



The INCEPTION Trial – Early ECPR for Refractory OHCA

Key Article: *Suverein MM, Delnoij TSR, Lorusso R, et al. Early extracorporeal cpr for refractory out-of-hospital cardiac arrest. N Engl J Med. 2023;388(4):299-309.*

Background

- There are approximately 350,000 OHCA that occur each year in the US, yet <20% survive and <7% have a good neurologic outcome.
- Multiple observational studies have found benefit in the use of ECMO for refractory OHCA, and in the past 2 years, we now have 3 RCTs to compare outcomes of ECPR vs. Conventional ACLS.
- We have discussed the role of ECMO to treat OHCA in the past, most recently the **ARREST Trial** which randomized 30 OHCA patients to a bundle of ECMO-facilitated resuscitation vs. Standard ACLS with standardized post-arrest care which resulted in 43% vs 7% neuro-intact survival.
 - Obviously, this trial wasn't definitive – it was small, had a fragility index of 1, and was performed at a highly experienced center with a small number of clinicians performing the clinical care of trial patients.
- Another trial we haven't discussed on CCPEM was the **Prague OHCA trial**, which was a single center RCT published in JAMA, which found a 31.5% vs. 22% difference in survival with good neurologic outcomes at 3 months. While not statistically significant, this was a much larger trial, including 256 patients, and *did find a statistical benefit in favor of ECPR at 30 days.*
- In an attempt to address some of the limitations of the previous literature, the INCEPTION trial was performed and just published in the January issue of NEJM.

Objective

- The INCEPTION trial was performed to compare the effect of extracorporeal CPR as with conventional CPR on survival with a favorable neurologic outcome at 30 days, in patients with refractory out-of-hospital cardiac arrest and an initial ventricular arrhythmia (primary cardiac cause).

Methods

- Multicenter, randomized trial from May 2017 – February 2021
- Location: 10 Centers in the Netherlands
- Patients
 - Included
 - Adults aged 18-70 years of age
 - Witnessed arrest
 - Initial ventricular arrhythmia (VT or VF)
 - Refractory cardiac arrest defined as > 15 minutes of ALS
 - Excluded patients with:
 - ROSC with sustained hemodynamic recovery within 15 minutes
 - Terminal heart failure or DNR code status
 - Severe pulmonary disease

- Disseminated cancer
 - Pregnancy
 - Bilateral femoral artery bypass surgery
 - Expected arrest to cannulation time estimated to be > 60 minutes
 - Severe volume depletion from nonsepsis causes
- Trial Procedures
 - At the 15-minute mark of ACLS, patients were screened for inclusion/exclusion criteria, the local hospital was notified, patients were packaged and transported to the nearest hospital.
 - After notification of the incoming patient, patients underwent a 1:1 permuted block randomization.
 - EMS teams were unaware of the trial-group assignment
 - If the patient had ROSC prior to cannulation, they remained in the assigned group for the intention to treat analysis.
 - Post-resuscitation care included:
 - TTM at all sites
 - Locally determined post-arrest care (no post-arrest care protocol)
- Primary outcome: Survival with favorable neurologic outcome (CPC score of 1 or 2) at 30 days
- Secondary Outcomes
 - Duration of CPR before ROSC
 - Total duration of CPR
 - ICU days
 - Hospital Days
 - Duration of mechanical ventilation
 - Long-term outcomes: 30d survival, 6-month survival, 6-month neurologic outcome
- Sample size:
 - Estimated 8% neuro-intact survival in ACLS group and 30% in ECLS group. So, 55 patients per group would be able to detect a difference.
 - After 70 patients, the sample size was increased to 134 patients because 6/27 patients in the ECPR group did not receive the assigned procedure b/c of pre-cannulation ROSC

Results

- Enrolled a total of 160 patients, 26 were excluded
 - **ECPR**: 70 patients randomized to ECPR (of which only 52 patients were attempted to ECMO, 46 patients were successfully started on ECMO)
 - **Conventional CPR**: 64 patients
- Demographics were well matched
 - Mean Age was 54-57 years old
 - 90% male
 - Most patients received mechanical CPR, Epinephrine, Amiodarone
 - Lactate was about 13 on admission in both groups
- Cardiac arrest data (ECPR vs. Conventional CPR)
 - Transport times were FAST
 - Arrest to EMS Transport: 21 vs. 25 minutes
 - Arrest to hospital arrival time: 36 vs. 38 minutes
 - ECMO cannulation times were variable, and slow at some centers
 - Median time from Arrest to ECMO flow: 74 minutes
 - **** 52 cannulations attempted across the 10 centers, with 46 being successful**

- **No initiation of E-CPR in 18 patients** (explained as a logistic failure, discontinuation of treatment, or patients achieved stable ROSC)
- Primary Outcome
 - **No difference** in 30d survival with favorable neuro outcome: ECPR: 14/70 (20%) vs. C-CPR: 10/62 (16%) $p=0.52$
- Secondary Outcomes
 - **No differences** in 3-month or 6-month outcomes

Limitations Identified by the Authors

- Early randomization led to large number of patients who had ROSC before ECLS which may have affected ability to detect an effect from the treatment strategy
- Lack of standardized protocols for ECPR at different institutions

Other limitations worth discussing:

- LARGE variation in cannulation times, procedural success rates, and care between 10 institutions.
- Some participating centers were building their ECPR program while still participating in the INCEPTION Trial. Several centers had never done ECPR prior to participating in INCEPTION. In fact, 4 centers enrolled 2 patients or less.
- This is really important, because the experience of each center will impact outcome in a complex procedure
- **ARREST and PRAGUE trials took place in experienced single centers** which may explain their positive results

Take Home Points

- **ECPR is not a cure for cardiac arrest, but is a potential therapy for the right patient to serve as a bridge to recovery or another definitive step to reverse their critical illness**
- **Experience in taking care of these patients is critical, the INCEPTION trial may have just shown us that ECPR is not a generalizable approach to cardiac arrest care**