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Clinical paper

Extracorporeal life support associated with hypothermia and normoxemia in refractory cardiac arrest☆

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ABSTRACT

Aim: We describe a 1-year experience with extracorporeal cardiopulmonary resuscitation (ECPR) for in-hospital (IHCA) and out-of-hospital cardiac arrest (OHCA) associated with intra-arrest hypothermia and normoxemia.
Methods: Since January 1st 2012, ECPR has been applied in our hospital to all patients less than 65 years of age and without major co-morbidities who develop refractory cardiac arrest (CA) with bystander CPR. Over a 1-year period of observation, we recorded 28-day survival with intact neurological outcome and the rate of organ donation.
Results: During the observational period, 24 patients were treated with ECPR, with a median age of 48 years. Ten patients had IHCA. Acute coronary syndrome and/or major arrhythmias were the main cause of arrest. Intra-arrest cooling was used in 17 patients; temperature on ECMO initiation in these patients was 32.9 °C [32–34]. The time from collapse to ECPR was 58 min [45–70] and was shorter in survivors than in non-survivors (41 min [39–58] vs. 60 min [55–77], $p = 0.059$). Non-survivors were more likely to have coagulopathy and received more blood transfusions. Six patients (25%) survived with good neurological outcome at day 28. Four patients with irreversible brain damage had organ function suitable for donation.
Conclusion: ECPR provided satisfactory survival rates with good neurologic recovery in refractory CA for both IHCA and OHCA. ECMO may help rapidly stabilise systemic haemodynamic status and restore organ function.

1. Introduction

Unexpected cardiac arrest (CA) remains a major problem worldwide[1,2] even though in-hospital survival has doubled from about 10% to more than 20% over the last decade.[3] Rates of clinically significant neurological disability among survivors have also decreased over time, with a risk-adjusted rate of 33% in 2000 to around 28% in 2009 in a large study by Girotra et al.[3] The outcome of CA survivors depends on several factors, including the location of arrest, with better outcomes for in-hospital (IHCA) compared to out-of-hospital (OHCA) CA, the initial rhythm (better outcomes for shockable than non-shockable rhythms), and the cause of cardiac arrest (better outcomes for cardiac origin than for others).[4–9] The duration of cardiopulmonary resuscitation (CPR) is also an important prognostic factor; indeed, the probability of achieving return to spontaneous circulation (ROSC) decreases rapidly when the duration of CPR exceeds 10 min and dramatically after 30 min.[2,10,11] Although hospitals that provide longer duration CPR may have higher ROSC and hospital discharge rates than others,[10] prolonged CPR is associated with a higher rate of unfavourable neurological outcome when compared to shorter CPR. Additional interventions to improve systemic perfusion and attenuate the extent of cerebral injury are, therefore, necessary in this setting.

Extracorporeal membrane oxygenation (ECMO) could facilitate ROSC and provides adequate organ perfusion, especially in the brain, during resuscitation. ECMO has been used as a therapeutic option during refractory CA since 1976, the so-called extracorporeal CPR (ECPR),[12] in specific situations, such as hypothermic CA, drug intoxication and in the post-operative period. In the recent AHA/ESC guidelines,[4] ECPR was only mentioned as a potential treatment to be considered in experienced centres where the technique is rapidly available, in patients with a short arrest period before CPR initiation and when the condition leading to the CA was reversible or amenable to coronary revascularisation or heart transplantation. Recent studies have suggested that ECPR may be effective for patients with refractory IHCA,[13–14] increasing the rate of successful defibrillation and extending the duration of

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resuscitation with good neurological recovery. For OHCA, the data are scarce and conflicting.[14,16] Moreover, previous studies have not considered the combination of intra-arrest hypothermia during ECPR or the control of blood oxygenation to avoid potential hyperoxia-induced injury during reperfusion.[17]

We report our experience with a 1-year programme of ECPR, used for IHCA and OHCA, combined with intra-arrest hypothermia and early oxygen control at the initiation of ECMO.

2. Patients and methods

This study was performed in the 35-bed Department of medico-surgical intensive care of the Erasme university hospital in Brussels, Belgium, where a 24/24-h ECPR programme was initiated on January 1st 2012. All consecutive patients undergoing ECPR for IHCA or OHCA were included in a prospective database. The local Ethics Committee approved the study.

2.1. Setting and study population

Erasme Hospital is a tertiary university hospital located in the west of Brussels. The hospital has 864 beds and a 24/24-h facility for coronary angiography and percutaneous coronary intervention (PCI). Patients with CA can be admitted by medicalised or non-medicalised ambulances, the staff of which are all aware of the ECPR programme. Patients were eligible for ECPR if the following criteria were met: (a) witnessed cardiac arrest with immediate CPR (<5 min from call to chest compression); (b) refractory CA, as defined by the absence of ROSC after 10 min of Advanced Life Support (ALS); (c) age less than 65 years and no major co-morbidity; (d) the ability to initiate ECMO within 1 h from arrest. Patients weighing less than 30 kg, patients with severe co-morbidities (terminal illness, cancer, end-stage liver cirrhosis, pre-existing severe cognitive impairment) and patients with CA associated with uncontrolled bleeding were not treated with ECPR. The age limit was chosen based on poor survival in previous reports in patients above that age who underwent ECPR[18] and local guidelines on left ventricular assistance device (LVAD) implantation. Indeed, LVAD implantation in Belgium is recommended only in patients who can be listed for cardiac transplantation and 65 years is the usual upper age limit for this procedure in our institution.

2.2. ECPR management

In patients with OHCA, the pre-hospital emergency medical team provided ALS according to the European guidelines,[19] including early defibrillation, intravenous line insertion, adrenaline (epinephrine) administration and endotracheal intubation. Mechanical chest compression (LUCAS device, Physio-Control, Medtronic, Kerkrade, The Netherlands) was initiated after 5-min of CPR in all patients. Intra-arrest hypothermia (Rhinochill device, Benechill Inc., San Diego, CA, USA) was implemented immediately after endotracheal intubation, whenever possible. After 10 min of CPR, the team leader called the senior intensivist at our institution, who evaluated the indication for ECPR. If the patient was eligible, the intensivist organised admission to the "shock-lab", a 4-bed unit fully equipped for aggressive management, which is located between the ICU and the Emergency Department (ED) and coordinated implementation of ECMO. The ECMO team includes one cardiothoracic surgeon and a resident in surgery, one intensivist, one perfusionist, two ICU nurses and one nurse from the operating room. In IHCA, patients are transferred from the floor to the "shock-lab" after 5–10 min of unsuccessful CPR. The senior intensivist then evaluates the patient for ECPR. In-hospital CPR was standardised as for OHCA. During all process, CPR was performed according to guidelines[19] up to ROSC or ECMO flow initiation, whichever came first.

On admission, absence of spontaneous circulation was confirmed and CPR was continued. If the rectal temperature was above 34 °C, 30 ml/kg intravenous cold (4 °C) saline fluid was rapidly infused to reach the desired temperature range of 32–34 °C. Veno-arterial ECMO was implanted surgically with femoro-femoral heparin-coated cannulation (20-22Fr arterial cannula and 22-24Fr venous cannula, Edwards Lifesciences, Irvine, CA, USA). A centrifugal blood pump (Revolution blood pump, Sorin, Milano, Italy) was initially set at a blood flow of 3–4 l/min (based on the body surface area). ECMO priming consisted of 700 ml of Plasmalyte solution (Baxter Healthcare Corporation, Deerfield, USA). At the end of the implantation, the leg was perfused with an anterograde single lumen 8Fr catheter (Arrow Inc., Reading, PA, USA) to prevent limb ischaemia (Electronic Fig. 1). Time to ECMO, defined as the time between collapse and ECMO initiation, was recorded. A heat exchanger on the ECMO circuit was used to maintain body temperature at 33 °C for 24 h. The patient was then slowly rewarmed (less than 0.5 °C per hour).

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During CPR, transoesophageal echocardiography was performed to identify a possible cause of the CA and to confirm the correct position of the venous cannula in the inferior vena cava at its entry to the right atrium. After ECMO implantation, the ICU physician inserted an echo-guided radial or brachial arterial catheter (Vygon, Ecouen, France) in the right arm. FiO_2 and air flow of the ECMO oxygenator (EOS, Sorin, Milano, Italy) were adapted to maintain PaO_2 between 60 and 150 mmHg and $PaCO_2$ between 35 and 45 mmHg, with a prior adaptation of the ventilator for a protective ventilation associated to the lowest FiO_2 using the right arm arterial catheter. When it was not achieved, veno-venous ECMO was added. Monitoring of heart function, and in particular the impact of ECMO on left ventricular afterload, was performed in all patients with echocardiography and/or with pulmonary artery catheter. Systemic anticoagulation was achieved by intravenous administration of unfractionated heparin; however, the timing of initiation of anticoagulation depended on the presence of clinical signs of bleeding and was generally started after 24 h. Optimal mean arterial pressure (MAP, usually >70 mmHg) was achieved by adjusting ECMO blood flow (to a maximum of 5 l/min) or by giving noradrenaline. In patients with no other obvious cause of cardiac arrest, PCI was performed just after ECMO implantation and haemodynamic stabilisation.

2.3. Definitions

Coagulopathy was defined as an international normalised ratio (INR) of the prothrombin time (PT) >1.5 or platelet count <50,000/μl.[20] Massive bleeding was defined as transfusion of 10 RBC units in 24 h or 4 RBC units in 1 h.[21] Patients with major bleeding were treated with fluids and blood products (to keep the haemoglobin level >7 g/dl and the ratio between RBC and fresh frozen plasma close to 1 after the fourth unit).

Acute renal failure was defined as a urine output <0.5 ml/kg for more than 6 h, and/or an increase in serum creatinine by at least 0.3 mg/dl.[22] Hypoxic hepatitis was defined as an increase in serum aminotransferase activity reaching at least 20-fold the upper limit of normal (normal ranges: serum aspartate transaminase (AST) ≤35 UI/L serum alanine aminotransferase (ALAT) ≤45 UI/L).[23]

The neurological assessment was performed at ICU and hospital discharge using Glasgow-Pittsburgh Cerebral Performance Categories (CPCs) at the discontinuation of sedative agent (midazolam