Clinical paper

Safety and feasibility of prehospital extra corporeal life support implementation by non-surgeons for out-of-hospital refractory cardiac arrest

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ABSTRACT

Background: Extra corporeal life support (ECLS) has been recently introduced in the treatment of refractory cardiac arrest (CA). Several studies have assessed the use of ECLS in refractory CA once the patients reach hospital. The time between CA and the implementation of ECLS is a major prognostic factor for survival. The main predictive factor for survival is ECLS access time. Pre hospital ECLS implementation could reduce access time. We therefore decided to assess the feasibility and safety of prehospital ECLS implementation (PH-ECLS) in a pilot study.

Methods and results: From January 2011 to January 2012, PH-ECLS implementation for refractory CA was performed in 7 patients by a PH-ECLS team including emergency and/or intensivist physicians and paramedics. Patients were included prospectively and consecutively if the following criteria were met: they had a witnessed CA; CPR was initiated within the first 5 min of CA and/or there were signs of life during CPR; an PH-ECLS team was available and absence of severe comorbidities. ECLS flow was established in all patients. ECLS was started 22 min (±6) after the incision, and 57 min (±21) after the onset of advanced cardiovascular life support (ACLS). In one patient, ECLS was stopped for 10 min due to an accidental decannulation. One patient survived without sequelae. Three patients developed brain death.

Conclusions: This pilot study suggests that PH-ECLS performed by non-surgeons is safe and feasible. Further studies are needed to confirm the time saved by this strategy and its potential effect on survival.

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1. Introduction

Extra corporeal life support (ECLS) has been recently introduced in the treatment of out-of-hospital cardiac arrest (OHCA).1–3 ECLS is the use of a mechanical device to temporarily support heart or lung function during cardiopulmonary failure, leading to organ recovery or replacement and allowing time for neurological assessment. Current guidelines state that ECLS should be considered where ECLS is readily available and when the time without blood flow is brief and the condition leading to the cardiac arrest is reversible (e.g. accidental hypothermia or drug intoxication), or amenable, to heart transplantation (e.g. myocarditis) or revascularisation (e.g. acute myocardial infarction).4–6 Improvement of survival was noted with ECLS for in-hospital cardiac arrest (IHCA).7–9 but its use is controversial in OHCA.10–12 A negative effect of prolonged CPR has been reported13,14 and several studies have evaluated the implementation of ECLS at hospital arrival.15–18 In contrast, there have been only case reports on pre-hospital ECLS insertion for OHCA.11–13 Obvious limitations to the use of pre-hospital ECLS include the complexity of out of hospital cannulation, instrumentation, and perfusion implementation.

Acute coronary artery thrombosis is the most frequent cause of OHCA.14,15 Percutaneous coronary intervention (PCI) seems to improve survival. Implantation of ECLS in refractory OHCA could allow direct transportation to a catheterization laboratory for PCI.
Pre-hospital ECLS could therefore potentially be a bridge to therapies treating the cause of arrest such as PCI. We therefore performed a prospective observational study to assess the feasibility and safety of pre-hospital extra corporal life support implementation (PH-ECLS).

2. Methods

2.1. Patients

From January 2011 to January 2012 all out-of-hospital refractory cardiac arrest patients treated by our mobile intensive care unit (MICU) were eligible for PH-ECLS treatment. This prospective observational study received approval from our institutional review board (CPP Ile de France II: A00829-34, Paris, France). According to French regulations for life-threatening situations, information was given to the patient’s relatives, and/or to the patient in cases of survival, after inclusion.

Cardiac arrest was defined as refractory after 30 min of unsuccessful advanced cardiovascular life support (ACLS) performed by a MICU team (one or two emergency physicians, one nurse, and one-paramedic).\(^{16}\) The delay of 30 min was chosen to follow French guidelines on the treatment of refractory cardiac arrest, and is supported by international guidelines.\(^ {17}\) The inclusion criteria were also chosen in accordance with French guidelines.\(^ {17}\) Patients were included if: (1) they had a witnessed cardiac arrest, (2) CPR was initiated within the first 5 min after the collapse (no-flow time) and/or there were signs of life during CPR (for example pupillary reactivity, spontaneous movement, or spontaneous breathing), (3) a PH-ECLS team was available (since this was a pilot study, a PH-ECLS team was not always available for logistical reasons), (4) known absence of severe comorbidities, (5) the cardiac arrest was not due to a toxic cause or severe hypothermia, and (6) age of less than 70 years.

2.2. ECLS protocol implementation

The PH-ECLS team included two senior emergency and/or intensivist physicians, one nurse, one paramedic and one logistician. All PH-ECLS team members had received special training in the management of ECLS from the intensive care unit (ICU) and cardiac surgery departments. The PH-ECLS team was equipped with a new generation of transportable ECLS devices (Cardiohelp\(^{6}\) Maquet\(^{6}\), Rastatt, Germany). All the equipment was pre-arranged in two portable bags. On-site transfusion of blood, frozen plasma and platelets was possible.

In Paris, management of OHCA involves 5 MICU stations with a total of 8 MICUs. On witnessed call and in suspected cases of sudden cardiac arrest, the closest emergency unit is dispatched on the scene. Out-of-hospital resuscitation is delivered by an emergency team, which includes at least one trained physician in emergency medicine according to the European Society of Cardiology guidelines. The SAMU (Service d’Aide Médicale Urgente) in Paris provides pre-hospital care for over 10 million inhabitants during the day and 2,250,000 during the night in an area of 105 km\(^2\). The PH-ECLS team was pre-alerted by the dispatch center of all cardiac arrest cases meeting the inclusion criteria. This team was ready to reach the scene in less than 10 min, by ambulance or car. After 10 min of ACLS, the MICU on scene (the first tier response) confirmed that ECLS was indicated, and the failure of ACLS. If the PH-ECLS team was not available, the patient was transported to a hospital for in-hospital cannulation after at least 20–30 min of ACLS according to French guidelines.\(^ {17}\) When available, the PH-ECLS team was then deployed as a second tier response. The MICU medical staff and the PH-ECLS team together made the definitive decision that ECLS treatment was indicated after 30 min of unsuccessful ACLS, after which the insertion procedure was then begun. (Fig. 1) During the cannulation the initial resuscitation continued without interruption including mechanical ventilation and automated chest compression (using Autopulse\(^{6}\) Zoll\(^{6}\) or LUCAS\(^{6}\) Jolife\(^{6}\)) until the start of ECLS.

ECLS insertion was done directly on site. The femoral area was chosen as the insertion site and cannulation implemented using the Seldinger technique. Insertion was performed after an incision and exposure of the Scarpa’s triangle to access the vessels. The femoral artery and the vein were partially separated on the anterior face. Insertion was done under visual guidance. During this time, the nurse primed the ECLS on site. The equipment included heparinized polyvinyl chloride tubing, a membrane oxygenator (HLS\(^{6}\), Maquet\(^{6}\), Rastatt, Germany) and venous and arterial femoral cannulae (HLS\(^{6}\), Maquet\(^{6}\), Rastatt, Germany). Pump flow was initially set at 2.5–4L per min. Arterial and central venous catheters with SCVO\(_2\) monitoring were inserted as soon as possible, continuously measuring the mean arterial blood pressure and allowing frequent blood sampling. To avoid limb ischemia an antegrade reperfusion catheter for the homolateral limb was inserted as soon as possible. To minimize the possibility of coagulopathy two units of blood and two of frozen plasma were transfused. This practice was warranted by the previously described high rate of disseminated intravascular coagulopathy (DIC) in refractory CA\(^{18}\) and the delay in obtaining blood products in a pre-hospital setting. The on site target objectives to optimize organ perfusion were a mean arterial blood pressure >60 mmHg. To reach this objective a dobutamine infusion associated with norepinephrine after fluid resuscitation was allowed. The ECLS hemoglobin-monitoring device was used continuously and a blood transfusion was performed to maintain a hemoglobin level at least at 10 g.dl\(^{-1}\). In case of clinical disseminated intravascular coagulation (DIC) or major bleeding during insertion, the MICU could transfuse more blood, frozen plasma, platelets, fibrinogen and tranexamic acid. At the start of the ECLS process, an injection of bicarbonate 8.4% was administered, and as soon as possible a blood sample would be drawn to adapt the therapy.

To guarantee the good placement of the venous cannula tip transthoracic echocardiography was performed during the pre-hospital phase.

Sterile insertion conditions were respected and infection prevented by intra-venous administration of 2 g of amoxicillin and clavulanic acid.

Hypothermia was also started in the pre-hospital phase by infusion of fresh saline serum (1 L) and by priming the ECLS with another 1.5 L.
2.3. In-hospital care

Possible causes of cardiac arrest were assessed by gathering past medical history and the circumstances of the arrest. Transthoracic echocardiography and electrocardiogram were performed as soon as an electrical activity was noted. Patients with a suspicion of acute myocardial infarction were transported directly to a cardiac catheterization laboratory and an immediate coronary angiogram followed if necessary by percutaneous coronary intervention (PCI) was performed.

In ICU, the target objectives were to optimize organ perfusion with a partial pressure of oxygen (PaO\textsubscript{2}) >100 mmHg, normocapnia, mean arterial blood pressure >60 mmHg, hematocrit level >35%. If; necessary fluids, blood transfusion or vasopressive drugs (nor-epinephrine or epinephrine) were administered. Dobutamine was systemically infused to prevent pulmonary edema under ECLS. If needed, an intra-aortic diastolic balloon pump was inserted via the contralateral femoral approach. The SCVO\textsubscript{2} was monitored con- tinuously, with an objective of SCVO\textsubscript{2} >70%. When the return of spontaneous circulation occurred, hemodynamic status was moni- tored by continuous cardiac output monitoring devices (Vigileo\textsuperscript{6}, Edwards\textsuperscript{6}), and by echocardiography at regular intervals.

Mild hypothermia, with a target body temperature between 32 and 34 °C, was maintained during the first 12–24 h, and neuro- muscular blocking agents with sedatives drugs were systematically administered. The depth of anesthesia was monitored by continued analyses of EEG (BIS\textsuperscript{8}), and neuromuscular responses by a “trend of four”. Minimum lung ventilation was maintained to avoid pul- monary collapse during ECLS with a tidal volume of 4–5 mL kg\textsuperscript{-1}, a respiratory rate of six breaths per minute and positive end-expiratory pressure of 5 cm H\textsubscript{2}O. To prevent the coagulation in the membrane oxygenator, unfractionated heparin was intravenously administered at a low dose during ECLS, with repeated controls to maintain an activated clotting time ratio >2.0. The hemostasis condition was carefully monitored. In case of DIC, transfusions of blood, frozen plasma, platelets and fibrinogen were performed. In cases of documented acute coronary syndrome aspirin (75 mg), and clopi-dogrel (75 mg) were administered daily. A proton pump inhibitor was also administered to prevent upper gastrointestinal bleeding. In case of inhalation, antibiotics were prescribed.

Sedation was stopped after a 12–24 h period of mild hypother- mia, and the patient’s neurological status (via clinical examination and electroencephalogram) was regularly checked.

The weaning and withdrawal from ECLS required echocar- diographic assessments of myocardial function (left ventricular ejection fraction >50%) and arterial blood PaO\textsubscript{2}-to-FIO\textsubscript{2} (fraction of inspired oxygen) ratio >150 mmHg. Pump flow was progressively reduced according to the hemodynamic status. Discontinuation of ECLS was based upon evidence of uncontrolled multiple organ fail- ure (MOF), massive bleeding or brain death.

2.4. Measurements

The following variables were recorded according to the Utstein reporting style for cardiac arrest: age, sex, delay from collapse to basic CPR and to advanced cardiovascular life support (ACLS), numbers of shocks delivered by an automatic external defibrillator, initial cardiac rhythm on ACLS, use of vasopressor and the sup- posed cause of cardiac arrest. During CPR, signs of life (respiratory gasps, movements, pupillary reactivity) were noted. We recorded all ECLS complications such as bleeding, disseminated intravascular coagulation (DIC), and infection. During the ECLS procedure, different times to the following end-points were collected: incision-time, venous cannula insertion-time, arterial cannula insertion-time and the starting of ECLS-time. During the hospitalization phase the length of stay and neurological evolution with the Glasgow Out- come Scale score (GOS) were noted.

2.5. Statistical analysis

Categorical variables were compared with χ\textsuperscript{2} test or Fischer’s exact test and continuous variables with Student’s t-test.

3. Results

During the study period, we performed PH-ECLS on seven out-of-hospital refractory cardiac arrest patients with presumed cardiac origin (Tables 1 and 2). The population characteristics were: mean age 42 years (±16), six men/one woman. The majority of car- diac arrests took place outside of the patient’s home (n=4, 57%) (Table 1). Five patients (71%) received shocks delivered by an automatic external defibrillator. The first rhythm noted by the MICU was ventricular tachycardia or fibrillation in five cases (71%). The causes of cardiac arrest were acute coronary syndrome (n=4, 58%), hyper- trophic cardiomyopathy (n=2, 29%), and cardiomyopathy-related dysrhythmia (1, 12%). The mean no-flow period was 4 min (±4); however only three patients had a no-flow period of less than 5 min. Four patients had signs of life during CPR at ECLS insertion time (57%).

ECLS flow was established in all patients. ECLS was started with an average of 22 min (±6) after the incision, and an average of 57 min (±21) after the onset of ACLS. The mean low flow period (the delay between starting CPR and establishing ECLS) was 72 min (±12 min). For one patient, the pump was stopped for 10 min during the pre-hospital phase after an accidental decannulation.

During the first 24 h after ECLS insertion, three patients (43%) required massive blood transfusions (of more than six red blood cell units), one patient received thrombolysis for suspected pulmonary embolism before ECLS, and DIC was present in two patients (29%).

Four patients (57%) underwent diagnostic procedures before ICU admission. A coronary angiogram was performed in four because of clinical and electrocardiographic findings suggesting acute coronary syndrome (3 patients) and a previously known coro- nary artery lesion in one. No significant coronary artery lesion was noted in the first three and the pre-existing coronary artery lesion was treated by balloon angioplasty in the last patient. Hyper- trophic cardiomyopathy was diagnosed in two patients (28%). One

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Results.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehospital ECLS</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>7</td>
</tr>
<tr>
<td>Mean age; mean ± SD</td>
<td>42; ±16</td>
</tr>
<tr>
<td>Site of cardiac arrest, n (%)</td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>3 (43)</td>
</tr>
<tr>
<td>Public location</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Street</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Sport</td>
<td>2 (29)</td>
</tr>
<tr>
<td>Ventricular fibrillation or tachycardia, n (%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>No flow (min); mean ± SD</td>
<td>4; ±4</td>
</tr>
<tr>
<td>Delay from cardiac arrest to effective ECLS (min); Mean ± SD</td>
<td>79; ±15</td>
</tr>
<tr>
<td>Delay from start CPR to effective ECLS (min); Mean ± SD</td>
<td>72; ±12</td>
</tr>
<tr>
<td>Delay from start ALS to effective ECLS (min); Mean ± SD</td>
<td>57; ±21</td>
</tr>
<tr>
<td>Delay from incision to effective ECLS (min); Mean ± SD</td>
<td>22; ±06</td>
</tr>
<tr>
<td>Survival at 7 days, n (%)</td>
<td>2 (28%)</td>
</tr>
<tr>
<td>Survival at 90 days, n (%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Brain death, n (%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>Organ donation, n (%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>DIC, n (%)</td>
<td>2 (29%)</td>
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</table>
patient (14%) had an immediate CT scan for suspected pulmonary embolism, which was not confirmed.

Six patients died. The length of stay was six days (±7.5). The causes of death were brain death (n = 3; 50%), refractory MOF (n = 1; 17%), post CPR thoracic trauma with hemorrhagic shock (n = 1; 17%), limitation of care for post anoxic coma (n = 1; 17%). In two patients with confirmed dead brain status, organ donation procedure was carried out after obtaining the consent of the families.

The survivor had hypertrophic cardiomyopathy with refractory ventricular fibrillation. CPR was performed immediately after the onset of arrest and the low-flow time was 75 min. The weaning and withdrawal from ECLS was possible at day Two. The patient received an implantable automatic defibrillator.

For one patient, a severe previous past medical history was identified in ICU which would have contraindicated the use of ECLS.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/age</th>
<th>No flow</th>
<th>First rhythm</th>
<th>Signs of life per CPR</th>
<th>Low flow CPR-ECLS</th>
<th>Diagnosis</th>
<th>Length of stay in ICU</th>
<th>CPC</th>
<th>Brain death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/54</td>
<td>9</td>
<td>VF</td>
<td>Y</td>
<td>88</td>
<td>Ischemic</td>
<td>1</td>
<td>5</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>M/34</td>
<td>0</td>
<td>VF</td>
<td>Y</td>
<td>75</td>
<td>Hypertrophic cardiomyopathy</td>
<td>21</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>M/46</td>
<td>5</td>
<td>VF</td>
<td>N</td>
<td>81</td>
<td>Ischemic</td>
<td>1</td>
<td>5</td>
<td>Y</td>
</tr>
<tr>
<td>4</td>
<td>F/29</td>
<td>12</td>
<td>VF</td>
<td>Y</td>
<td>80</td>
<td>Rhythmic</td>
<td>4</td>
<td>5</td>
<td>Y</td>
</tr>
<tr>
<td>5</td>
<td>H/28</td>
<td>16</td>
<td>VF</td>
<td>Y</td>
<td>98</td>
<td>Hypertrophic Cardiomyopathy</td>
<td>3</td>
<td>5</td>
<td>Y</td>
</tr>
<tr>
<td>6</td>
<td>H/45</td>
<td>1</td>
<td>AS</td>
<td>N</td>
<td>52</td>
<td>Cardiomyopathy-related dysrhythmia</td>
<td>12</td>
<td>5</td>
<td>N</td>
</tr>
<tr>
<td>7</td>
<td>H/59</td>
<td>4</td>
<td>AS</td>
<td>N</td>
<td>72</td>
<td>Ischemic</td>
<td>2</td>
<td>5</td>
<td>N</td>
</tr>
</tbody>
</table>

M, male; F, female; VF, ventricular fibrillation; AS, asystole; Y, yes; N, no; CPC, cerebral performance category scale.

4. Discussion

The main result of this study is that PH-ECLS is feasible and safe when performed by experienced and trained MICU teams.

To our knowledge, this is the first study of pre-hospital use of ECLS by emergency and/or intensive care physicians in the field. Previous studies have reported ECLS implantation by emergency or intensivist physicians in settings such as ICU and emergency departments (ED). Arlt and Lebreton reported two cases of PH-ECLS implementation; however the procedure was performed by a surgical team dispatched to the scene. In one case, the surgical ECLS team was already on standby at the scene, and in the other ECLS was implemented after prolonged resuscitation of a pediatric patient. No survival was observed in these two cases.

Obvious limitations to the pre-hospital use of ECLS are difficulties of cannulation, complexity of ECLS priming and logistic considerations in a non-controlled environment. In our report, we observed that adequate training of emergency and/or intensivist physicians by a cardiac surgical team and a previous experience acquired in ICU, allowed for successful cannulation without major complication in the pre-hospital setting. This included theoretical and practical training with a cardiac surgeon. The management of ECLS, training was done in collaboration with a cardiac surgery team and the industry. From a logistics point of view, experience with ECLS during transport was gained from the inter-hospital exchanges of Acute Respiratory Distress Syndrome (ARDS) patients related to a H1N1 pandemic flu outbreak.

New generations of ECLS devices were specially designed for transportation. This was especially helpful as it simplified procedures for the circuit priming and the pump settings were established and taught to nurses and paramedics.

A key factor in successful insertion may also be the technique we have adapted for this procedure. This insertion technique is simpler to perform than complete surgical denudation during the on going cardiac massage on a patient lying on the floor. We also decided not to use the more classic percutaneous insertion, suggested for use in emergency departments, partly because ultrasonography was not easy to perform at the scene. Furthermore, ultrasound vessel tracking during cardiac arrest was difficult due to the absence of flow and the movements induced by the CPR. Moreover, this technique allows an effective ECLS implementation for all patients, in contrast to the percutaneous technique described in ED, which has had a high rate of failure.

There were no major vascular complications due to the insertion (for example retroperitoneal bleeding or aortic or ilio-femoral dissection). One patient had an accidental decannulation, forcing the pump to be stopped for 10 min, in order to re-insert the cannulae. Patient mobilization must therefore be carefully monitored at each step.

No early infection was noticed. The massive transfusion was due to DIC, and not a direct complication due to the ECLS insertion. The rate of DIC is high in refractory CA. Prolonged low-flow likely contributed to DIC in this case.

The training of the team and the simplified technique we developed allowed insertion times within in the same range as surgical in-hospital insertion (Fig. 1). In our study, the mean time of ACLS to ECLS was 57 min, which is similar to the time noted by Chen et al. who performed ECLS insertion in-hospital refractory cardiac arrest. In this study, a surgical team was on the site of in-hospital arrest in 5–7 min, and an incision was performed 10 min after onset of ACLS.

Our study was not designed to assess survival. However, in this small study, one patient survived with no neurological damage.

Comparison of studies on cardiac arrest is difficult due to patient selection. No and low flow delays remain important predictive factors for survival. Chen et al. observed a better survival rate (15%) but ECLS implementation was done in-hospital after 10 min of ACLS decreasing significantly the duration of low-flow. Conversely, pre-hospital insertion may have a positive effect on survival by shortening the duration of CPR during transportation to the hospital. In the same setting in Paris, Le Guen et al. observed a delay to ECLS of 120 min with a survival rate of 4% as compared to 79 min in our study and survival rate of 14%.

In our study, we found a high rate of brain death. This was probably due to a no-flow time longer than 5 min. This time may have been underestimated by the MICU, because it is particularly difficult to assess it in a pre-hospital setting. No-flow duration remains the most important predictor of mortality in OHCA. The high rate of organ donation performed in our study may be an indirect positive effect of this strategy. PH-ECLS may have allowed better organ conservation and a decrease in the DIC rate, probably by limiting ischemic-reperfusion lesions.

This study suggests that PH-ECLS is safe and feasible when performed by a non-surgical team. It may be an alternative to the insertion of ECLS in-hospital. Further studies are needed to confirm the time saved by this strategy and the effect on survival.

Disclosures

None.
Conflict of interest statement

All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence this work.

References