Outcomes of Venoarterial Extracorporeal Membrane Oxygenation for Cardiac Arrest in Adult Patients in the United States

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BACKGROUND: Factors associated with poor prognosis following receipt of extracorporeal membrane oxygenation (ECMO) in adults with cardiac arrest remain unclear. We aimed to identify predictors of mortality in adults with cardiac arrest receiving ECMO in a nationally representative sample.

METHODS AND RESULTS: The US Healthcare Cost and Utilization Project’s National Inpatient Sample was used to identify 782 adults hospitalized with cardiac arrest who received ECMO between 2006 and 2014. The primary outcome of interest was all-cause in-hospital mortality. Factors associated with mortality were analyzed using multivariable logistic regression. The overall in-hospital mortality rate was 60.4% (n=472). Patients who died were older and more often men, of non-White race, and with lower household income than those surviving to discharge. In the risk-adjusted analysis, independent predictors of mortality included older age, male sex, lower annual income, absence of ventricular arrhythmia, absence of percutaneous coronary intervention, and presence of therapeutic hypothermia.

CONCLUSIONS: Demographic and therapeutic factors are independently associated with mortality in patients with cardiac arrest receiving ECMO. Identification of which patients with cardiac arrest may receive the utmost benefit from ECMO may aid with decision-making regarding its implementation. Larger-scale studies are warranted to assess the appropriate candidates for ECMO in cardiac arrest.

Key Words: cardiac arrest ■ extracorporeal cardiopulmonary resuscitation ■ extracorporeal membrane oxygenation ■ mortality ■ outcomes ■ survival

The use of venoarterial extracorporeal membrane oxygenation (ECMO) for refractory cardiac arrest has significantly increased over the past decade, yet extracorporeal cardiopulmonary resuscitation is limited to a Class 2b recommendation in the most recent American Heart Association guidelines for select patients as rescue therapy when conventional efforts are failing and when it can be implemented expeditiously by skilled providers. The majority of contemporary data on the efficacy of ECMO in cardiac arrest is provided by single-center studies with differing selection criteria and conflicting results. A recent national analysis has reported higher mortality in patients hospitalized with cardiac arrest who received ECMO compared with those who did not, but the use of more stringent selection criteria has been shown to improve outcomes. The identification of factors associated with a worse prognosis is important to enable the selection of patients with cardiac arrest who may benefit the most from ECMO. This study was therefore designed to identify the predictors of all-cause mortality in adults hospitalized with cardiac arrest receiving ECMO using the largest publicly available all-payer inpatient database in the United States.
What Is New?

- The in-hospital survival rate in a nationally representative sample of adults hospitalized with cardiac arrest who received extracorporeal membrane oxygenation in the United States was 40%.
- A variety of patient, demographic, and procedural factors were identified as independent predictors of mortality in this study population.

What Are the Clinical Implications?

- The poor prognostic factors identified may aid clinical decision-making regarding the implementation of extracorporeal membrane oxygenation in patients with cardiac arrest and highlights the need for large clinical trials to determine the patients who may receive the utmost benefit from this intervention.

Nonstandard Abbreviations and Acronyms

NIS  National Inpatient Sample

RESULTS

The overall in-hospital mortality rate of patients with cardiac arrest who received ECMO was 60.4% (n=472). The demographics, comorbidities, and clinical presentation of the study population are summarized in Table 1. Patients who died were older than those who survived to discharge (mean age, 52.2±16.2 versus 49.1±17.0; P<0.01) and more likely to be men (66.9% [n=316] versus 59% [n=183]; P=0.03). Patients who died were also more often of non-White race (P=0.04) and more likely to have a lower household income (P<0.01). The rates of comorbidities assessed were similar between the 2 study groups. Patients who died had lower rates of ventricular tachycardia (26.8% versus 19.7%, P=0.02) than those who survived, but the difference in rates of ventricular fibrillation did not reach statistical significance (32.6% versus 28.7%, P=0.08). Patients who died were also less likely to receive percutaneous coronary intervention (13.8% versus 19.7%, P=0.03).

Table 2 summarizes the results of the multivariable logistic regression model for predictors of mortality in this population. In the risk-adjusted analysis, factors independently associated with mortality included older age (odds ratio [OR], 4.1; 95% CI, 1.9–8.9 [P<0.01]), male sex (OR, 1.61; 95% CI, 1.16–2.22 [P<0.01]), higher annual income (OR, 0.62; 95% CI, 0.39–0.96 [P=0.04]), presence of ventricular arrhythmia (OR, 0.7; 95% CI, 0.5–1.0 [P=0.05]), occurrence of
The largest cohort study to date focused on adults with cardiac arrest receiving ECMO in the United States. Our analysis of a nationally representative sample has several significant findings. First, ≈40% of adults hospitalized with cardiac arrest who received ECMO survived to hospital discharge. Second, patients who died were older, male, and with lower annual income. Finally, absence of ventricular arrhythmia, lack of percutaneous coronary intervention, and presence of therapeutic hypothermia were independently associated with worse outcomes in this patient population.

Survival rates of patients with cardiac arrest receiving venoarterial ECMO have widely varied in previous studies from 8% to 75%.5,7–19 The majority of data on the efficacy of venoarterial ECMO in patients with cardiac arrest is confined to single-center series. These small studies have differing criteria for the implementation of venoarterial ECMO in cardiac arrest, including cardiac arrests occurring in different settings, and hence—unsurprisingly—report conflicting outcomes. The largest study assessing the use of ECMO in adults hospitalized with cardiac arrest has reported a higher risk-adjusted likelihood of mortality in patients receiving ECMO.13 Given that decisions to implement ECMO in patients with cardiac arrest are largely made on a case-by-case basis and that ECMO is reserved for rescue therapy, the overall mortality rate reported in this nationally representative sample suggests that a survival rate of 40% can be achieved with evidence-based implementation criteria in patients who are not otherwise responding to standard therapy.
While systematic reviews have attempted to perform meta-analyses on the outcomes of patients receiving venoarterial ECMO in cardiac arrest and its associated prognostic variables using single-center data, these analyses report a low quality of evidence and are uniformly limited by heterogeneity and significant bias—often precluding meaningful analysis.\textsuperscript{20–23} The identification of which patients with cardiac arrest will receive the utmost benefit from ECMO initiation has therefore remained unclear. The size of this study provides sufficient power for a reasonable number of covariates to be included in the risk-adjusted regression model, enabling the identification of a variety of demographic and therapeutic factors associated with mortality in hospitalized adults with cardiac arrest who received ECMO. The presence of percutaneous coronary intervention and shockable rhythms as significant predictors of survival in our model is consistent with the ability of venoarterial ECMO to provide end-organ perfusion while reversible causes are being treated. The American Heart Association guidelines available during the study period recommended therapeutic hypothermia for unconscious patients with spontaneous circulation after out-of-hospital cardiac arrests with shockable rhythms,\textsuperscript{24} therefore this variable may well serve as a surrogate for this subset of patients in our study. Therapeutic hypothermia is often used for patients with hypoxic encephalopathy following return of spontaneous circulation, so the variable may represent an indication of severity. Other variables that could not be captured from the NIS database and were found to be independently associated with survival in single-center studies may be used with discretion to supplement the mortality predictors we have identified (high lactate, low arterial pH, shorter cardiopulmonary resuscitation duration, time to venoarterial ECMO, and presence of return of spontaneous circulation before venoarterial ECMO initiation).\textsuperscript{25–27} The poor prognosticators identified may be used to aid clinicians who are called to the bedside to decide whether a patient with cardiac arrest is an appropriate candidate for venoarterial ECMO and may be used in the design of randomized controlled trials to assess the suitability of this intervention.

Social determinants of health contribute to pervasive disparities that continue to exist in health care.\textsuperscript{28,29} The association of household income and non-White race with worse outcomes in this study suggests that socioeconomic disparities similarly exist among the study population. Further research assessing disparities in venoarterial ECMO practice is needed to explore the mechanisms contributing to and perpetuating these disparities that may be targeted by interventions and inform ethical clinical decision-making in the field.

**Limitations**

Given that the NIS collects billing-related data, the use of this administrative database may be subject to coding errors. This analysis is also subject to confounding bias: despite the number of variables included in our multivariable model, several clinical variables such as medications, laboratory data, hemodynamics, duration of cardiopulmonary resuscitation and other interventions were not available and therefore could not be assessed. The granularity of the NIS enabled the capture of hospitalized patients who experienced a cardiac arrest and received ECMO during their hospitalization; the study population is therefore not limited to patients receiving extracorporeal cardiopulmonary resuscitation and may include some patients who received ECMO at other points in their hospitalization. There are also limited data available on the use of venoarterial ECMO, eg, the duration of therapy and timing of initiation. This study was limited to in-patient mortality, and important secondary outcomes such as neurological function and longer-term outcomes could not be assessed. Finally, data are only available up to 2014 in this study. Outcomes of extracorporeal cardiopulmonary resuscitation will have likely improved since this time period given the greater experience and improved extracorporeal life support technology available, but the predictors of mortality are unlikely to have changed.

**CONCLUSIONS**

In this nationally representative sample of adults with cardiac arrest receiving ECMO, demographic and therapeutic factors are independently associated with mortality. Identification of which patients with cardiac arrest may receive the utmost benefit from ECMO may aid with decision-making regarding its implementation and support the design of future large randomized controlled trials required to assess the optimal patient population to receive ECMO in cardiac arrest.

**ARTICLE INFORMATION**

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**Disclosures**

None.
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