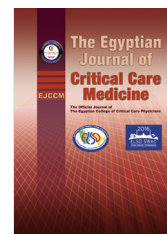The Egyptian College of Critical Care Physicians

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ORIGINAL ARTICLE

Extracorporeal cardiopulmonary resuscitation

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Abstract ECPR is defined as the rapidly-deployed application of venoarterial extracorporeal membrane oxygenation, in patients with cardiac arrest, during cardiopulmonary resuscitation before the return of ROSC. ECPR is one of the most rapidly growing segments of ECLS, and is becoming more widespread. Consideration for institution of ECPR is given to patients with witnessed arrest, good quality CPR instituted within 5 min of arrest, in whom ROSC does not occur within 15 min, and who can complete cannulation within 30–60 min. Patients from both inpatient and out-of-hospital settings are candidates if they meet these criteria. Deep hypothermic cardiac arrest, such as cold-water drowning, should receive consideration for ECPR even after considerable duration of arrest. Available outcome data are based on retrospective observation studies, some with propensity matching, and suggests a higher chance for survival with ECPR. Published outcomes from ECPR, however, are difficult to interpret, since many centers classify their use of ECLS after ROSC, in addition to ECLS before ROSC, as ECPR. Both children and adults are candidates for ECPR, but the experience in children is weighted heavily toward those with a diagnosis of cardiac disease and arrest occurring within closely monitored units.

1. Introduction

Extracorporeal cardiopulmonary resuscitation (ECPR) refers to the use of rapid-deployment venoarterial extracorporeal membrane oxygenation to provide circulatory support during cardiac arrest, when conventional CPR has failed to provide return of spontaneous circulation (ROSC) [1,2], or when repetitive arrests occur without sustained ROSC. Venoarterial (VA) ECMO is the required mode of support since cardiac output is absent or at best inadequate and intermittent. ECPR has sometimes been used to refer to extracorporeal support of low cardiac output states following ROSC, but the Extracorporeal Life Support Organization (ELSO) does not include this scenario in its definition of ECPR [2].

ECPR is one of the most rapidly growing segments of ECLS as reported to the ELSO Registry. In the interval 2012 through 2015 there were 869 neonatal, 1106 pediatric, and 1337 adult cases reported. This number underrepresents

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the actual number, as a number of centers performing ECPR are not ELSO centers and are not reporting their data.

2. Rationale

Several factors have been associated with survival following cardiac arrest [3–10]. Included are the initial rhythm and whether it is shockable, and the presence of comorbidities, which may be related to initial rhythm. The time to initiation of external chest compressions, and the adequacy of those compressions are both important factors. The time to defibrillation in the presence of a shockable rhythm and the time to return of spontaneous circulation (ROSC) are also major determinants.

ECPR has the potential to modify some of these factors, although data are lacking to demonstrate any direct influence. The institution of support provides definitive and immediate return of circulation, albeit not spontaneous, thereby providing adequate organ perfusion not possible with CPR. Improved perfusion of the myocardium may allow success at defibrillation, or elimination of myocardial hypoxemia that may have led to non-shockable rhythms, thereby allowing return of myocardial function. External circulation can permit rapid institution of hypothermia during the resuscitation phase, greatly reducing exposure to higher temperatures at the time of reperfusion.

3. Patient selection

In the adult population, there is sufficient experience with ECPR to provide guidance for selecting patients who may benefit [11]. As new data accumulate, it is likely that criteria for consideration will change. One of the difficult decisions to make is when to consider conventional resuscitation measures inadequate and an indication to initiate ECPR. Too early implementation would lead to application in many patients who would have recovered conventionally, whereas too late implementation could lead to application beyond the period of reversibility. The rate of ROSC decreases with time, with half or more of patients recovering from in-hospital and out-of-hospital cardiac arrest within 10–15 min, and the great majority within 20 min [12,13]. The target to initiation of support would be ideally 30 min, but no more than 60 min, from onset of conventional resuscitation. Beginning the decision-making within 10 min and completing by 15 min would allow identification of patients with low chance of ROSC with conventional means and allow for ECPR within the allowable time limits [11].

The arrest should be witnessed, and the duration of no-flow prior to resuscitation efforts should be less than 5 min. Good-quality CPR should have been provided at all times, which may best be performed with properly adjusted mechanical compression devices. Additional considerations include the presence of comorbidities, especially cardiovascular, and the pre-arrest functional status. Patients sustaining cardiac arrest in both the inpatient and out-of-hospital setting should be considered.

ECPR is now the treatment of choice for deep hypothermic (< 20 °C) cardiac arrest refractory to conventional resuscitation efforts. Variance on the times to conventional CPR and time to ECPR can be afforded these patients, since experience suggests good outcomes with therapy delayed to as long as 226 min [14].

4. Technical considerations

As a rapidly-deployed procedure, ECPR programs benefit from simplified pre-primed circuits positioned in a strategic location, trained individuals to perform percutaneous or surgical cannulation, and a cross-discipline organization structure supported by defined protocols.

5. Extracorporeal circuit

Centrifugal pump systems with hollow-fiber membrane oxygenators have numerous advantages that make them most suitable for ECPR. These components can be quickly primed and have reasonably small priming volumes. The centrifugal pump is afterload-dependent, and circuit rupture is non-existent when properly assembled and operated, eliminating the need for pre- and post-pump pressure monitoring. The pump provides a controlled inlet pressure, allowing augmented venous return without the need for gravity-facilitated hydrostatic pressure, allowing the pump to be positioned close to the patient. Hollow-fiber membrane oxygenators prime quickly without residual deadspace.

The size of the extracorporeal circuit depends on patient size. Circuits with ¼″ tubing size are used for pediatric circuits for body weights up to about 15 kg. Larger children and adults are managed with ⅜″ tubing size circuits. Centrifugal pumps currently are available in one size with ⅜″ inlet and outlet ports, and require downsizing for pediatric circuits. Membrane oxygenators are available in adult (⅜″ connector), and pediatric (¼″ connector) sizes, with some manufacturers providing a neonatal size. The membrane oxygenator should have a rated flow at least 1.5 times the expected maximum flow for the patient.

The use of pre-primed circuits eliminates any time lost to priming at the time of cardiac arrest. Circuits primed with crystalloid alone (free of glucose, protein and blood products) have been shown to be infection free for 14 days [15] and up to 30 days [16]. It is likely that longer durations of storage are safe, but data are lacking. A potential approach to prolonged storage is to sample the circuit for bacterial antigens or culture at intervals and discard the circuit if contamination is found. Although microporous hollow-fiber membrane oxygenators lose some function after pre-priming [17], modern nanoporous "plasma tight" hollow-fiber membrane oxygenators do not appear to lose any functional capacity when stored for 2 weeks [18], and there does not appear to be any leaching of plasticizers into the prime [19].

The introduction of small-footprint, portable, integrated ECLS systems has streamlined the initiation of ECLS, and has demonstrated functionality during transport [20] and in-hospital support [21].

6. Cannulation

The cannulation sites for arteriovenous support in the adult depend on the circumstances surrounding resuscitation. Patients in the emergency department or hospital ward who are not post-op cardiac patients will usually undergo

cannulation of the femoral vessels. Unilateral femoral cannulation is frequently used when one clinician is performing both cannulations. When two clinicians are available, then each can cannulate on a different side without interference, reducing the time to cannulation. An advantage of the femoral site is that it does not interfere with external chest compressions.

The choice between percutaneous and surgical approaches to the femoral vessels is largely dependent on the skill and preference of the clinician. Percutaneous cannulation can be performed quickly, but in the absence of spontaneous circulation, identification of vessel location and size is problematic, and the failure rate may be higher. The use of ultrasound may mitigate these issues, but adds to the procedure time. In settings where percutaneous cannulation is limited to surgeons who may not be in the department, the placement of small vascular catheters by non-surgeons can reduce the time to complete cannulation with the larger ECMO cannulae [22]. Surgical cannulation allows ready identification of vessel anatomy, but limits the procedure to surgeons who may not be readily available. This approach is typically limited to institutions with full-time availability of surgical staff. The surgical approach is also the only option for failed percutaneous cannulation.

Cannula size is chosen to provide an extracorporeal flow of 4–5 L/min, sufficient to maintain full circulatory support. The venous cannula must be large enough to accommodate flow at pressure gradients of 50 mmHg, typically 24–28 Fr. Arterial cannulae are necessarily smaller due to femoral artery size, and range from 16 to 19 Fr. When placed surgically, the femoral artery is ligated, and a 6–8 Fr. antegrade cannula must be added to the reinfusion limb of the circuit to prevent limb ischemia and loss. An antegrade cannula is commonly required after percutaneous cannulation, but can also be placed percutaneously.

Postoperative cardiac patients in the intensive care unit may be candidates for central cannulation. The incision and sternum can be reopened, with cannulation of the right atrium and aorta. Support can continue through the open chest, and if recovery is adequate, decannulation can be performed. If support will be of a longer duration, conversion to peripheral cannulation is desirable to reduce infectious and bleeding complications. Central cannulation outside the operating suite requires prior planning with adequate equipment and resources available in the unit.

7. Complications

As with extracorporeal support for any indication, ECPR is associated with the risk of complications ranging from minor to fatal. ECPR is instituted as rapid-deployment venoarterial ECMO, with the risk of vascular injury leading to failure to cannulate or to bleeding complications. Failure to maintain adequate flow can lead to suboptimal support and non-survival. Intracranial hemorrhage is a serious complication which can greatly decrease chance of survival. Reperfusion injury can contribute to multiple organ failure, sepsis and neurologic injury.

8. Outcomes

The use of ECPR in adults is increasing significantly, with more patients reported to the ELSO Registry in the past 3 years than all previous years combined. The reported cumulative survival is 29% [23]. Although not high, it is likely that the majority of the patients would not have survived otherwise. Survival in single center studies is reported to be higher.

In a meta-analysis of 11 observational studies of adult ECPR in the inpatient setting, the overall survival to discharge was 40% [24]. The definition in this study included post-ROSC ECLS. When restricted to pre-ROSC ECLS, the survival was 48%, with a pre-ECLS time of 40 min. Shorter pre-ECLS time was associated with 1.9 odds of survival compared to the whole group. A prospective observational study of ECPR compared with conventional CPR using propensity matching in 172 patients with in-hospital arrest revealed a higher survival to discharge, as well as 30-day and 1-year survival [25]. In a recent retrospective analysis of conventional CPR compared with ECPR in 353 patients with in-hospital cardiac arrest, ECPR was associated with improved short-term and long-term survival [26].

Deep hypothermic cardiac arrest managed with ECPR appears to have a better prognosis than standard extracorporeal rewarming, preventing death from cardiopulmonary complications associated with lung reperfusion [27]. In this series of 59 patients, 25 treated with ECPR survived, a 6.6-fold increase over standard rewarming.

The application of ECPR in the pediatric population is dominated by its use in patients with congenital heart disease in the inpatient setting. A study of children and infants with heart disease based on the ELSO Registry analyzing 492 patients demonstrated a 42% survival, with predictors for mortality including single ventricle physiology, prior Stage 1-type procedure, and extreme acidosis [28]. It is unclear if this cohort included patients who may have received post-ROSC support that was classified as ECPR, as the ELSO Registry does not enforce this definition. A report from the Hospital for Sick Children on 80 children receiving ECPR indicated a 30% survival with favorable neurologic outcome [29]. Nearly 90% of this group had a cardiac diagnosis. A survival rate of 73% with grossly normal neurologic function was reported in a cohort of 32 patients in a retrospective study, in a group of patients of whom 82% were cardiac patients [30]. In a cohort of 31 patients with predominantly cardiac disease, 23% survival with good function was reported [31]. This group found no relationship between duration of CPR prior to ECPR and outcome.

In a mixed group of 54 pediatric inpatients with both cardiac and non-cardiac causes analyzed retrospectively, a survival of 46% was reported [32]. The survival rate for cardiac and non-cardiac causes were approximately equal, with 44% of non-cardiac causes surviving.

9. Ethical and cultural considerations

Introduction of extracorporeal circulation into resuscitation from cardiac arrest poses new potential issues of an ethical nature. These issues relate to decisions on both initiation and termination of support. The basic principles of autonomy, beneficence, non-maleficence and justice become more complex during extracorporeal resuscitation efforts. The patient usually has not provided any information about his or her right to refuse treatment, and decisions are usually made in urgency by the healthcare team. While data are accumulating

regarding the benefits of ECPR versus conventional CPR, we still don't have clear guidance. We usually don't have the ability to identify futility prior to ECPR, and we have a technology that can artificially support life until terminated. As a resource limited in availability, we are unable to provide ECPR equally to all patients who may potentially benefit.

While we now rely on guidance from the application of conventional CPR to help with decisions on introducing ECPR, new challenges with ECPR are emerging. For example, there is the potential for irreversible neurologic injury to develop while being supported on ECPR. In countries that do not recognize brain death, this can pose ethical dilemmas. There is also the possibility of a patient recovering neurologic function following ECPR, but without recovery of cardiac function or candidacy for transplantation. Withdrawal of support in this case is now a very different scenario since the patient can participate in decision making [33], but was not a participant when ECPR was initiated.

10. Summary

ECPR is defined as the application of venoarterial extracorporeal membrane oxygenation, in patients with cardiac arrest, during cardiopulmonary resuscitation before the return of ROSC. The technique is technically challenging but feasible. Consideration for institution of ECPR is given to patients with witnessed arrest, good quality CPR instituted within 5 min of arrest, in whom ROSC does not occur within 15 min, and who can complete cannulation within 30–60 min. Available outcome data are based on retrospective observation studies, some with propensity matching, and suggest a higher chance for survival with ECPR. Published outcomes from ECPR, however, are difficult to interpret, since many centers classify their use of ECLS after ROSC, in addition to ECLS before ROSC, as ECPR. Both children and adults are candidates for ECPR, but the experience in children is weighted heavily toward those with a diagnosis of cardiac disease and arrest occurring within closely monitored units.

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