for ECPR. Further studies are needed to better define its role and application; however, at the present time, ECPR should be considered in appropriate patients in hospitals where ECLS programs exist.

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Conflicts of interest

There are no conflicts of interest.

References

1 O'Rourke PP, Crone RK, Vacanti JP, Ware JH, Lillehei CW, Parad RB, *et al.* Extracorporeal membrane oxygenation and conventional medical therapy in neonates with persistent pulmonary hypertension of the newborn: a prospective randomized study. Pediatrics 1989; 84:957–963.

2 Edwards MO, Kotecha SJ, Kotecha S. Respiratory distress of the term newborn infant. Paediatr Respir Rev 2013; 14:29–37.

3 Meliones JN, Custer JR, Snedecor S, Moler FW, O'Rourke PP, Delius RE. Extracorporeal life support for cardiac assist in pediatric patients.Review of ELSO Registry data. Circulation 1991; 84(Suppl):III168–II I172.

4 O'Rourke PP, Stolar CJ, Zwischenberger JB, Snedecor SM, Bartlett RH. Extracorporeal membrane oxygenation: support for overwhelming pulmonary failure in the pediatric population.Collective experience from the extracorporeal life support organization. J Pediatr Surg 1993; 28:523–528; [discussion 528-9].

5 Noah MA, Peek GJ, Finney SJ, Griffiths MJ, Harrison DA, Grieve R, *et al.* Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A (H1N1). JAMA 2011; 306:1659.

6 Richardson ASC, Schmidt M, Bailey M, Pellegrino VA, Rycus PT, Pilcher DV. ECMO Cardio-Pulmonary Resuscitation (ECPR), trends in survival from an international multicentre cohort study over 12-years. Resuscitation 2017; 112:34–40.

7 Thiagarajan RR, Barbaro RP, Rycus PT, Mcmullan DM, Conrad SA, Fortenberry JD, *et al.* Extracorporeal Life Support Organization Registry International Report 2016. ASAIO J 2017; 63:60–67.

8 Conrad S, Rycus P. Extracorporeal membrane oxygenation for refractory cardiac arrest. Ann Card Anaesth 2017; 20:S4–S10.

9 Donoghue AJ, Nadkarni V, Berg RA, Osmond MH, Wells G, Nesbitt L, *et al.* Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. Ann Emerg Med 2005; 46:512–522.

10 Niemann JT. Differences in cerebral and myocardial perfusion during closed-chest resuscitation. Ann Emerg Med 1984; 13:849–853.

11 Herlitz J, Engdahl J, Svensson L, Ängquist KA, Young M, Holmberg S. Factors associated with an increased chance of survival among patients suffering from an out-of-hospital cardiac arrest in a national perspective in Sweden. Am Heart J 2005; 149:61–66.

12 Carew H, Zhang W, Heart TR. Chronic Health Conditions and Survival following Out-of-Hospital Ventricular Fibrillation Cardiac Arrest. Heart 2007; 93:728–731.

13 Andersen LW, Berg KM, Saindon BZ, Massaro JM, Raymond TT, Berg RA, *et al.* Time to epinephrine and survival after pediatric in-hospital cardiac arrest. JAMA 2015; 314:802.

14 Idris AH, Guffey D, Aufderheide TP, Brown S, Morrison LJ, Nichols P, *et al.* Relationship between chest compression rates and outcomes from cardiac arrest. Circulation 2012; 125:3004–3012.

15 Wallace SK, Abella BS, Becker LB. Quantifying the effect of cardiopulmonary resuscitation quality on cardiac arrest outcome. Circ Cardiovasc Qual Outcomes 2013; 6:148–156.

16 Thiagarajan RR. Extracorporeal membrane oxygenation to support cardiopulmonary resuscitation: useful, but for whom? Crit Care Med 2011; 39:190–191.

17 Cave DM, Gazmuri RJ, Otto CW, Nadkarni VM, Cheng A, Brooks SC, *et al.* Part 7: CPR Techniques and Devices: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010; 122(Suppl 3): S720–S728.

18 Goldberger ZD, Chan PS, Berg RA, Kronick SL, Cooke CR, Lu M, *et al.* Duration of resuscitation efforts and survival after in-hospital cardiac arrest: an observational study. Lancet 2012; 380:1473–1481.

19 Conrad SA, Grier LR, Scott LK, Green R, Jordan M. Percutaneous cannulation for extracorporeal membrane oxygenation by intensivists. Crit Care Med 2015; 43:1010–1015.

20 Bellezzo JM, Shinar Z, Davis DP, Jaski BE, Chillcott S, Stahovich M, *et al.* Emergency physician-initiated extracorporeal cardiopulmonary resuscitation. Resuscitation 2012; 83:966–970.

21 Weinberg A, Miko B, Beck J, Bacchetta M, Mongero L. Is it safe to leave an ECMO circuit primed? Perfusion 2015; 30:47–49.

22 Laussen PC, Guerguerian AM. Establishing and sustaining an ECPR program. Front Pediatr 2018; 6:152.

23 Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, *et al.* Therapeutic hypothermia after out-of-hospital cardiac arrest in children. N Engl J Med 2015; 372:1898–1908.

24 Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, *et al.* Therapeutic hypothermia after in-hospital cardiac arrest in children. N Engl J Med 2017; 376:318–329.