

Extracorporeal Cardiopulmonary Resuscitation in Adults. Interim Guideline Consensus Statement From the Extracorporeal Life Support Organization.

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All authors take responsibility for the integrity of the submission from inception to published article. ACR, JET, VN, LR conceived study design, ACR, JET drafted the work; all authors revised the article for important intellectual content, had final approval of the work to be published, and agree to be accountable to for all aspects of the work.

01 3 2021 67 3 378037 221 228 01 03 2021 01 03 2022 01 03 2022 23 03 2021 17 06 2024 This file is available for text mining. It may also be used consistent with the principles of fair use under the copyright law. Veno-arterial extracorporeal membrane oxygenation (ECMO) is increasingly being deployed for selected patients in cardiac arrest who do not attain a native circulation with conventional CPR (ECPR). This ELSO guideline is intended to be a practical guide to implementing ECPR and the early management following establishment of ECMO support. Where a paucity of high-quality evidence exists, a consensus has been reached amongst the authors to provide guidance to the clinician. This guideline will be updated as further evidence in this field becomes available.

Extracorporeal cardiopulmonary resuscitation (ECPR) is the application of extracorporeal membrane oxygenation (ECMO) in patients where conventional cardiopulmonary resuscitation (CCPR) measures are unsuccessful in achieving a sustained return of spontaneous circulation

(ROSC) 1 . 1 The primary purpose of ECPR is to restore the circulation and gas exchange. By providing organ perfusion, it provides time for the delivery of interventions necessary to regain an adequate native circulation. These may include percutaneous coronary intervention (PCI) and recovery from myocardial stunning, pulmonary thrombectomy, rewarming, or toxin clearance.

ECPR is a time-sensitive, complex intervention that requires teamwork, clearly defined roles, and well trained health care providers. 2 ECPR can be deployed both for patients with in-hospital cardiac arrest (IHCA) and out of hospital cardiac arrest (OHCA). ECPR should be considered after 10–15 minutes of unsuccessful conventional resuscitation efforts, 2 because organisation and preparation for ECPR will take some time and it has been clearly shown that time to ECMO correlates with neurological outcome. 3 , 4

Currently, there are no published randomized controlled trials comparing outcomes of ECPR to CCPR. Observational studies comparing ECPR to historical controls and case matched controls have demonstrated favorable results for ECPR. 5 – 9 However, these studies are heterogeneous and survival ranges from 15–50%. Among adult ECPR patients recorded in the international ELSO dataset, survival to hospital discharge is 29%. 10

At the time being we do not know whether the number of neurological injured patients will increase with growing use of ECPR. A major task for the future will be to develop better neuro-prognostication tools. In the current observational studies in selected populations, 5 , 8 – 10 >85% of survivors of cardiac arrest treated with ECPR had neurologic outcomes fall into favorable neurologic performance categories (cerebral performance categories (CPC) 1 or 2). 5 , 8 , 9 Future trials involving ECPR should endeavor to report neurological outcomes as well as mortality.

This document contains numerous additional literature references, organized by topic, found in the Supplemental Content .

Robust data to identify those who may benefit from ECPR are lacking. Protocols and guidelines strive to identify cases most likely to survive with favorable neurologic outcome—such as those patients who are witnessed to arrest and in whom high quality CPR was initiated rapidly, in addition to cardiac arrests with a presumed reversible pathology, such as acute coronary occlusions. 1 , 11 – 13

We recommend that locally agreed inclusion criteria be formulated to guide clinicians on balancing the wise use of resources amongst patients who are thought to have an improved chance of survival following cardiac arrest (TABLE 1).

Decision making for ECPR is often time critical and relies on incomplete information. As such, it may be reasonable to start ECPR as a bridge-to-seeking further information regarding appropriateness of ongoing support. Institutions may choose to use alternative inclusion criteria for OHCA vs IHCA given differences in etiology and expected survival.

The optimal time before initiation of ECPR in cases of refractory cardiac arrest is not well defined. If initiated too early, ROSC may have been gained with CCPR avoiding the additional risks of V-A ECMO. If initiated too late, the risk of hypoxic ischemic injury to the brain and other organs increases significantly; resuscitation related organ trauma and coagulation disorders may also increase. Among observational studies, shorter intervals between the cardiac arrest and ECPR initiation correlate with improved survival. 4 , 14 , 15

The time required to establish ECMO support is highly dependent upon the capabilities of the resuscitation team and patient factors. It may be achieved in as little as 10 minutes but may take longer. 9 We therefore advise early assessment for ECPR candidacy. It is reasonable to consider commencing cannulation after 10–20 minutes of failed resuscitation efforts. Beyond 20 minutes of refractory arrest, the probability of ROSC and survival with CCPR is <5%; 16 , 17 thus, the risks of

V-A ECMO and ECPR at this point, with appropriately selected patients and providers, may be justified.

A maximum arrest duration before ECPR becomes futile has also not been well defined. Neurologically intact survival has occurred following over 3 hours of mechanical CPR before ECPR in the context of a hypothermic arrest. In contrast, among non-hypothermic arrests, the majority of survivors were established on ECMO support in < 60 minutes from onset of cardiac arrest. In one center, ECPR survival after 90 minutes of CCPR was 14%. ¹⁸ Until there are more robust data to the contrary, we recommend that the goal of ECPR is to establish adequate ECMO flow within 60 minutes of onset of cardiac arrest.

The optimal location to provide safe and timely cannulation for ECPR in a hospital may differ between institutions depending on infrastructure, staffing, and other logistical considerations. Deployment of ECPR does not require an operating theatre. Some centers have proven the feasibility of providing prehospital ECPR to minimize low flow time. ⁶ It is uncertain at present if provision of a prehospital ECPR system rather than transport of the OHCA patient to a center that provides ECPR leads to improved outcomes.

In the absence of definitive evidence, it is recommended that patients in refractory cardiac arrest who are suitable for ECPR should be transported to the nearest hospital which can provide this support as fast and as safely as possible. Early notification of a potential ECPR case is reasonable to gain time for hospital staff to mobilize the required team. If transport to a hospital-based ECPR setting is undertaken, EMS systems should strive to minimize interruptions to high-quality CPR during the extrication, transport, and hospital hand over. Automated mechanical compression devices may facilitate this.

Before further data become available, at the present time it is recommended to reserve out of hospital ECPR to highly specialized teams, possibly in the setting of controlled clinical trials. ⁶

The goal of ECPR is the rapid restoration of adequate organ perfusion with cardiopulmonary support utilizing V-A ECMO.

The cannulation phase commences with skin preparation to the femoral areas with antiseptic solution at which point modification to the ACLS algorithm should occur. Concurrently the following processes must occur:

External cardiac massage must continue throughout the cannulation phase, which may be assisted by application of an automated mechanical compression device. Studies comparing the mechanical chest compression devices with human-performed chest compression during CCPR have shown similar survival outcomes. We, therefore, extrapolate that a mechanical chest compression device may offer advantages during a prolonged resuscitation attempt during ECPR by reducing staff physical fatigue, providing more space around the patient and minimizing body movements during the cannulation. ^{8 , 19}

Some mechanical chest compression devices require careful positioning over the lower third of the sternum in the midline and must be checked regularly throughout application. Migration towards the upper abdomen reduces the effectiveness of compressions and is potentially harmful. ²⁰

Percutaneous ECMO cannulation has been shown to be effectively performed by providers from many disciplines, including surgeons, ^{19 , 21} intensivists, ²² cardiologists, ⁹ and emergency physicians. ^{19 , 21 , 23} However, those performing this technically challenging procedure must have the requisite training to develop the required skills, and sufficient volume of experience to maintain competency. Ideally, cannulators should be performing conventional vascular access procedures regularly. We advise that the decision to initiate cannulation occur after a risk/benefit assessment of the most skilled immediately available provider, within the context of patient specific

cannulation complexities and the risk of continued CCPR.

The common femoral artery and vein may be accessed using a modified Seldinger technique. 22 The femoral vessels should be imaged with ultrasound in real time to increase first-pass success rates. In suspected pulmonary embolism as the cause for arrest, ultrasound visualisation of the vessels is particularly important to exclude inadvertent cannulation of a thrombosed vein. Chest compression pauses, if required, should be kept to a minimum during cannulation. The first cannula may be flushed with heparinized saline and/or periodically back-flushed, to prevent clot formation whilst the second cannula is inserted. This step is not required for the second cannula as connection to the pre-primed circuit is imminent.

There is no strong preference regarding the side and, in case of difficulty, unilateral cannulation of both femoral vessels is acceptable. Time to support takes precedence over these other considerations. If two trained operators are available, contralateral cannulation may be faster.

The venous and arterial guidewires should be imaged prior to cannula insertion to confirm correct location and avoid inadvertent non-physiological support. 24 This may be performed with bedside vascular ultrasound in combination with transthoracic or transesophageal echocardiography (for imaging of wires in the hepatic IVC and abdominal aorta) or with fluoroscopy. 24 If available, fluoroscopy offers advantages in that it can evaluate the course and size of the vasculature. However, cannulator preference with alternative methodologies are acceptable; minimizing time to support remains the priority. Intra-arrest transesophageal echocardiography, in the hands of experienced providers, can facilitate placement and is supported by specialty guidelines. 25

Observational series suggest that ultrasound-guided placement of a smaller distal antegrade perfusion cannula (sometimes called distal limb perfusion cannula) in the ipsilateral superficial femoral artery, perfused off the side port on the arterial cannula, is associated with reduced critical limb ischemia. 26 Leg perfusion could also be via retrograde flow via cannulation of the dorsalis pedis or posterior tibial arteries. This distal perfusion cannula is not required for initial deployment—priority should be given to therapies such as coronary catheterization—but should be sited ideally within 4 hours to reduce the risk of limb ischemia and subsequent need for fasciotomy or limb amputation. 27 The use of calf tissue oxygen saturation with NIRS may provide monitoring of leg perfusion and onset of ischaemia.

Arterial (antegrade and retrograde) and venous cannulation can also be acquired via surgical cut down techniques. The main advantage of cut down technique is direct visualization of the vessels while cannulating. This can be used to salvage a failed percutaneous access attempt. Cut down approaches may increase subsequent bleeding or infection from cannulation sites.

Cannula size should be guided by the relative balance between vessel size and the anticipated need for flow. Some data suggest increased limb ischemia with larger cannula size 28 though this has not been confirmed in other studies. Arterial 15–17 Fr and 19–25 Fr multi-stage venous cannula provide satisfactory blood flow, 29 though smaller cannulae may be acceptable for small patients. 28 A single stage drainage cannula is also acceptable. Most circuits can deliver >4 L/min blood flow with a 15 Fr arterial return cannula. For large males, a 17–19 Fr arterial return cannula may be used. Significant arterial vasospasm may be seen in prolonged cardiac arrest after multiple doses of IV adrenaline, which may impede percutaneous cannulation.

Standard ACLS therapies should be applied throughout the resuscitation until the cannulation procedure commences. The code leader should not be engaged in the ECMO cannulation process, but should provide oversight of the parallel conventional and ECMO resuscitation. Extreme caution should be applied when defibrillating the patient once guide wire insertion commences, due to the risk of electrocution of the cannulators. It may be reasonable to suspend further defibrillation attempts from this point until the patient is established on V-A ECMO support. Brief rhythm and pulse checks may still occur at the discretion of the code leader, as ROSC may allow the

cannulation team more time for cannulation. End tidal CO₂ and tissue oxygenation monitoring may help in assessing CCPR quality and ROSC detection. 30 – 32

Pauses to chest compressions for any reason should be kept to a minimum. Adrenaline, and other drug administration may continue through the cannulation phase as directed by the code leader. When V-A ECMO support is imminent, as the circuit is being connected to the cannulae, adrenaline boluses should be discontinued as there is a risk of significant hypertension on establishment of a circulation with V-A ECMO blood flow.

The primed circuit is connected to the inserted ECMO cannulae using a technique to purge all air from the lines, thereby avoiding risk of air embolism. There is no need to warm the saline prime in the circuit prior to V-A ECMO support in ECPR (FIGURE 1).

The console operator should increase pump RPM to generate positive pressure in the return limb of the circuit prior to releasing the final clamp, this ensures antegrade circuit flow. Gradual increases in V-A ECMO support should occur over 20 seconds, aiming for a blood flow of 3–4 L/min. The goal of ECMO support is to halt ongoing global ischemia. The minimum flow rate required to achieve this goal is uncertain. Serial measurement of lactate to assess clearance and monitoring of organ function may be used to guide support. 33

Once V-A ECMO blood flow is ≥ 3 L/min, mechanical compressions should be discontinued as an adequate circulation has been established. Vasopressor and inotrope infusions, if running, may need to be weaned rapidly.

The access cannula position should be confirmed with fluoroscopy or echocardiography prior to cannula securing and dressing. The tip of the drainage cannula should be positioned in the Right Atrium. Both cannulas should be secured once an acceptable position is achieved.

Mean Arterial Pressure measurement: This is best achieved with a right-sided upper limb arterial line (radial or brachial). Right upper limb blood gas sampling gives the easiest indicator of native circulation P a O₂ which may represent the cerebral oxygen delivery depending on the mixing point in the aorta between native circulation and V-A ECMO blood flow. 34 Until an arterial line is placed, non-invasive measurement using a Doppler and a cuff will assist with initial vasopressor dosing.

An optimal MAP target following ECPR has not been identified. We recommend titrating vasopressors to MAP target ≥ 60 mmHg for organ perfusion pressure and < 80 mmHg to minimize risk of LV distension. Animal data suggest higher MAP targets during initial reperfusion may improve neurological outcome.

Titrate sweep gas flow mechanical ventilation if ROSC has occurred by frequent ABGs monitoring to avoid hypocarbia

Address potential drainage insufficiency (drainage line chatter) with fluids / transfusion / weaning of V-A ECMO blood flow if excess to requirement; total circulation is made up of native cardiac output, if present, plus ECMO blood flow.

Ensure correct placement of endotracheal tube.

Perform bedside ultrasound: cardiac, thoracic, and abdominal imaging to identify possible complications (pneumothorax, thoracic/abdominal bleeding) and assess valve competence and LV distension.

Establish end-tidal CO₂ monitoring to assess native cardiopulmonary circulation.

Formal laboratory bloods including cross match.

Check circuit blood flow stability. Unstable (falling) ECMO circuit blood flow should prompt a search for intra-abdominal, including retroperitoneal, and thoracic sources of hemorrhage, cardiac tamponade (associated with prolonged chest compression or trauma), or ECMO driven left ventricular distension with pulmonary congestion.

Restoration of a potentially perfusing rhythm increases likelihood of native circulation with left ventricular (LV) ejection and thus reduces risks of LV distension, valvular regurgitation, pulmonary edema and intracardiac thrombus formation. Patients in refractory arrhythmias should have another attempt at electrical cardioversion after several minutes of extracorporeal support. The restoration of coronary perfusion pressure with the V-A ECMO along with improving acid base status may lead to a successful cardioversion at this point. However, coronary ischemia and other reversible factors need to be addressed. Therefore, multiple attempts should be avoided unless these factors are resolved.

Peripheral V-A ECMO may increase LV afterload. If LV distension and pulmonary congestion occur, consideration to LV venting should be given. Options include: an intra-aortic balloon pump, direct LV vent, Impella® or atrial septostomy. 35

Consider mechanical ventilation with PEEP ≥ 10 cmH₂O for reducing LV afterload and preventing or treating pulmonary oedema. Reduce minute ventilation, due to reduced pulmonary blood flow, to achieve low normal etCO₂. Lack of etCO₂ may indicate absent native circulation.

Hyperoxia may be associated with worse neurologic outcome after cardiac arrest, including in the ECPR population. 36 Avoidance of hyperoxia can be achieved through careful blending of ECMO fresh gas flow with an air and oxygen mix. We recommend targeting a patient arterial oxygen saturation of 92–97%.

Carbon dioxide (CO₂) targets after resuscitation from cardiac arrest are conflicting, but a predominance of studies demonstrates increasing mortality with initial hypocarbia. 37 There is insufficient data among ECPR specific populations to provide further recommendations.

Targeted Temperature Management (TTM) can be precisely achieved using the heat exchanger on the ECMO oxygenator. Based on protocols with best outcomes and consensus, we advise on 33–36 for 24 hours, then gradual rewarming to 37C. 8 , 9

Siting a distal limb perfusion cannula is known to be associated with decreased limb ischemia in V-A ECMO. 26 Accordingly, we recommend a distal perfusion cannula should be sited on the side of arterial cannulation. This should be performed within 4 hours of cannulation, though this should not delay cardiac reperfusion or urgent diagnostic imaging for bleeding or pulmonary embolism if these are required. 27

Studies suggest improved outcomes in cardiac arrest patients treated with percutaneous coronary interventions. ECPR series targeting cardiac arrest believed to be due to acute coronary etiologies, that utilized protocolised catheterization post cannulation are associated with increased survival. 8 , 9 , 19 Accordingly, we recommend emergent coronary angiography for all ECPR patients without an obvious alternate non-cardiac cause, independent of age and presenting rhythm.

The cardiology team should be informed at the time of set-up for all ECPRs and be presented with the history and 12-lead ECG post cannulation for assessment.

In adults, as well as initial ultrasound, we recommend routine CT imaging is performed in all ECPR cases as soon as practical. If the cause of the cardiac arrest is unclear, or if there are signs for significant internal haemorrhage, CT should take place immediately after the cannulation, otherwise

after coronary angiography.

If the cause of the arrest is unclear, consider: CT brain

CT pulmonary angiography (timing of contrast administration and ECMO blood flow may need to be adjusted to improve image quality)

If the cause for cardiac arrest is identified in the cath lab, consider imaging: CT brain

If there is evidence falling ECMO blood flows or drainage insufficiency (drainage line chatter), these additional scans may be useful: CT abdomen/pelvis

The rationale for routine CT imaging is to identify causes of the cardiac arrest, early identification of catastrophic brain injuries and solid organ bleeding from prolonged mechanical chest compressions. If patient has drainage insufficiency and an abdominal ultrasound scan is suggestive of free fluid, arterial phase CT scan of abdomen and pelvis should be considered to rule out injury to liver and spleen. This often occurs early and may present with falling ECMO blood flow or drainage insufficiency. Liver and splenic lacerations are commonly amenable to embolization with interventional radiology.

Early echocardiography to assess bi-ventricular and valvular function is helpful in predicting complications of ECMO support. The presence of greater than mild aortic regurgitation dramatically increases the likelihood of catastrophic LV distension and pulmonary oedema.

Once the etiology of the cardiac arrest is addressed, native cardiac function may return and be sufficient for separating from V-A ECMO support after a period of recovery. There is a lack of consensus on the timing of weaning and decannulation for V-A ECMO, though a period of 3 to 4 days ECMO support is typically seen. 10, 33 Premature decannulation results in haemodynamic deterioration and either urgent re-cannulation for support or cardiovascular collapse and possible death, whilst prolonging ECMO support unnecessarily may lead to significant morbidity and mortality.

V-A ECMO weaning usually consists of serial reductions in blood flow until a flow of 0.5–1.0 L/min is achieved, with serial echocardiographic and haemodynamic assessment at each stage. Even with this minimal ECMO flow, right ventricular (RV) preload is reduced and, hence, right heart function is not tested under fully unsupported, loading conditions.

Trial off support, either by using an arteriovenous bridge within the circuit, or by clamping, allows temporary separation of ECMO from the patient. However, it requires intermittent circuit clamping and carries a significant risk of circuit thrombosis.

Once a successful weaning study has been completed, flow should be increased to 2 L/min until time of decannulation to minimize the risk of circuit thrombosis.

Some patients will survive ECPR neurologically intact, but fail to recover sufficient myocardial function for successful weaning and decannulation; for these, long term mechanical cardiac support such as ventricular assist device (VAD) and/or cardiac transplantation may be the only option for survival. 33, 38 We recommend early discussion with a referral center that offers durable VAD and cardiac transplantation for these patients.

For those patients that are not weanable and who are not considered candidates for durable VAD or cardiac transplantation, terminal decannulation with palliation may have to be considered.

Brain death is a common mode of death following ECPR and organ donation may be considered in this circumstance. Declaration of brain death has to follow national guidelines and may need an adjusted protocol with on-going ECMO support. Organ donation is also possible following circulatory death after withdrawal of ECMO support.

Consent for ECPR therapy from those receiving CCPR is not possible. Further, it is unlikely that an appropriate consent process can take place with next of kin during this time. Whereas ELSO Guidelines for ECMO initiation recommend consent prior to initiation of ECMO, with a clear treatment plan including the rationale for withdrawing care due to lack of recovery or ineligibility for long-term mechanical support, this is usually not possible among those considered for ECPR. Patients are initiated on ECPR based on the presumption that they would want all efforts pursued.

We recommend that institutions offering ECPR develop a guideline for ECPR treatment which includes eligibility, goals of treatment, and a timeline with conditions for stopping ECMO in those without neurological recovery, or in those ineligible for long term mechanical cardiac support due to insufficient cardiac recovery. After ECPR initiation an immediate meeting should take place with the next of kin to explain the basics of ECPR, the institutional guidelines of care for ECPR, and obtain consent for continued treatment.

The provision of ECPR should not be first entertained during CPR, but rather requires careful organizational consideration. An institution wanting to provide ECPR should engage in a multi-disciplinary discernment process of clinicians and administrators to include: a needs assessment, program feasibility and sustainability, expectations, and resource availability. 19 Program development should consider human resources, infrastructure already in place and the resources required to maintain competency. Eligibility criteria need to be developed which are clear and reproducible.

Given the complexities of instituting ECPR and its infrequent usage even in large centers, we advocate for regular system and team-based simulation with simulators that can be used to practice cannulations with ongoing resuscitation measures. This training should be the cornerstone for any ECPR program development to aid in the delivery of consistent and safe care.

A quality improvement strategy needs to be developed to monitor process metrics and outcomes. With the added complexities of ECPR initiation, there is risk to the quality of CCPR. Quality of care metrics for both CCPR and ECPR processes should be identified and monitored. Case reviews should be performed for every ECPR case, identifying areas for improvement and reporting institutional goal performance metrics. Goal metrics and outcomes should be monitored and reported.

We recommend each institution has a robust process for clinical governance of their ECPR program with multi-disciplinary input and review. Demographic, outcome, and complication data should be collected and reported to the institution providing oversight of the service and consideration given to contributing to an international dataset, such as ELSO, to allow for benchmarking and research opportunities.

Providing ECPR for those with OHCA poses additional logistical obstacles. Integrated prehospital protocols are required to identify appropriate patients early, provide pre-arrival notification to hospital teams and facilitate timely transport to hospital with continued high quality resuscitative efforts. Prehospital teams should identify methods to mitigate the risk to CCPR quality during extrication and transport, and should participate in ECPR simulation exercises.

Regardless of specific details of protocol, only a very small proportion of patients with OHCA will ultimately be considered eligible for ECPR. 39 Thus, prehospital resuscitation for the remaining patients with OHCA should ideally not be altered, which poses the risk of worsening CCPR quality in the majority of arrests, which could decrease overall survival. Thus, clear collaboration of hospital

and prehospital systems is required in order to identify ECPR-candidates in the prehospital setting to achieve early transport to hospital.

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Sustained ROSC is deemed to have occurred when chest compressions are not required for 20 consecutive minutes following cardiac arrest.

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FIGURE 1: Cannulation sequence of events

(unless other favorable prognostic features are present: e.g. periods of intermittent ROSC / hypothermia pre-arrest / young age / signs of life during CPR)