

REVIEW ARTICLE

The Practice of Emergency Medicine

The state of emergency department extracorporeal cardiopulmonary resuscitation: Where are we now, and where are we going?

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Abstract

Extracorporeal cardiopulmonary resuscitation (ECPR) has emerged in the context of the emergency department as a life-saving therapy for patients with refractory cardiac arrest. This review examines the utility of ECPR based on current evidence gleaned from three pivotal trials: the ARREST trial, the Prague study, and the INCEPTION trial. We also discuss several considerations in the care of these complex patients, including prehospital strategy, patient selection, and postcardiac arrest management. Collectively, the evidence from these trials emphasizes the growing significance of ECPR as a viable intervention, highlighting its potential for improved outcomes and survival rates in patients with refractory cardiac arrest when employed judiciously. As such, these findings advocate the need for further research and protocol development to optimize its use in diverse clinical scenarios.

KEYWORDS

cardiac arrest, extracorporeal cardiopulmonary resuscitation, extracorporeal life support, extracorporeal membrane oxygenation, resuscitation

1 | INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) continues to be a leading cause of morbidity and mortality with approximately 313,000 deaths annually in the United States and 4–5 million worldwide.^{1,2} Even with efforts to implement high-quality chest compressions^{3,4} and cardiac defibrillation⁵ interventions repeatedly associated with improved outcomes, neurologically intact survival remains extremely poor in patients with refractory cardiac arrest, often failing to surpass 10%.^{6,7} As a result of these stagnant outcomes,⁸ there is growing interest in the application of extracorporeal membrane oxygenation (ECMO) as a means to restore systemic circulation.⁹ The use of ECMO in this setting is referred to as extracorporeal cardiopulmonary resuscita-

tion (ECPR). ECPR can be and has been performed throughout the hospital¹⁰ or prehospital setting;¹¹ ECPR most recently came to the forefront in the context of the emergency department (ED),^{12,13} where it became known as ED ECMO.¹⁴ Although the use of ECPR may also include noncardiac arrest etiologies—acute respiratory distress syndrome, severe refractory hypercapnia, and massive pulmonary embolism—the predominant use of ECPR is in the setting of cardiac arrest. Compared with conventional advanced life support (ALS) therapies, ECPR has increased survival rates from 10 to 30% at high volume programs in select trials.^{15–17} In addition to stable and augmented perfusion, ECPR allows for the cessation of external chest compressions, which in turn decreases trauma, stress, and frequent interruptions.^{18–23}

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TABLE 1 Trial characteristics and outcomes.

	ARREST	Prague OHCA	INCEPTION
ECPR/invasive group	15	124	70
CCPR group	15	132	64
Age (mean, SD)	59 (10)	57 (14)	55 (11)
Male sex (%)	25 (83%)	212 (83%)	39 (29%)
Primary rhythm:			
VT/VF	30 (100%)	156 (61%)	132 (99%)
PEA	0	45 (17%)	NA
Asystole	0	55 (22%)	NA
Bystander CPR (%)	25 (83%)	252 (98%)	130 (97%)
Defibrillation attempts (prehospital, mean, SD)	6 (3)	4 (3)	9 (6)
Mechanical CPR (%)	30 (100%)	218 (85%)	120 (90%)
Lactate on admission (mmol/L, mean, SD)	11.1 (3.8)	11.5 (4.9)	13.5 (4.6)
pH on admission (mean, SD)	6.95 (0.11)	6.99 (0.23)	6.92 (0.17)
Cannulation location	Cardiac catheterization laboratory	Cardiac catheterization laboratory	Emergency Department
Cannulator specialty	Interventional cardiology	Interventional cardiology	Surgery, interventional cardiology, intensivists
Time from 911 to VA ECMO initiation (min, mean, SD)	59 (28)	62.0 (11.3)	74.7 (18.2)
Six-month survival (CPC 1–2) ^a			
ECPR/invasive group	6 (43%)	39 (32%)	14 (20%)
CCPR group	0	29 (22%)	10 (16%)

Abbreviations: CCPR, conventional cardiopulmonary resuscitation; ECPR, extracorporeal membrane oxygenation; PEA, pulseless electrical activity; VT, ventricular tachycardia; VF, ventricular fibrillation.

^aCPC 1–2 applicable to only the Prague and INCEPTION trials.

Achieving sustained programmatic success in the application of ECPR, however, is extremely complex, relying on a multidisciplinary effort to minimize time spent in a low-flow state.^{14,23} From prehospital organization,^{24,25} procedural expertise,²⁶ and postresuscitation management,²⁷ it is an intricate framework that demands meticulous attention to detail. With the ED playing a central role in the care of these patients,²⁸ this review article looks to summarize the application of ECPR, including its current evidence, implementation, and inherent risks and benefits. We also characterize a potential future of ECPR.

2 | EVIDENCE BEHIND ECPR

Coupled with the increasing interest in ECPR is a growing body of evidence assessing its efficacy. There are now several randomized control trials (RCTs) evaluating the therapeutic effect of ECPR in refractory OHCA patients. Notably, these include: the Advanced Reperfusion Strategies for Patients with OHCA and Refractory Ventricular Fibrillation Trial (ARREST),¹⁶ the Prague OHCA study,¹⁵ and the Early

Initiation of Extracorporeal Life Support in Refractory OHCA Trial (INCEPTION).²⁹ A summary of these trials is shown in Table 1.

In 2020, Yannopoulos et al¹⁶ performed a single-center trial, randomizing patients with refractory cardiac arrest due to ventricular fibrillation or pulseless ventricular tachycardia (VF/VT), to either ECPR or conventional cardiopulmonary resuscitation (CCPR). Patients in the ECPR arm received bundled protocol care, including mechanical CPR, and postcannulation coronary catheterization and temperature control.¹⁶ The results of the ARREST trial demonstrated that patients treated with ECPR had improved survival to hospital discharge of 43%, compared with 7% in the control, CCPR group. Enrollment was stopped early after 30 patients had been enrolled by the data safety monitoring board on the basis of significantly improved survival in the ECPR group.

The Prague OHCA study, also a single-center RCT, enrolled 256 patients with OHCA who were randomized between a “hyperinvasive” approach and standard care.¹⁵ The hyperinvasive group likewise received bundled care, including early transport to an ECPR-capable hospital, use of mechanical CPR during transport, and early evaluation for ECPR upon hospital arrival. Distinct from the ARREST trial,

Prague OHCA also included patients with nonshockable rhythms. Of note, due to the duration of time from prehospital randomization to coronary catheterization laboratory cannulation, of the 124 patients enrolled in the hyperinvasive strategy, only 66% were cannulated for ECPR. Twenty-seven percent of the patients randomized to the ECPR arm had achieved sustained ROSC upon admission prior to ECPR cannulation. The primary outcome of neurologically intact survival at 180 days was 31.5% in the ECPR arm versus 22% in the standard arm ($p = 0.02$). Interestingly, the survival rate in the control group was nearly twice as high compared with the existing literature and experiences. Despite the 10% survival benefit seen in the ECPR arm, the trial was stopped early for futility when the prespecified between-group difference of 15% was not maintained; this failure can be attributed in part to unplanned crossover ($n = 20$) and exclusion from ECPR cannulation in the ECPR arm ($n = 34$).

Finally, the INCEPTION trial was a multicenter RCT based in the Netherlands, which enrolled 134 patients with a primarily shockable rhythm (VT/VF) who failed to achieve sustainable ROSC within 15 min of ALS.²⁹ Patients were randomized 1:1 to ECPR versus conventional CPR. Neurologically intact survival (CPC 1–2) was not significant between groups (14, ECPR vs. 10, CCPR; $p = 0.518$).

Seemingly, all three trials studied the same invasive intervention, each, however, yielded distinct results, and each trial was conducted in different regions of the world, with different cannulator specialties, contributing to some uncertainty regarding the efficacy of ECPR.³⁰ Despite evaluating similar primary outcomes, the results of each trial demonstrate the differences in the functional implementation of ECPR within a given system. For instance, the ARREST trial aimed to evaluate the efficacy of ECPR in a highly specific patient population with a small team of experienced cannulators at a single center. Both the Prague OHCA study and INCEPTION trial were generally considered more pragmatic. Prague included nonshockable initial rhythms, which are known to have lower survival for OHCA.⁸ Cannulation success was lower in INCEPTION, with a rate of successful cannulation of 88% (46 out of 52) among patients in whom cannulation was attempted. Further, 56% of patients were cannulated in the ED (as opposed to the coronary catheterization laboratory [ARREST and Prague]), with the others in the Intensive Care Unit. These differences highlight the importance of the question of ECPR effectiveness when applied to a more real-world setting. Enrollment of patients with nonshockable rhythms (ie, asystole and pulseless-electrical activity) (eg, Prague study) as well as inclusion of multiple centers with inherent variation in ECPR practice, including less protocolized postcannulation care (eg, INCEPTION), demonstrate the effect of a less tightly controlled use of ECPR. Last, it is worth noting that the length of stay was 2 days for patients receiving ECPR in the INCEPTION trial, potentially indicating that care was withdrawn early due to unfavorable neurological outcomes. Although this is a common practice,³¹ influenced by the difficulty waiting for eventual neurologic outcomes,²³ it is worth noting that guidelines recommend neuroprognostication be delayed at least 72 h following cardiac arrest.³²

3 | ECPR IMPLEMENTATION

Despite the appearance of the diverging outcomes amongst the three RCTs as outlined above, a common theme does emerge: ECPR is an inherently complex intervention, where success is dependent on patient selection, proficient proceduralists, and a highly organized systematic approach. Nonetheless, even under the most ideal circumstances when these parameters are achieved, implementation of ECPR for refractory OHCA does not necessarily guarantee positive outcomes. Below we outline some of the fundamental considerations when implementing an ECPR program.

3.1 | Scene transport

Integrating an ECPR program into an existing Emergency Medical Services (EMS) system poses several unique challenges. In recent years, the prevailing prehospital culture for patients with OHCA prioritized on-scene resuscitation.³³ Although more recent analyses have called this into question,³³ if patients are indeed intended for ECPR, minimization of low-flow time needs to be a primary motivator of prehospital care.²⁵ EMS professionals should prioritize rapid transport of refractory OHCA patients to an ECPR-capable center.²⁴ With a sharp decline in favorable neurological outcomes after 30 min following cardiac arrest, it is clear that every minute counts.³⁴ Mean on-scene times for EMS in the ARREST and INCEPTION trials were 23 and 13 min, respectively.^{16,29} On-scene times such as these are achieved by establishing a “load and go” policy wherein, after no more than three defibrillations, if ROSC is not achieved, EMS should transport to an ECPR capable center.

Although on-scene and transportation durations contribute to the total duration of low-flow, so too does the in-hospital time, including the time for cannulation. Despite having the shortest prehospital time, the mean low-flow time in the INCEPTION trial was 74 min, which is longer than that in the ARREST trial and Prague OHCA study (59 and 61 min, respectively).^{15,16,29} Although factors of the time differential between these trials are many, the cannulators in both the ARREST and Prague Trials had performed over 100 cannulations previously,³⁵ in contrast to the INCEPTION trial, where the cannulators had performed less than 50 cannulations at each participating center.²⁹ Achieving mastery in ECPR cannulation demands a comprehensive understanding of vascular anatomy, meticulous hand-eye coordination, and an ability to work swiftly under high-pressure and technically challenging circumstances. Skillful ECPR cannulation requires the practitioner to navigate through layers of tissue and vessels with utmost precision to ensure optimal blood flow and avoid complications such as vessel perforation or thrombosis. As ECPR serves as a last resort for patients unresponsive to conventional resuscitation methods, procedural proficiency in cannulation becomes a pivotal factor in enhancing patient outcomes and increasing the chances of successful resuscitation and subsequent recovery.

3.2 | Cannulators and cannulation location

As of 10 years ago, there was considerable heterogeneity amongst health care professionals who were performing cannulation.³⁶ Cardiothoracic surgeons are the primary cannulators in a majority of ECPR centers in the United States; however, emergency physicians, intensivists, vascular surgeons, and interventional cardiologists are amongst that contingency as well.³⁶ This diversity of cannulators is represented in the recent trials. In the INCEPTION trial, surgeons, interventional cardiologists, and intensivists all performed cannulation, whereas in the ARREST and Prague study, interventional cardiologists were the cannulators. The EROCA ECPR feasibility trial utilized emergency physicians.²⁵ This varied composition of cannulators highlights a central staffing challenge. As we know from surgical literature, surgeon volume correlates with good outcomes.^{37,38} If this is extrapolated to ECPR cannulation, then how do we ensure sufficient procedural volume for any one proceduralist given the low volumes of ECPR?²⁷ If we want to ensure any one proceduralist is not overly worked, we need multiple capable proceduralists for 24/7 coverage, but this in turn leads to lower volumes for each cannulator. A second challenge is to determine the ideal location for cannulation: the ED, cardiac catheterization laboratory, the operating room, intensive care unit, or even in the prehospital setting? At this time, there are no studies that directly assess the ideal *specialty* or *location* to perform ECPR. In the above-mentioned trials, the primary location for cannulation was either in the ED or cardiac catheterization laboratory. Each location has benefits and limitations. The operating room has more resources, but these may not be needed for most patients and requires a greater effort to get patients there. Most advanced fluoroscopically capable locations such as the coronary catheterization laboratory add the benefit of being able to perform coronary angiography in addition to fluoroscopic confirmation of vascular access and assessment for vascular injury but are limited in that few interventional cardiologists routinely manage cardiac arrest resuscitations, and again the location requires more effort to get patients there. The ED is the easiest to get to, but may not have the resources of the other locations. The goal is to have an integrated process where additional ancillary staff and resources are available and the team has practiced this exercise to near perfection.

One potential solution that maintains high volumes for a given cannulator, but limits the demands on them overall is to limit the number of cannulators and also limit the time of day during which ECPR is offered. An analysis of in-hospital ECPR has previously showed that ECPR was preferentially offered during daytimes and weekdays³⁹ and was associated with improved outcomes during that time,¹⁰ despite the observation that cardiac arrests occurred equally throughout the hours and days.

3.3 | Patient selection

Patient selection is an essential process that involves identifying individuals who could potentially benefit from this salvage therapy. The

selection criteria usually encompass several factors: age, presenting rhythm, delivery of bystander CPR, total low flow time, underlying health conditions, and etiology of cardiac arrest.^{14,16} The strictness with which these factors are applied will have a broad impact on case volume, ability to maintain expertise, observed survival rates, as well as cost and resource utilization. As a general rule, the more limited the entry criteria are, the higher the observed survival. However, each institution must ultimately tailor their ECPR program to meet the needs of their community with their available resources.

3.4 | Postarrest management

The final link in the chain of resuscitation is postcardiac arrest management.⁴⁰ Optimally multifaceted, postarrest management should further optimize care by immediately treating the underlying arrest etiology while simultaneously addressing the injurious pathophysiological effects from a low-flow state.⁴¹ Percutaneous coronary intervention (PCI) is arguably required for ECPR with initial shockable rhythms, if not also in cases where noncoronary causes of arrest can be excluded. Acute thrombotic occlusive coronary lesions, with or without ST elevation on EKG, are leading causes of sudden OHCA with initial shockable rhythms.⁴² Although the COACT trial demonstrated that immediate PCI in initial nonshockable rhythm OHCA was not beneficial,⁴³ ECPR patients by definition have refractory arrest at the time of cannulation, making them distinct in this regard from the patients in the COACT trial who achieved ROSC. Studies suggest that PCI after ECPR is strongly associated with adjusted survival,²⁷ thus, until proven otherwise, it can be argued that patients with refractory arrest characteristic should be considered for immediate coronary angiography if other causes cannot be excluded.⁴¹

Beyond coronary angiography, other sudden cardiac arrest etiologies that can be diagnosed and treated once ECMO support has been established include: acute pulmonary embolism, tamponade, toxins and medication overdoses.⁴⁴ Although respiratory failure—hypercapnic or hypoxic—will improve on an extracorporeal circuit, patients who progress to cardiac arrest due to these causes have likely sustained prolonged periods of hypoventilation and/or hypoxemia that can cause irreversible cerebral injury. Thus, although venovenous cannulation in patients with respiratory failure prior to cardiac arrest may be warranted, even in the ED,⁴⁵ using ECPR for a respiratory arrest is probably not the best use of this resource and may be less likely to result in neurologic survival.

4 | RISKS AND BENEFITS

Given its complex and invasive nature, there are inherent risks and potential complications that must be considered when utilizing ECPR. One major concern is the risk of bleeding and coagulopathy, often worsened by the use of anticoagulation during cannulation and exposure to the extracorporeal circuit.⁴⁴ Vascular complications, including perforation or dissection, can lead to hemorrhage or occlusion, poten-

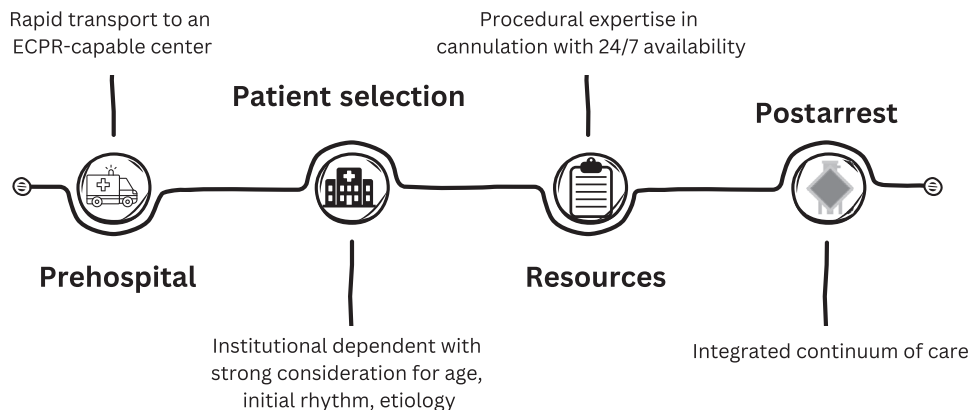


FIGURE 1 Considerations for extracorporeal membrane oxygenation (ECPR) in patients with refractory out-of-hospital cardiac arrest (OHCA).

tially resulting in limb ischemia.⁴⁶ Additionally, there is the possibility of clot formation and systemic embolization within the extracorporeal circuit, which can impede blood flow to vital organs. Furthermore, ECPR patients can experience multisystem organ failure from prolonged hypoperfusion in addition to the trauma from external chest compressions.⁴⁷⁻⁴⁹ Neurologic injury is also a common life-limiting problem,⁵⁰ requiring early and ongoing neuroprognostication.

Indirect risks, such as cost and resource utilization, must also be considered. Hospital length of stay is variable,⁵¹ influenced in aggregate by early withdrawal of care³¹ and the burden of comorbid injuries sustained.^{49,51} In the ARREST trial, this includes an average of 10 days to extubation, 22 days in the intensive care unit, and 26 days total in the hospital. Survivors will also frequently require intensive rehabilitation following hospital discharge. Compared with patients receiving ECPR, healthcare costs associated with conventional CPR are often less since, in general, they do not survive to hospital admission.⁵² To date, no trial-based cost-effectiveness studies have been published. However, limited studies suggest that ECPR is cost effective.^{53,54}

The most direct benefit of ECPR is the absolute increase in survival in the roughly 30% of patients with refractory cardiac arrest.⁹ Further, there is a potential indirect benefit to cardiac arrest patients through the implementation and maintenance of an ECPR program, which often leads to a well-organized, systematic approach to cardiac arrest that includes coordinated prehospital resuscitation, high-quality ALS and postarrest care, therein benefiting all OHCA patients.⁴⁴ This effect was noted by the Prague ECPR study within the control group.¹⁵ Finally, metrics that are often not captured in trial data but should also be accounted for includes organ donation and the opportunity for families to say goodbye to their loved one. Ultimately, balancing these risks against potential benefits is critical in determining the appropriateness of ECPR for individual patients.

5 | DISCUSSION

Optimal ECPR is predicated upon a system of comprehensive and multidisciplinary care for patients with refractory cardiac arrest

(Figure 1).¹⁴ This system involves a well-coordinated sequence of actions, starting with early identification of eligible candidates based on specific criteria (e.g., age, witnessed arrest, and potentially reversible causes). Once identified, rapid initiation of ECPR involves establishing extracorporeal circulation via cannulation of large blood vessels, thereby facilitating oxygenation and circulation outside the body. This intricate procedure demands procedural expertise, teamwork, and meticulous monitoring to ensure optimal blood flow and prevent complications. ECPR is integrated within a continuum of care, encompassing postresuscitation management, cardiac catheterization to address underlying causes, targeted temperature management to mitigate brain injury,⁵⁵ and ongoing monitoring of cardiac function⁵⁶ and neurological status.^{57,58} The collaborative efforts of healthcare professionals from various disciplines are fundamental to this system, allowing for swift and strategic decision-making throughout each stage of care, ultimately increasing the potential for improved patient outcomes.

Although ECPR has shown promise as a potentially life-saving intervention,⁵⁹ there are several knowledge gaps that still need to be addressed. Among them include optimal patient selection. As only the Prague trial included nonshockable initial rhythms,¹⁵ there is debate as to the benefit of ECPR for these patients, as the beneficial effect is less pronounced.¹⁷ Additionally, determining when to transition from conventional CPR to ECPR requires more clarity. Finally, although ECPR guidelines exist from the Extracorporeal Life Support Organization⁶⁰ along with Delphi best practice recommendations from recognized experts,²⁸ RCT level data are limited. There is a need for prospective trials to test published recommendations, including optimal prehospital management, patient selection, arrest management, cannulation, imaging, and circuit and postresuscitation management within the context of an ECPR patient.

Finally, it is important to understand that individual death and failure are inherent to this process. Although ECPR has demonstrated a survival benefit in trials, >50% of patients with refractory OHCA treated with ECPR still die despite treatment. Other patients survive and subsequently suffer neurologic and/or physical morbidity. Institutions that perform ECPR—or are looking to establish a program—must

consider community needs, logistics, ability to maintain procedural excellence and outcomes to maximize patient benefits.

6 | CONCLUSION

ECPR holds immense promise in revolutionizing the management of patients with refractory cardiac arrest. Its potential benefits—in terms of improved survival rates and neurologic outcomes—cannot be overstated. However, the complexity of implementing ECPR, both in terms of technical expertise and resource allocation, underscores the need for careful planning and rigorous training. As we look to the future, ongoing research, technological advancements, and a collaborative effort among healthcare professionals will likely expand the utility of ECPR, with the intent of achieving sustainable improved survival outcomes in this specific patient population.

AUTHOR CONTRIBUTIONS

Study design: A. C. and J. T. *Study conduct:* A. C. and J. T. *Data acquisition and analysis:* A. C. and J. T. *Drafting the manuscript:* A. C. and J. T. All authors revised the article for important intellectual content and had approved the final manuscript for publication. A. C. had full access to the study data and takes responsibility for the data integrity, accuracy, and integrity of the submission as a whole.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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