Extracorporeal Cardiopulmonary Resuscitation (ECPR) by Cause of Cardiac Arrest

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June 23, 2020

Abstract

Background: Extracorporeal cardiopulmonary resuscitation (ECPR) has emerged as a rescue strategy for non-responders to conventional CPR (CCPR) in cardiac arrest. Definitive guidelines for ECPR deployment do not exist. Prior studies suggest that arrest rhythm and cardiac origin of arrest may be variables used to assess candidacy for ECPR. Aim: To describe a single center experience with ECPR and to assess associations between survival and physician-adjudicated origin of arrest and arrest rhythm. Methods: A retrospective review of all patients who underwent ECPR at a quaternary care center over a 7-year period was performed. Demographic and clinical characteristics were extracted from the medical record and used to adjudicate origin of cardiac arrest, etiology, rhythm, survival, and outcomes. Univariate analysis was performed to determine association of patient and arrest characteristics with survival. Results: Between 2010 and 2017, 47 cardiac arrest patients were initiated on extracorporeal membrane oxygenation (ECMO) at the time of active CPR. ECPR patient survival to hospital discharge was 25.5% (n=12). Twenty-six patients died on ECMO (55.3%) while 9 patients (19.1%) survived decannulation but died prior to discharge. Neither physician-adjudicated arrest rhythm nor underlying origin were significantly associated with survival to discharge, either alone or in combination. Younger age and arresting in the emergency department were significantly associated with survival. Nearly all survivors experienced myocardial recovery and left the hospital with a good neurological status. Conclusions: Arrest rhythm and etiology may be insufficient predictors of survival in ECPR utilization. Further studies are needed to determine evidenced based criteria for ECPR deployment.

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Conclusions : Arrest rhythm and etiology may be insufficient predictors of survival in ECPR utilization. Further studies are needed to determine evidenced based criteria for ECPR deployment.

Introduction :

Sudden cardiac arrest in adults has low survival rates despite the widespread implementation of cardiopulmonary resuscitation (CPR)[1]. Hospital cardiac arrest survival to discharge can be less than 20%[2–4]. Moreover, the odds of survival decline with increasing duration of CPR[5,6].

Extracorporeal membrane oxygenation (ECMO) during CPR, referred to as ECPR, can provide complete cardiopulmonary support and has emerged as a strategy to provide temporary perfusion and oxygenation for patients in cardiac arrest. The data in support of ECPR over conventional CPR (CCPR) remain mixed and are limited by the heterogeneity of a small number of studies.

Propensity matched observational studies comparing ECPR with CCPR suggest improved in-hospital and 1-year survival, as well as improved neurological outcomes with ECPR[7–10]. A large meta-analysis found that for adult patients with in-hospital cardiac arrest thought to be of cardiac origin, ECPR was associated with significantly improved survival and neurological outcomes compared to CCPR [11]. Others, however, have found no clear benefit in survival to hospital discharge with ECPR[12].

There are no definitive initiation criteria for ECMO deployment during in-hospital CPR. Among patients who undergo ECPR, approximately 20-40% survive to discharge, with younger age being a potential predictor for favorable neurological outcome[13–20]. Factors that have been reported to correlate with survival in ECPR include younger age[17], shorter CPR duration[16,21], normal pre-cannulation renal function[22], a simplified acute physiology score II of less than 80[23], a serum lactate less than 4.6 mmol per liter[24], or a diagnosis of acute myocarditis[19].

The prognostic significance of the arrest rhythm, arrest etiology, and cardiac versus non-cardiac origin of cardiac arrest in ECPR remains controversial. A meta-analysis of 856 patients who underwent ECPR for in hospital cardiac arrest demonstrated that an initial shockable rhythm was associated with survival. However, no significant association was found between survival and cardiac versus non-cardiac origin of arrest[25]. In contrast, a comparison of ECPR and CCPR found a higher rate of intensive care unit survival and long term favorable neurological outcome in ECPR patients with a non-cardiac origin of arrest[10]. Other studies report survival rates of 20% in patients with non-shockable rhythm at time of ECPR, suggesting a shockable rhythm should not be a solitary prerequisite for ECPR, however no information on cardiac arrest origin or etiology was included[26].

The high study heterogeneity and low level of evidence limits the external validity of many meta-analyses. What is defined as cardiac versus non-cardiac origin is often not explicitly stated and may be variable between different studies, and underlying etiologies of cardiac arrest are not always available or reported.

In light of the expanding utilization of ECPR and lack of definitive criteria for optimal patient selection, we performed a single center retrospective observational study of adults with cardiac arrest who received ECPR at a large quaternary care center, determined the predominant arrest rhythm and underlying etiology in each case by physician-adjudicated chart review, and defined each cardiac arrest as cardiac or non-cardiac in origin based on the etiology. The purpose of this study was to report the association between ECPR survival and cardiac versus non-cardiac origin of arrest, both alone and combined with arrest rhythm.

Methods and Materials:

A retrospective cohort review was performed on all entries in the Extracorporeal Life Support Organization (ELSO) registry from November 1, 2010 to July 31, 2017 at the Massachusetts General Hospital (MGH), a large quaternary care center in Boston, Massachusetts (USA). Patients who were undergoing CPR in hospital at the time of ECMO initiation as documented in the procedural report were included. Patients who underwent ECMO cannulation but for whom immediate durable flow through the ECMO circuit could not be initiated were excluded. Baseline characteristics were extracted from the medical record. The study was approved by the Partners Institutional Review Board.

This study's primary outcome was survival to hospital discharge. Etiology of cardiac arrest was adjudicated by two reviewers (NM & LXM) and categorized by cardiac origin (defined as an etiology of acute coronary syndrome, primary arrhythmia in the absence of overlapping etiology, acute heart failure, and tamponade) or non-cardiac origin (defined as pulmonary embolism, drug toxicity, sepsis, perioperative shock, or air embolism). When multiple potential etiologies were present, the primary cause as adjudicated by the care team was selected. Cardiac arrest rhythm was ascertained from the procedural report and categorized as either pulseless ventricular tachycardia/ventricular fibrillation (VT/VF) or pulseless electrical activity (PEA).

ECMO-related complications were assessed. Major bleeding was defined as Bleeding Academic Research Consortium category 3-5[27]. Additional outcomes assessed included de novo renal replacement therapy, cerebrovascular events, limb ischemia, and cerebral performance category (CPC). CPC scores 1 through 5 correlated to good cerebral performance (able to work, minor deficits), moderate cerebral disability (persistent deficits but mostly independent), severe cerebral disability (dependent on others), coma or vegetative state, and brain death, respectively[28].

Descriptive statistics were used to quantify baseline patient characteristics, clinical features, ECMO utilization, and survival rates. Categorical variables were reported as counts and percentages and compared using the Fisher's exact test. Continuous variables were reported as medians with interquartile ranges and compared with the Wilcoxon two-sample test. Statistical significance was assessed at a nominal α level of 0.05. All reported P values were 2-sided. Analysis was performed in R 4.0.0 (R Core Team, 2020).

Results:

Between November 2010 and September 2017, 47 cardiac arrest patients were initiated on ECMO at the time of active CPR for cardiac arrest. Baseline characteristics for survivors and non-survivors are described in Table 1. ECPR patients were more commonly male (n=33; 70.2%) with a median age of 53 years. The majority of patients had underlying cardiovascular disease, including 20 patients (42.6%) with known cardiomyopathy and 27 (57.4%) with coronary artery disease.

Arrest and cannulation locations are described in Table 2. Forty-five patients (95.7%) experienced an in-hospital cardiac arrest while two patients experienced an out-of-hospital arrest but were cannulated in the hospital while receiving CPR (4.3%). The most common locations for both arrest and cannulation were the cardiac catherization lab and the intensive care unit.

Arrest rhythms were either PEA (n=25; 53.2%) or pulseless VT/VF (n=22; 46.8%). Arrest etiologies included acute coronary syndromes (n=17; 36.2%), acute heart failure syndromes (n=10; 21.3%), pulmonary embolism (n=7; 14.9%), primary arrhythmia (n=5; 10.6%), drug toxicity or overdose (n=2; 4.3%), and other causes (n=6; 13%), including tamponade (n=2), air embolism (n=1), perioperative hemorrhagic shock (n=1), and sepsis/endocarditis (n=2) . In total, 4 patients (8.5%) experienced arrest post-cardiotomy (from tamponade, PE, VT storm, and VF), with 50% of these patients dying while on ECMO and the remaining surviving to discharge.

Overall, 34 patients (72.3%) were adjudicated to have a primary cardiac origin of their cardiac arrest. There was no significant association found between etiology of arrest, arrest rhythm, or cardiac versus non-cardiac origin of arrest and survival to discharge. Similarly, no combination of arrest origin (cardiac or non-cardiac) and arrest rhythm (PEA or VT/VF) was significantly associated with survival to discharge [Table 3].

ECMO characteristics are described in Table 4. Almost all patients underwent peripheral cannulation. Following cannulation, 22 (46.8%) were underwent targeted temperature management, 19 (40.4%) had a subsequent revascularization procedure, and 6 (12.8%) had a venting ventricular assist device placed. Median time on ECMO support was 3.00 days.

ECMO-related complications included major bleeding (n=28; 59.6%), renal replacement therapy (n=24; 51.1%), cerebrovascular accident (n=10; 21.3%), and limb ischemia (n=8; 17.0%) [Table 5].

Overall ECPR patient survival to hospital discharge was 25.5% (n=12). Twenty-six patients died on ECMO (55.3%) while 9 patients (19.1%) survived ECMO decannulation but died prior to discharge. The majority of patients who survived to discharge experienced myocardial recovery (n=10; 83%); one patient underwent orthotopic heart transplantation (8.3%), one received a durable ventricular assist device (8.3%), and 2 required new dialysis at discharge (16.7%). Most survivors had a favorable CPC score of 1 at discharge (n=9; 66.7%) [Table 6]. Median intensive care unit and hospital length of stay for survivors was 28.5 [IQR 13.50, 39.50] and 35.50 days [IQR 21.75, 49.50] respectively. Causes of death in non-survivors are listed in Table 7.

In univariate analysis, characteristics associated with survival to discharge include younger age (median 44.0 [IQR 45.00,64.00] in survivors versus 60.00 in non-survivors [IQR 46.00, 6.65]; p 0.034) and arrest location in the emergency department (33.3% of survivors versus 2.9% of non-survivors; p=0.012). Arrest etiology of pulmonary embolism approached but did not cross the pre-established threshold for significance (33.3% of survivors versus 8.6% of non-survivors, p=0.060).

Discussion:

In this single-center experience, we demonstrated that neither physician adjudicated arrest rhythm (VT/VF versus PEA) nor underlying origin of the cardiac arrest (cardiac versus non-cardiac) were significantly associated with the primary outcome of survival to discharge following ECPR, either alone or in combination. Of the multiple baseline, peri-arrest, and on-circuit characteristics assessed, only younger age and arresting in the emergency department were significantly associated with survival following ECPR, and of the range of arrest etiologies described, only pulmonary embolism approached significance. We found that while ECPR therapy was associated with a high complication burden, with the majority of patients experiencing major bleeding or requiring de novo renal replacement therapy, of the patients who survived to discharge, nearly all experienced myocardial recovery and left the hospital with a good functional neurological status. Of the patients who did not survive, the most common cause of death was the decision to pursue comfort measures only in the setting of multiorgan failure.

The initiation of ECMO at the time of in-hospital cardiac arrest with active CPR remains an evolving treatment strategy without a robust evidence base to discern who benefits most from its deployment. Our study had the advantage of detailed physician review of cardiac arrest origin, etiology, and rhythm and highlights the heterogeneity in adjudicated causes of cardiac arrest preceding ECPR initiation. In doing so, it adds to the existing literature that underscores the salient challenge in predicting survival following ECPR: the complex and heterogeneous epidemiology of cardiac arrest as a whole.

The most parsimonious approach to predicting survival in ECPR may center on a clinical assessment of the reversibility of either the proximal cause of arrest or the clinical characteristics surrounding it. Historically, factors associated with survival in CCPR have included findings such as shockable arrest rhythm[29] and cardiac origin of cardiac arrest[1]. We found no such relationship with survival in ECPR. This study adds to the growing body of literature that suggests these traditional risk stratifiers may not be reliable indicators of survival in ECPR and thus may not deserve a prominent role in the decision to provide extracorporeal support during CPR.

As the utilization of ECPR as a salvage therapy for patients with complete cardiopulmonary collapse expands, more work is needed to identify the patients for whom this resource intensive therapy with high morbidity and mortality would provide a durable benefit. Our results suggest that younger age, pulmonary embolism, and arresting in the emergency department may be associated with survival in ECPR. This does not imply that these should be entertained as possible initiation criteria, but rather that they should serve as hypothesis generating metrics for prospective evaluation of the potential for survival that this population represents.

Younger age may speak to the physiologic reserve required to tolerate not just the arrest event itself and attendant ischemic risks, but also the subsequent ECMO therapy and its high complication burden. Arrest location in the emergency department may be related to the heightened staff awareness regarding potential for decompensation, allowing for swifter response, though the intensive care unit will have as much or more monitoring potential. Therefore, it may also be that compared to patients who present and arrest in the emergency department, those who are already admitted and then arrest as an inpatient may have a poorer prognosis due to their relative comorbid state secondary to their initial, non-arrest presenting diagnosis. Nevertheless, the overall high functional status of those who survive to discharge, despite the high frequency of significant underlying conditions as described in Table 1, can justify the use of this therapy even in patients with multiple pre-existing medical problems.

This study has several important limitations. First, it was subject to limitations inherent in a retrospective, observation design. Second, our findings reflected a small set of ECPR patients at a single center, limiting its generalizability. Third, we were lacking what may arguably be the most important prognostic factors in ECPR: the time from arrest onset to cannulation, and the duration and quality of CPR provided prior to ECMO initiation. It may be that arrest origin, etiology, and rhythm gain prognostic significance when considered alongside these resuscitation metrics. For example, there is evidence that taking into account initial rhythm along with low flow time could help predict neurological outcomes[1,31]. Ultimately, the potential for ECMO as a rescue strategy may be limited at its onset by the extent of ischemic damage suffered prior to it its initiation. Future prospective studies of ECPR should focus on variables which might capture the depth and severity of ischemic insults sustained in the period after arrest but before ECMO deployment, especially those variables which have the potential to be easily incorporated into future advanced cardiovascular life support protocols. Finally, this study does not account for potential improvements in ECPR initiation and post-ECPR care over time, nor do we provide the total number of patients placed on venoarterial ECMO over the duration of the study period. The current registry also does not include cardiac arrest patients for whom ECMO support was considered but ultimately not provided. While emblematic of the challenges with ECPR studies, our findings should be viewed as primarily hypothesis generating and complimentary to the existing evidence base with similar limitations.

Conclusion:

Physician adjudicated etiology and origin of cardiac arrest, even when considered along with arrest rhythm, may not be predictive of survival to discharge in ECPR. Patients who are younger, arrested in the emergency department, and arrested from a pulmonary embolism may represent a population who benefits from ECPR that warrants future study. The excellent neurological status of those who survive to discharge demonstrated in this study serves as a justification for its continued use and optimization.

The lack of correlation between etiology, origin, rhythm, and outcome is indicative of the underlying heterogeneity of arrest patients. This heterogeneity poses a fundamental challenge to studying the appropriateness of ECPR across the diverse care settings and patient populations. Ultimately, ECPR survival may depend more on resuscitation metrics such as CPR duration or quality than patient- or arrest-specific characteristics. In order to determine who may benefit most, we must focus on improving our ability to clinically phenotype peri-arrest patients, as well as understanding how the epidemiology of in-hospital cardiac arrest is changing over time as medical advances continue to alter the natural history of many common underlying conditions and risk factors. Further studies are needed to elucidate the factors that can help determine who will derive the greatest benefit from ECPR in order to better guide institutions on how to deploy this resource-intensive but potentially life-saving therapy.

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