Extracorporeal Cardiopulmonary Resuscitation for Refractory Ventricular Fibrillation
A Rescue Bridge To Reperfusion

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**Abstract**: Accumulating evidence suggests benefit of extracorporeal cardiopulmonary resuscitation (E-CPR) in patients with refractory cardiac arrest by using veno-arterial extracorporeal membrane oxygenation. Appropriate patient selection for E-CPR is cumbersome and still debated. We describe a 56-year-old male who developed refractory ventricular fibrillation upon arrival at the emergency department and was successfully treated by urgent E-CPR. Patient selection, complications and the need to adapt the chain of survival are discussed.

**Key words**: E-CPR (extracorporeal cardiopulmonary resuscitation); ECMO (extracorporeal membrane oxygenation); ECLS (extracorporeal life support); out-of-hospital resuscitation; resuscitation

**Introduction**

Conventional management of out-of-hospital cardiac arrest still lacks a satisfactory rate of survival with favourable neurological outcome. Recently, encouraging results have been reported on extracorporeal cardiopulmonary resuscitation (E-CPR) for refractory in- and out-of-hospital cardiac arrest (1-5). Generally, E-CPR is applied by peripheral veno-arterial extracorporeal membrane oxygenation (VA-ECMO). This approach is supported by current guidelines if patient-specific circumstances are optimal, yet, the latter remains ill-defined (4, 6). We report the successful use of E-CPR in a patient with refractory primary ventricular fibrillation (VF).

**Case**

A 56-year old male, known with hypertension, presented with an acute inferior myocardial infarction (Fig. 1) and received acetylsalicylic acid (500 mg) and prasugrel (60 mg) in the ambulance. On arrival at the emergency department, he developed VF and despite advanced life support (ALS) no return of spontaneous circulation occurred. After 15 minutes of resuscitative efforts, VF was considered refractory and E-CPR logistics were initiated as circumstances were judged to be favourable: witnessed ‘in-hospital’ cardiac arrest, immediate professional resuscitation, adequate end-tidal CO₂, defibrillatable rhythm and a medical team readily available to initiate E-CPR. During continued ALS, percutaneous bi-femoral access was achieved (28F venous-, 21F arterial cannula) and after 55 minutes of CPR peripheral VA-ECMO (Prolonged Life Support, Maquet®) at maximum pump flow (4.5 L min⁻¹) was initiated, allowing immediate induction of therapeutic hypothermia (32°C) and zero-balance ultrafiltration. Perfusion of the lower extremities was impaired after bi-femoral cannulation. Yet, placement of selective distal perfusion was omitted to allow immediate cardiac revascularization. Coronary angiography revealed an isolated right coronary occlusion (Fig. 2). After intravenous bolus of unfractionated heparin (10 000 IU) and abciximab (0.25 mg/kg), thrombosisuction, stenting and defibrillation, sinus rhythm ensued. After 60 minutes of VA-ECMO, echocardiography revealed sufficient contractile recovery to wean from extracorporeal support.

The clinical course was complicated by profound rectal bleeding in the absence of transmural intestinal ischemia on exploratory laparotomy. This adverse event necessitated multiple transfusions and cessation of therapeutic hypothermia. On day
two bilateral lower leg compartment syndrome was treated by fasciotomy. Acute kidney injury required continuous renal replacement therapy for 9 days, which recovered completely. A systemic inflammatory response syndrome (SIRS) in the absence of sepsis responded to pharmacological intervention (hydrocortisone 100 mg t.i.d., noradrenaline).

On day two, the patient showed clinical signs suggestive for complete neurological recovery (Glasgow Coma Scale : E4M6Vtube), and could be weaned from mechanical ventilation and discharged home in a good general condition without any neurological sequelae on day 26 after cardiac arrest.

**DISCUSSION**

This case exemplifies the encouraging perspectives of E-CPR reported recently. The favourable neurological outcome observed after a prolonged period of no-flow- and low-flow ischemia supports this novel resuscitation strategy for refractory, seemingly futile situations (1-4). Although E-CPR has been shown to improve survival (~15-30%) if conventional resuscitation fails, adequate patient selection remains a major point of concern (3, 4). Although no definite criteria for E-CPR exist, a witnessed cardiac arrest, ventricular fibrillation as initial rhythm, a presumed age < 65 years, absence of severe comorbidities, admission during regular working hours seem important prerequisites to allow a satisfactory outcome (3, 4, 6).

E-CPR has to be readily available to keep post-arrest ischemic intervals as brief as possible. A low-flow ischemia time ≤ 100 minutes has been proposed as possible indication for E-CPR (4). Although shorter periods, i.e., < 60 minutes as met by our case, might be more appropriate to avoid unfavourable neurological sequelae and systemic inflammation and multi-organ failure.

Despite the short period of low-flow ischemia (< 60 minutes), our patient developed a systemic inflammatory response syndrome (SIRS). SIRS is a clinical syndrome that is characterised by a dysregulated inflammation and affects the whole body. Causes can be infectious and non-infectious (7). Global ischemia and the blood contact with the VA-ECMO circuit are likely non-infectious causes in our case. Moreover, release of various pro-inflammatory mediators ensues after restoration of blood flow, whereas anti-inflammatory mediators such as nitric oxide and prostacyclin are depressed. These complex and intermingled mechanisms promote the SIRS response and potentially exaggerate tissue damage (8).

STEMI warrants early revascularization. The preferred strategy is early, primary PCI and combined inhibition of thrombocyte aggregation and anticoagulation (9). After cardiac arrest marked alterations in coagulation properties have been reported (8). Therapeutic hypothermia, E-CPR, antplatelet therapy and anticoagulation will significantly derange the coagulation system and face clinicians with intriguing dilemmas in individuals resuscitated by E-CPR. In this case all therapeutic efforts to adequately revascularize the myocardium led to profound rectal bleeding and the decision was made to cessate the therapeutic hypothermia.

Vascular complications related to cannulations in VA-ECMO remain an important point of concern and as much as 18% of patients receiving VA-ECMO have been reported to develop limb ischemia (10). Unfortunately, our patient showed bilateral compartment syndrome of both lower extremities after an episode of global low-flow ischemia. On the arterial side, the compartment syndrome is likely promoted by ischemia-reperfusion injury after transient absence or compromise of perfusion distal to the cannula insertion site in the femoral artery. On the venous side, the large-sized cannula might have caused venous congestion.
within the leg, although no evident clinical signs, e.g., swelling, pointed in that direction.

Whether the sizes of the cannulae chosen in our case have importantly contributed to this complication remains elusive. Ganslmeier et al. showed no differences in leg ischemia using varying cannula sizes (13-19 Fr) using percutaneous access. Moreover, survival was shown to be independent of ischemic complications. Although, in an emergency situation, as in our case, the use of ultrasound may not always be possible, it has been shown that percutaneous cannula placement is safe, accurate and achieves optimal flows if the vessel can properly be visualized (13).

In general, the percutaneous Seldinger technique for vessel cannulation may be preferred for E-CPR due to ease and speed. In order to improve its success rate and avoid vascular complications, ultrasound guidance should be considered if available. However, in patients with known occlusive arterial disease or small vessels it may be virtually impossible to apply percutaneous acces and thus surgical exploration is warranted as suggested by Bidas et al. (11). Alternatively, a hybrid technique, in which the artery is exposed by cut down and the actual cannulation is performed with a Seldinger technique can also be considered if vascular access is extremely difficult (12).

Currently, most operators prophylactically insert a distal perfusion catheter in the femoral artery in order to prevent limb ischemia. This procedural step is imperative in elective and semi-elective cannulations of the femoral artery, since limb ischemia might occur in up to 21% of patients who do not receive adequate antegrade perfusion (14). Importantly, patients who receive prophylactic antegrade perfusion have been reported to remain free of limb ischemia during extracorporeal support (14). In our case, we omitted distal, antegrade femoral artery perfusion due the urgency of E-CPR, but in retrospect this decision might not have been ideal although rapid weaning from extracorporeal support was realised within an hour.

Early detection of limb ischemia or compartment syndrome is essential in limiting damage and permanent functional sequelae. Clinically, we monitor the cannulated extremities by visual inspection, surface temperature, and capillary refill properties every hour. In addition, continuous measurement of oxygen saturation of the toes, Doppler detection of peripheral pulses is performed every hour. Every 8 hours creatinine kinase levels are measured. Recently, near infrared spectroscopy (NIRS), a non-invasive technique to measure tissue oxygenation has been advocated as complementary technique to monitor limb ischemia (15). Although NIRS has been proven useful to detect ischemia after femoral artery cannulation its clinical usefulness has yet to be determined (15).

In this case, the prerequisites for a successful outcome after E-CPR were optimally met and a full recovery was accomplished despite the occurrence of several complications. The patient collapsed on the hospital doorstep and the E-CPR team was readily available. Yet, especially in out-of hospital arrest, it remains extremely challenging to limit no-flow and low-flow ischemic intervals. In order to strive for minimal delays and optimal outcome after E-CPR all crucial elements of the ‘chain of survival’ have to be considered. In this context, a practical ‘hyperinvasive approach’ incorporating E-CPR has recently been proposed for out-of-hospital cardiac arrest and awaits further evaluation (16).

A more widespread acceptance of E-CPR will depend on accumulating evidence for appropriate patient selection, well-organised logistics, optimised post-E-CPR care and superior outcome compared to conventional treatment.

References