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# NEVER SAY NEVER: SUCCESSFUL EXTRACORPOREAL CARDIOPULMONARY RESUSCITATION (ECPR) FOLLOWING A PROLONGED OUT-OF-HOSPITAL CARDIAC ARREST DUE TO SPONTANEOUS CORONARY ARTERY DISSECTION

Laura Canziani, Francesca Orlando, Michele Villa, Tiziano Cassina

Department of Cardiac Annaesthesia and Intensive Care, Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, Lugano, Switzerland

**Corresponding author:** Laura Canziani **e-mail:** laura.canziani@eoc.ch

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## ABSTRACT

*Introduction:* Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) may be a life-saving rescue therapy for patients with severe cardiac disease of any origin and circulatory failure. Data in the literature have demonstrated that the use of advanced mechanical circulation has resulted in improvements in both survival and quality of life; despite this, cardiogenic shock and refractory cardiac arrest remain conditions with high mortality. Opportune identification of patients who can benefit from it may improve outcomes. However, the shortage of guidelines on indications often results in a high mortality rate and poor outcome. Due to ethical issues, randomised controlled studies with VA-ECMO have not been conducted so no recommended evidence-based guidelines exist for VA-ECMO patient-selection criteria. Therefore, the indications depend only on expert opinion after reviewing the literature.

*Case description:* We report the case of a young female patient who presented with an out-of-hospital cardiac arrest (OHCA) due to spontaneous coronary dissection. She was treated with extracorporeal cardiopulmonary resuscitation (ECPR) with excellent results in terms of short and long-term survival, and neurological outcome. This was despite the presence of several clinical and laboratory negative prognostic factors on the basis of the current literature, and the lack of general consensus among the relevant medical personnel.

*Conclusion:* We were able to explain the favourable outcome only on the basis of clinical data. We can conclude that the availability of advanced resources in the area (timeliness of the rescues, quality of the resuscitation, an advanced haemodynamic management centre nearby) has contributed to determining the complete clinical and neurological recovery of the patient.

## KEYWORDS

Extracorporeal cardiopulmonary resuscitation (ECPR), out-of-hospital cardiac arrest (OHCA), hyperlactacidemic metabolic acidosis, neurological outcome

## LEARNING POINTS

- Extracorporeal cardiopulmonary resuscitation to rescue patients with cardiac arrest refractory to conventional cardiopulmonary resuscitation could represent a life-saving technique in carefully selected patients.

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- Refractory out-of-hospital cardiac arrest with evolution to a non-shockable rhythm and severe lactic acidosis are conditions that should not rule out ECPR.
- Evidence-based selection of ECPR patients remains challenging, but it could be considered as a therapeutic option in dedicated specialised centres.

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## INTRODUCTION

Cardiac arrest (CA) is the cessation of myocardial mechanical activity and circulation, which can be confirmed by the absence of a detectable pulse, unresponsiveness and absence of a normal breathing pattern[1].

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is one of the mechanical devices that has been increasingly utilised for organ and circulatory support during refractory CA[2]. Such support in patients where cardiopulmonary resuscitation (CPR) measures are unsuccessful in achieving a sustained return of spontaneous circulation (ROSC), is referred to as extracorporeal cardiopulmonary resuscitation (ECPR)[3]. The use of this technology is time-sensitive and requires specialised equipment and trained providers[4].

Currently, there are only two randomised controlled trials reporting outcomes of ECPR. Observational studies comparing ECPR to historical controls and case-matched controls have demonstrated favourable results for ECPR[5,6]. However, these studies are heterogeneous and survival ranges from 15–50%. Based on the 2015 American Heart Association guideline (updated in 2019), ECPR is given a class IIb recommendation if it is performed rapidly in a specialised centre, and should be used in patients with a potentially reversible aetiology.

We report the case of a young woman suffering from a refractory out-of-hospital cardiac arrest (OHCA) who, despite not meeting all the inclusion criteria suggested in the current scientific literature, was treated with ECPR with an unexpected favourable outcome.

## CASE DESCRIPTION

A 33-year-old woman in good health lost consciousness while in the waiting room of an ambulatory medical centre. She was rescued by the staff present and once the absence of circulation was ascertained, resuscitative manoeuvers were immediately undertaken with external chest compression and an electric shock, given the automated external defibrillator (AED)'s detection of a shockable rhythm. Ventricular fibrillation (VF) was confirmed and a total of six defibrillations were delivered, without getting a return of spontaneous circulation (ROSC) and subsequent transition to pulseless electrical activity (PEA).

The patient was transferred to our haemodynamics unit supported by automated mechanical chest compressor (Autopulse®), and mechanically ventilated after approximately 65 minutes of advanced CPR. There was a prolonged low flow time, the presence of a non-shockable rhythm and a first arterial blood gas analysis showing a critically hyperlactacidemia metabolic acidosis (pH 6.52, lactates 17.52 mmol/l, BE −34.5 mmol/l). After an interdisciplinary discussion, support was changed to an extracorporeal mechanical circulatory support via right femoral veno-arterial access. Approximately 75 minutes after the first symptom, circulation was restored. This allowed for coronary examination, which showed a spontaneous dissection of the ostial left anterior descending (LAD) artery, which was treated by angioplasty and a stent on the CT/LAD and thromboaspiration on the apical LAD. At the end of the procedure, pulsatility of the circulation was resumed with restoration of a sinus rhythm.

After placement of a retrograde perfusion cannula at the level of the femoral artery to ensure a good perfusion of the right lower limb, the patient was transferred to our intensive care unit, haemodynamically supported by VA-ECMO. An initial transoesophageal echocardiography showed severely reduced left ventricular function (FE 25–30%) with septal, apical and anterior wall akinesia.

In the first hours after hospitalisation we could progressively reduce external haemodynamic support, allowing complete weaning after about 48 hours.

The course is characterised by incipient multi-organ failure secondary to post ischaemic insult and venous congestion of the first phase.

On the first day after the CA, upon sedation cessation there was a transient interaction with the patient. However, this was followed by a sudden worsening of the neurological picture with loss of contact: a cerebral CT scan revealed small bilateral subdural blood collections that did not justify neurological impairment. An electroencephalogram revealed moderate diffuse slowing of baseline electrical activity with preserved reactivity, consistent with a nonspecific encephalopathy.

A brain MRI showed multiple diffuse cerebral ischaemic lesions secondary to brain hypoperfusion, and likely thromboembolic events. Thirteen days after the CA, alongside the improvement on the metabolic level, the patient recovered consciousness and a gradual recovery of neurological function followed. Despite the subsequent improvement in gas exchange, it proved impossible to wean the patient off the ventilator because of concomitant neuromyopathy related to the prolonged ICU stay. Therefore, on day 15 a tracheostomy was performed from which the patient was weaned 14 days later, maintaining adequate respiratory exchanges. One week later, the patient was fully alert and able to interact coherently with caregivers and family members; at the time of discharge from the ICU (30 days after the CA) she had an excellent neurological outcome (Cerebral Performance Category scale 2, (CPC 2). The two-year follow-up showed a full recovery with the same quality of life as before the accident.

## DISCUSSION

Use of ECPR for refractory OHCA has been associated with survival rates between 6.9% and 56%[7-10], but the selection criteria between studies varies and may be responsible for the wide range of results. Robust data to identify those patients who may benefit from ECPR are lacking because of the observational nature of investigations, or difficulties in carrying out randomised trials. Protocols and guidelines strive to identify cases most likely to survive with a favourable neurological outcome, such as those patients who are witnessed arresting and where high-quality CPR was initiated rapidly, in addition to a CA with a presumed reversible pathology[11].

The selection criteria adopted at our Institute for the management of patients with out-of-hospital cardiac arrest due to refractory TV/VF (ROSC not obtained after three defibrillation attempts) include the evaluation to an early VA-ECMO in cases of OHCA of probable cardiac origin, ventricular arrhythmia as the first rhythm, age between 18 and 75 years, no contraindications to the use of the automatic chest compressor, and transfer time to the competence centre of up to 40 minutes.

We report this case given the important therapeutic success achieved, despite the initial clinical presentation and the presence of numerous unfavourable prognostic factors. When the patient arrived at our haemodynamics unit, several healthcare providers including cardiac-anaesthesiologists, cardiologists and cardiac-surgeons were unsure about the efficacy or otherwise of continuing resuscitative manoeuvers by ECPR. In addition to the prolonged resuscitation time – although the presenting rhythm was VF – there had been an evolution towards PEA, which was also a negative prognostic element as it suggested an evolution of ischaemic damage.

According to Extracorporeal Life Support Organization guidelines (2021) and until there are more consistent data, it is reasonable to establish adequate ECMO flow within 60 minutes of onset of a CA.

The severe hyperlactacidemic metabolic acidosis also suggested an inauspicious evolution, at least from the neurological point of view, not only on the basis of studies concerning the subject, but also on the basis of our clinical experience. In a recently published retrospective analysis, OHCA patients that had an arterial pH <7.03 prior to the initiation of ECPR had unfavourable neurologic outcomes when compared to patients that had pH ≥ 7.03[12]. Bartos et al. also observed a significant association between neurologically favourable survival and lower serum lactic acid level, higher arterial pH, higher $PaO_2$ and lower $PaCO_2$, with each value being obtained upon arrival of the patient[13]. A meta-analysis by Debaty et al. found that initial shockable rhythm, shorter low flow time, higher arterial pH and lower serum lactate on admission were associated with a favourable outcome in OHCA patients undergoing ECPR[14]. Aside from lab values, the cardiac rhythm preceding ECPR initiation should also be considered. A multi-centre observational study examined the relationship between arrest rhythm and neurological outcome among patients treated with ECPR for OHCA.

Ventricular fibrillation or pulseless ventricular tachycardia (pVT) that was sustained until the initiation of ECPR was significantly associated with a favourable neurological outcome, and patients who initially had VF or pVT but converted to PEA or asystole had no benefit from ECPR[15].

The ARREST trial, the first randomised clinical trial of ECPR versus standard advanced cardiac life support (ACLS) for refractory OHCA with VF[16], was stopped early for prespecified superiority criteria after enrolment of only 30 patients. It demonstrated a significantly higher survival-to-discharge for ECPR compared to standard ACLS (43% vs 7%) and more favourable neurological and functional outcomes at 3 and 6 months. However, a second recently completed randomised clinical trial, the Prague OHCA trial, compared a bundle of interventions including prompt intra-arrest transport, in-hospital ECPR and rapid invasive treatment (n=124), to standard ACLS (n=132) in OHCA of presumed cardiac cause. This trial demonstrated a non-statistically significant difference in the primary outcome of 6-month survival with functional recovery favouring ECPR (31.5% vs 22%, p=0.09)[17]. In a Japanese prospective study, one-month survival with CPC 1–2 was > 30% with low flow time of 40 minutes in those with shockable rhythms, compared to <15% in non-shockable rhythms[18].

Other retrospective analyses have shown favourable outcomes despite prolonged low flow time (>45 minutes) when restricted to younger patients (≤ 43 years)[19].

These data demonstrated how the application of a composite of stringent criteria (age ≤ 65, witnessed CA with bystander CPR, no major comorbidity and the beginning of ECMO within 1 hour from the arrest) could improve the rate of survival with a favourable functional outcome.

In addition to the lack of well-defined inclusion and exclusion criteria, the use of VA-ECMO for resuscitation faces a number of potential complications including haemorrhage, limb ischaemia, renal failure, neurologic injury, infections, and mechanical issues of the ECMO circuit.

On the other hand, we were dealing with a healthy young patient with a proven CA for which resuscitative manoeuvers had begun immediately and with a potentially reversible underlying cause. It was these aspects that led us to proceed with the placement of mechanical haemodynamic support, which consequently allowed the underlying cause to be treated by coronary examination.

## CONCLUSION

The neurological outcome in the medium and long term came as a surprise to those involved.

Survival is a universally reported endpoint, but does not sufficiently characterise the success of ECPR. Measures of functional status, such as the CPC score or modified rankin scale (mRS) are used to assess early post-arrest outcomes. Beyond survival with neurological recovery, it is important to understand long-term functional status and quality of life. In our case, not all presenting criteria were consistent with those reported in the literature; however, our patient had a CPC score of 2 and an mRS of 2, 30 days after CA. The 18 months follow-up showed a Glasgow outcome scale-extended (GOSE) of 8 and an mRS of 0, confirming full recovery and optimal quality of life.

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