CASE REPORT

Extracorporeal cardiopulmonary resuscitation in a patient with severe lactic acidosis: hope for the nearly dead

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Abstract
We present the case of a 45-year-old patient who was brought to our emergency department with an out-of-hospital cardiac arrest. The patient arrived 45 minutes after collapse due to ventricular fibrillation. The initial rhythm at arrival to the emergency department was asystole. His laboratory results showed profound lactic acidosis (lactate of 21 mmol/l and pH of 6.6). Time to arrival, rhythm at presentation and the observed lactic acidosis were all interpreted as prognostic signs of a poor outcome but, despite that, it was decided to treat the patient with extracorporeal cardiopulmonary resuscitation (ECPR). Subsequently percutaneous coronary intervention was performed. In contrast to the poor prognosis, the patient was discharged on day 6 with no discernible neurological deficit. This case illustrates that despite biochemical data suggesting profound tissue ischaemia/hypoxia, the outcome of ECPR may be excellent. Such data cannot be reliably used as a single indicator to decide whether or not ECPR should be initiated.

Introduction
Survival rates in the Netherlands after out-of-hospital cardiac arrest (OHCA) are low.[¹] With each minute of cardiopulmonary resuscitation (CPR) the probability of a good neurological outcome decreases and the vast majority of patients with good neurological outcome achieve return of spontaneous circulation (ROSC) within the first 16 minutes of CPR.[²,³] In selected patients with treatable causes of cardiac arrest, most prominently ventricular fibrillation (VF) in coronary artery disease, the use of extracorporeal cardiopulmonary resuscitation (ECPR) could potentially improve survival and neurological outcome, even after longer CPR times.[⁴,⁵] Survival rates may further improve when the chain of care is optimised.[⁶] We present a case of a young patient with OHCA due to VF who received ECPR after 75 minutes of CPR. Although he presented with a very high lactate and very low pH, he still made an excellent neurological recovery. In this case report, the implications of these findings, the relevant state of the literature regarding this topic and lessons for clinical practice are discussed.

Case report
A 45-year-old man was brought to our emergency department after an out-of-hospital cardiac arrest. The patient had an unremarkable medical history and became unwell when exercising in the gym. Bystanders performed basic life support. Ambulance personnel arrived at the scene within 5 minutes. First cardiac rhythm was VF, which the ambulance personnel promptly converted by two defibrillations. ECG showed ST-segment abnormalities suggesting acute lateral ischaemia. After a short (5 minute) period of ROSC, the VF returned and the patient was shocked again without return to sinus rhythm. The patient received amiodarone and was shocked multiple times. Thirty minutes after cardiac arrest a transient agitational state was observed, while the patient was receiving CPR with the aid of an external device (LUCAS®), which was interpreted as a sign of life. Hereafter the rhythm of the patient changed from VF to pulseless electrical activity and later to asystole. Subsequently, 45 minutes after the initial cardiac arrest, the patient arrived at the emergency department in asystole. The patient was intubated and CPR was continued. Arterial blood gas analysis showed severe acidosis (pH 6.6) and lactataemia (21 mmol/l). A bedside cardiac ultrasound could not generate any reliable images. During rhythm checks pulseless electrical activity was observed. Since the patient was young, the initial rhythm was VF and no sustained return of spontaneous circulation (ROSC) was obtained during conventional treatment, it was decided to initiate ECPR. Our protocol states that patients are only eligible for ECPR if they can be cannulated within 60 minutes after cardiac arrest. Partially due to the long prehospital period, this was not achievable in this case. However, since the patient had shown signs of life after his initial collapse, it was felt that it was reasonable to extend the time limit in this case, although
ECPR in a patient with severe lactic acidosis

the severe lactic acidosis was interpreted as a poor prognostic indicator. Sixty-five minutes after initial cardiac arrest the patient was transferred to the catheterisation lab for venoarterial extracorporeal membrane oxygenation (VA-ECMO) placement and percutaneous coronary intervention. At the time of arrival to the catheterisation room the rhythm had changed back to pulseless electrical activity, but fortunately during cannulation ROSC was obtained although this was accompanied with a low cardiac output. Ultrasound-guided cannulation of the right common femoral artery and vein was performed, and 17 Fr and 25 Fr cannulas were inserted respectively. Eighty-five minutes after initial cardiac arrest or 55 minutes after the last sign of life, the VA-ECMO was running. A distal perfusion cannula was placed in the femoral artery to preserve flow to the right leg. ECMO flow was increased to approximately 4.3 l/min. Clinically, our patient rapidly improved with VA-ECMO. Peripheral oxygen saturation was measurable for the first time. Angiography of the coronary arteries showed an occlusion of the proximal left anterior descending artery, which was successfully treated by implanting a drug-eluting stent. Approximately 60 minutes after starting ECMO, the acidosis improved (pH >7) and lactataemia decreased. Chest X-ray and ultrasonography of the lungs revealed severe pulmonary oedema, which clinically resulted in ‘Harlequin syndrome’. Harlequin syndrome is a clinical syndrome that can develop during peripheral VA-ECMO where the heart pumps poorly oxygenated blood and the ECMO pumps highly oxygenated blood into the aorta, resulting in different oxygen saturation between the upper and lower parts of the body. After increasing PEEP, and increasing ECMO flow, peripheral oxygen delivery improved. Cardiac ultrasound showed opening of the aortic valve; no inotropic support or intra-aortic balloon pump was necessary to support the circulation. Liver function tests were elevated and clinical signs of intestinal ischaemia developed, which were both a result of the ischaemic period. Kidney function, however, was preserved. Cardiac output, when estimated with ultrasound, improved during the first few days of treatment and after temporarily decreasing the ECMO flow, cardiac output improved furthermore. After three days, VA-ECMO could be terminated. In the first days after ECMO initiation the patient was sedated but after ECMO removal, the sedation was stopped. Fortunately, neurological recovery was swift and excellent. He could be extubated on day 5 and had no discernible neurological deficit. The patient was transferred to the cardiology department six days after his initial cardiac arrest without inotropic support and neurologically intact.

Discussion

Overall survival after out-of-hospital cardiac arrest is low. Functional neurological recovery (defined as a modified Rankin Scale 0-3 or a Cerebral Performance Category (CPC 1-2) correlates with the initial rhythm and in the Netherlands is seen in 13.2-18.7% of the patients. With every extra minute of CPR, the probability of a good neurological outcome declines. The fastest way to restore adequate circulation is through ROSC. The vast majority of patients with functional neurological outcome achieve ROSC within the first 16 minutes of CPR. After this time, using our current treatment protocols, the chances of survival with functional neurological recovery are very poor. ECPR, however, may be able to improve circulation and expand time to definitive treatment in cardiac arrest and improve outcome in selected patients. Initial studies have had substantial variations in outcomes in ECPR recipients. Stricter patient selection was deemed to be necessary and shorter low-flow times before initiation of ECPR showed improved outcomes. Recent data from centres of excellence have shown that ECPR with strict inclusion criteria could significantly improve survival with functional neurological outcome. In a recent review and meta-analysis by Debaty et al., substantial variations were observed in functional neurological outcome across primary studies on ECPR in
OHCA. The best results were reported by Yannopoulos et al. in 2016. In this study of 18 patients who suffered an OHCA and received ECPR, half of the population had a functional neurological outcome (CPC 1-2) with no major ECMO-related complications. Overall, the other studies in the meta-analysis by Debaty et al. showed 15% functional neurological outcome, which is still a major leap from outcomes during conservative treatment of OHCA. In our centre, current inclusion criteria for ECPR are: age 18-70 years, witnessed arrest, first rhythm VF or ventricular tachycardia, basic life support initiated within five minutes of collapse. On top of that, our protocol demands that initiation of cannulation for ECPR should be achievable within 60 minutes of initial cardiac arrest. If a patient shows signs of life during CPR, there is room to consider extending this time frame, as happened in this case. Patients who fulfill all the criteria mentioned above are candidates for ECPR. In very specific situations, after consulting with the ECPR team, a patient with an initial non-shockable rhythm (asystole or pulseless electrical activity) may receive ECPR support. At present, the reason for excluding non-shockable rhythms in general is the far worse outcomes of these patients as compared with patients presenting with a shockable rhythm. A recent paper reported observational evidence that shorter low-flow duration, shockable cardiac rhythm, higher arterial pH and lower serum lactate concentration on hospital admission are associated with better outcomes for ECPR recipients after OHCA. Although exact levels of lactate and pH did not reliably predict mortality in this small series, the mean pH and lactate in non-survivors of ECMO after OHCA in this report were pH <7 and lactate >10 mmol/l. In contrast to these results, the outcome in the case presented here shows that both lactate and pH have limitations in predicting functional neurological outcome. Based upon this outcome, we feel that if a patient has a short no-flow time and a limited low-flow time and fulfills all the inclusion criteria, ECPR should not be withheld solely because of severe acidosis or a high lactate level.

To achieve a short low-flow time patients have to be transported to hospital as soon as possible. Alternatively, as has been implemented in Paris, ECMO teams may travel to the patient in order to start ECMO in an out-of-hospital setting. In patients with witnessed OHCA and shockable rhythm who do not achieve ROSC within the first 16 minutes of CPR, there is not much to be gained from further attempts to achieve ROSC in the field. Given the fact that ECPR offers a new treatment modality, it seems reasonable to transport patients who do not achieve ROSC early to an ECPR equipped centre. At this moment, several randomised multicentre trials, such as the INCEPTION trial (ClinicalTrials.gov Identifier: NCT03101787), are investigating the role of ECPR in OHCA. Taken together, the case described above illustrates that, in selected cases, ECPR can be of major benefit to patients with OHCA, independent of a longer downtime and biochemical data suggesting profound tissue ischaemia/hypoxia. In the coming years, multicentre studies will evaluate whether the benefits of ECPR translate to larger patient groups, which patient criteria can predict optimal use of ECMO and what paradigm shifts with regard to out-of-hospital care are required to optimise outcome in these patients.

**Disclosures**

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**References**