

with the potential for improved ROSC and patient survival if and when equipment and training is readily available.

Expert Opinion: In patients with OHCA and a refractory (defined as no termination after 3 shocks) shockable rhythm, double sequential or vector change defibrillation, when equipment and training is available, can be considered.

Extracorporeal membrane oxygenation-assisted CPR

With the increasing use of venoarterial extracorporeal membrane oxygenation (ECMO) in patients in cardiogenic shock, there has been a parallel increase of extracorporeal CPR (eCPR) for patients with refractory cardiac arrest. The applications of eCPR restores systemic perfusion thereby allowing time for targeted investigations and therapies. However, eCPR is resource- and cost-intensive, and RCTs of eCPR have yielded conflicting results.

In a small single-centre feasibility study with expedited transport to the ED for eCPR initiation (< 30 minutes from 911 call to ED arrival, for shockable and non-shockable rhythms), none of the 15 patients enrolled survived, including the 5 who received eCPR of whom 3 received eCPR within 30 minutes of arrival to the ED.⁶¹ In the single-centre **Advanced Reperfusion Strategies for Refractory Cardiac Arrest (ARREST)** trial eCPR was evaluated in 30 patients with refractory OHCA with VF refractory to 2 shocks and an anticipated transfer time < 30 minutes.⁶² Exclusion criteria included catheterization lab unavailability or contraindication to emergent angiography, trauma or burn-related injury, drowning, or known overdose. Upon arrival to hospital, patients were randomized to receive eCPR in the catheterization lab or standard ACLS in the emergency room. Survival to hospital discharge was higher with eCPR compared with standard ACLS (42.9% vs 6.7%). Survivors in the eCPR group had favourable functional status (CPC < 2) and modified Rankin score of < 2 up to 6 months post discharge. This trial was terminated early because of the superiority of eCPR and ethical concerns of withholding therapy.

In the Hyperinvasive Approach in Cardiac Arrest trial, an early invasive strategy (eCPR if ROSC was not obtained en route or upon hospital arrival) vs standard ACLS in 256 OHCA patients with shockable and nonshockable rhythms was evaluated.⁶³ Patients were identified by dispatch and randomized in the field via a call with an eCPR centre physician. The study included patients (18-65 years old) with a witnessed arrest of presumed cardiac cause, with a minimum of 5 minutes of ACLS without ROSC. Exclusion criteria included suspected or confirmed pregnancy, stroke, known severe chronic organ dysfunction, and bleeding diathesis or recent intracranial bleeding. The investigators reported no statistically significant difference in survival with good neurological outcome (CPC 1-2) at 180 days for the eCPR (31.5%) and standard treatment (22.0%) arms ($P = 0.09$). The risk of bleeding was higher with eCPR (31.0%) than in the standard group (14.5%). The trial was terminated early because of futility criteria.

In the recent multicentre **Early Initiation of Extracorporeal Life Support in Refractory Out of Hospital Cardiac Arrest (INCEPTION)** trial eCPR (upon hospital arrival) compared with standard ACLS in 160 patients aged 18-70 years with a witnessed cardiac arrest due to a shockable rhythm without

ROSC after > 15 minutes of CPR was evaluated.⁶⁴ The investigators excluded patients with > 60 minutes between initial cardiac arrest to initiation of cannulation, those with advanced comorbidities, or patients who had a valid do not resuscitate order. The investigators reported no significant difference in survival with a favourable neurological outcome (CPC 1-2) at 30 days (20.0% with eCPR vs 16.1% with ACLS; $P = 0.52$). Notably, the median time from initial cannulation to start of ECMO flows were longer in the INCEPTION trial compared with in the ARREST and Prague OHCA trials, potentially reflecting varying experience and logistics among the participating centres.

A summary of patient, prehospital, and hospital-based variables potentially associated with eCPR outcomes is presented in **Table 3**. No RCTs have evaluated eCPR for patients with IHCA.

Expert Opinion: eCPR should not be routinely used, but may be considered in highly selected patients with refractory cardiac arrest (> 5-15 minutes) with limited comorbidities and a witnessed cardiac arrest with a targeted cardiac arrest to cannulation time of < 60 minutes.

Expert Opinion: Extracorporeal CPR can be considered in centres with established venoarterial ECMO programs and formalized integrated eCPR clinical pathways.

Expert Opinion: If eCPR is considered, the target arrest to cannulation time is < 60 minutes and the target hospital arrival to cannulation time is < 30 minutes.

Cardiac Arrest Regionalized Systems of Care

A meta-analysis of observational studies showed that patients with OHCA who are admitted to high OHCA volume centres (> 40-100 OHCA cases per year) have lower mortality rates.⁶⁵ In addition, a prospective before and after study in the state of Arizona of OHCA emergency medical services triage to specialized cardiac arrest centres reported improved survival and favourable neurologic outcomes.⁶⁶ International societies have advocated for regionalization of OHCA care including timely transfer to centres capable of comprehensively centralizing OHCA care, but randomized studies were

Table 3. Patient, prehospital, and hospital-based variables potentially associated with eCPR outcomes

Patient variables	Target metrics
Associated with favourable outcomes	Prehospital
• Shockable rhythm • Reversible etiology • Witnessed arrest	• Estimated hospital transfer time < 30 minutes • Operationalized eCPR pathway within EMS • Advance care or critical care paramedics
Associated with poor outcomes	Intrahospital
• Older age • Comorbidities • Prolonged no or low flow time	• Cardiac arrest to eCPR flow time < 60 minutes • eCPR team available for cannulation on arrival • Established VA-ECMO program • Multidisciplinary team

eCPR, extracorporeal cardiopulmonary resuscitation; EMS, emergency medical services; VA-ECMO, venoarterial extracorporeal membrane oxygenation.