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Should All Shock Centers Offer ECPR? Balancing Futility, Cost Effectiveness, and Hope

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Abstract

There are over 400,000 out-of-hospital cardiac arrests (OHCA) in the United States annually. Of those, 50% are refractory cardiac arrest, defined as the lack of return of spontaneous circulation (ROSC) after 30 minutes of appropriate cardiopulmonary resuscitation (CPR) in the absence of hypothermia. Extracorporeal cardiopulmonary resuscitation (ECPR) has been increasingly used given its potential to improve survival and offer improved neurological outcomes.

Keywords: ECPR; extracorporeal cardiopulmonary resuscitation; cardiac arrest; out-of-hospital cardiac arrest, OHCA

Background

Out-of-hospital cardiac arrest (OHCA) carries a significant socioeconomic burden to society. Following OHCA, outcomes are favorable in patients younger than 75 years, with shockable rhythms (ventricular tachycardia or fibrillation), and adequate cardiopulmonary resuscitation (CPR) of less than 30 minutes. As the duration of CPR increases, the survival and likelihood of a favorable neurological outcome decreases dramatically, with very poor outcomes after 30 minutes of CPR. In light of retrospective data on OHCA and survival, extracorporeal cardiopulmonary resuscitation (ECPR) has been recently recognized as a potential approach to modulate this outcome and extend favorable outcomes to 45 minutes for those in refractory cardiac arrest [1].

For successful implementation of ECPR in OHCA, the connection between emergency medical service and extracorporeal membrane oxygenation (ECMO) teams, the different disciplines, proper training, and operator familiarity with performing ECPR are all critical elements. Japan, Korea and, to a lesser extent, Taiwan have the highest rate of ECPR use worldwide. Currently, ECPR is only offered in select, pocketed locations in the United States.

Based out of Minneapolis, Minnesota, the ARREST trail was led by Dr Yannopoulos et al.[2] ARREST was the first US-based, randomized trial of ECPR. The study included adults aged 18 to 75 years presenting to the University of Minnesota Medical Center (MN, USA) with OHCA and refractory ventricular fibrillation, no ROSC after three shocks, automated CPR with a Lund University Cardiac Arrest System (LUCAS), and an estimated transfer time shorter than 30 minutes. Patients were randomized on arrival to the emergency room into one of two treatment arms: standard advanced cardiovascular life support (ACLS) or early ECMO-facilitated CPR.[2] A treatment algorithm for triage and management after arrival to the emergency department was used.

Survival to hospital discharge was observed in 1 (7%) of 15 patients (95% credible interval 1·6–30·2) in the standard ACLS treatment group versus 6 (43%) of 14 patients (21·3–67·7) in the early ECMO-facilitated resuscitation group. One of the primary concerns of offering ECPR up front in OHCA

is poor neurological outcomes with cerebral performance category (CPC) scores of over 4. However, the ARREST trial revealed that the neurological function was mainly preserved, and functional status scores were significantly improved after physical therapy and rehabilitation.[2]

It is important to consider complications of ECPR. ECPR should not be viewed as a *nothing to lose* solution because there are adverse events. Over time, ultrasound and fluoroscopy have led to less complications: about 36% if not used, compared to 8% when used.[3] Limb ischemia was between 3% to 15%, infection 8% to 20%, and bleeding at the CPR site, insertion site, and abdominal bleeding were 28%, 49%, and 14%, respectively.

Based on the ARREST trial, the Minnesota Mobile Resuscitation Consortium (MMRC) brought the ECPR to the community. ECMO teams were deployed from an ECMO center to regional facilities to perform ECPR quickly. Their outcomes were surprisingly good, with 27 of 58 patients (47%) surviving to hospital discharge and 25 of 58 with favorable neurological outcome with a CPC score of 1 or 2. The data further validates the ARREST trial results.

Belohlavek et al. randomized 256 patients in a single center clinical trial in Prague, the Czech Republic, of adults with witnessed OHCA of presumed cardiac origin without ROSC to either an invasive strategy group of 124 patients (mechanical compression, followed by intra-arrest transport to a cardiac center for ECPR and immediate invasive assessment and treatment) vs regular ACLS in the standard strategy group.[6] Thirty-nine patients (31.5%) in the invasive strategy group and 29 (22.0%) in the standard strategy group survived to 180 days with good neurologic outcomes (odds ratio [OR], 1.63 [95% CI, 0.93-2.85]; difference, 9.5% [95% CI, −1.3 to 20.1; P = .09). At 30 days, neurologic recovery had occurred in 38 patients (30.6%) in the invasive strategy group and in 24 (18.2%) in the standard strategy group (OR, 1.99 [95% CI, 1.11-3.57]; difference, 12.4% [95% CI, 1.9-22.7]; P = .02), and cardiac recovery had occurred in 54 (43.5%) and 45 (34.1%) patients, respectively (OR, 1.49 [95% CI, 0.91-2.47]; difference, 9.4% [95% CI, −2.5% to 21%]; P = .12). Bleeding occurred more frequently in the invasive strategy vs standard strategy group (31% vs 15%, respectively). Unlike the ARREST trial, the bundle of early intra-arrest transport, ECPR, and invasive assessment and treatment did not significantly improve survival with neurologically favorable outcome at 180 days compared with standard resuscitation.[6] However, this study included shockable and nonshockable rhythms; 64% of patients had an arrest of over 45 minutes; LUCAS system was not used uniformly.

When combining data from the two clinical trials, especially OHCA with shockable rhythms, there is a clear mortality benefit from ECPR in OHCA.

Ongoing Clinical Trials of ECPR

There are currently several ongoing ECPR trials including EROCA, APACAR2, ECPB4OHCA, and INCEPTION. The INCEPTION study is being done in the Netherlands, where emergency medicine physicians follow a different approach and are cannulating patients on ECMO.[7]

A recent meta-analysis of ECPR with hypothermia favors therapeutic hypothermia with an odds ratio of survival of 2.27 (1.60, 3.23).[5] Among 374 patients in the HYPO-ECMO randomized clinical trial, which is a clinical trial of patients who were eligible if they had been endotracheally intubated and were receiving venoarterial ECMO for cardiogenic shock for <6 hours. It was conducted in the intensive care units at 20 cardiac shock care centers in France between October 2016 and July 2019. Patients were randomized to either early moderate hypothermia (33-34 °C; n = 168) for 24 hours or strict normothermia (36-37 °C; n = 166). At 30 days, 71 patients (42%) in the moderate hypothermia group had died vs 84 patients (51%) in the normothermia group (adjusted odds ratio, 0.71 [95% CI, 0.45-1.13], P = .15; risk difference, −8.3% [95% CI, −16.3% to −0.3%]).[8]

Conclusion

All shock centers should consider implementing an ECPR program and therapeutic hypothermia. ECPR improves outcomes, and development of these programs is valuable in managing refractory cardiac arrest, while also benefiting patients in the timely implementation of ECMO, particularly those with potentially reversible causes.

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