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Extracorporeal life support following out-of-hospital refractory cardiac arrest

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Abstract

Introduction Extracorporeal life support (ECLS) has recently shown encouraging results in resuscitation of in-hospital (IH) refractory cardiac arrest. We assessed the use of ECLS following out-hospital (OH) refractory cardiac arrest.

Methods We evaluated 51 consecutive patients who experienced witnessed OH refractory cardiac arrest and received automated chest compression and ECLS upon arrival in the hospital. Patients with pre-existing severe hypothermia and who experienced IH cardiac arrest were excluded. A femoro-femoral ECLS was set up on admission to hospital by a mobile cardiothoracic surgical team.

Results 51 patients were included, mean age 42 $\pm$ 15 years. The mean delays from arrest to cardiopulmonary resuscitation and ECLS were respectively 3 [25-75 interquartile 1-7] and 120 [102-149] min. Initial rhythm was ventricular fibrillation in 32 (63%) patients, asystole in 15 (29%) patients, and pulseless rhythm in 4 (8%). ECLS failed in 9 (18%) patients. Only two (4%, 95% confidence interval 1-13%) patients were alive at day 28 with a favourable neurological outcome. There was a significant correlation (R=0.36, p=0.01) between blood lactate and delay between cardiac arrest and onset of ECLS, but not with arterial pH or blood potassium. Deaths were the consequence of multi-organ failure (n=43, 47%), brain death (n=10, 20%) and refractory hemorrhagic shock (n=7, 14%), and most patients (n=46, 90%) died within 48 hours.

Conclusions This poor outcome suggests that the use of ECLS should be more restricted following in OH refractory cardiac arrest.

Introduction

Out-of-hospital (OH) cardiac arrest remains an important cause of unexpected death in developed countries. It still has a low survival rate despite access to improved emergency medical care, spread of automatic defibrillation [1], and regularly updated international guidelines [2]. Recent studies have indicated to unchanged or slightly better survival rates after OH cardiac arrest over the past decades [3,4]. Initial rhythm and cardiac origin are independent predictors of successful cardiopulmonary resuscitation (CPR) with better outcome related to a shockable rhythm such as ventricular fibrillation than asystole [5,6]. Survival rate rapidly decreases with time and a refractory cardiac arrest, defined as persistence of circulatory arrest despite more than 30 min of appropriate CPR, is usually considered as a condition associated with no survival [7], except in some particular conditions such as hypothermia [8].

Extracorporeal life support (ECLS) has been suggested as a therapeutic option in refractory cardiac arrest since 1976 [9]. However, the use of this technique has remained limited to hypothermic cardiac arrest and those occurring during the perioperative period of cardiothoracic surgery, mainly because the results of the initial trials were disappointing [10,11]. The ease of use of more recent miniaturized ECLS devices has permitted a wider use of the technique. Encouraging results have been published recently by several teams in France, Taiwan, Japan, and United States [12-16]. In these studies, most cardiac arrests occurred in the hospital, and survival with good neurological outcome has been observed in up to 20 to 30 % of cases [12-16]. Therefore, ECLS has been assigned a low-grade recommendation in recent guidelines for in-hospital (IH) cardiac arrest [17].

However, the good results obtained in IH cardiac arrests should not be extrapolated to OH cardiac arrests, mainly because there may be a longer delay in ECLS initiation [18]. Our primary aim was to review use of ECLS for OH refractory cardiac arrest.

Materials and methods

This prospective observational study received approval from our Institutional Review Board (CPP Pitié-Salpêtrière 2008/0701 Paris, France). Informed consent was waived due to life threatening emergencies and the absence of any therapeutic alternative. Information to the relatives of the patient (or to the patient in case of survival) was delivered after inclusion as appropriate in a life-threatening context.

Patients

Over a 32-month period (from January 2008 to August 2010), all patients who were referred to our ICU for OH refractory cardiac arrest were eligible for enrollment into this study. They were included prospectively and consecutively if the following criteria were met: 1) witnessed OH cardiac arrest; 2) refractory cardiac arrest, defined as the absence of return of spontaneous circulation (ROSC) after 30 min of CPR; 3) CPR pursued until arrival at our ICU; 4) mobile cardiothoracic surgery team available; 5) lack of known severe co-morbidities that should have preclude admission into an ICU. Patients who experienced IH cardiac arrest were excluded as well as patients who were severely hypothermic (body temperature <32°C) before CPR. Young children (<30 kg) were not included because our institution exclusively takes care of adults and because specific sizes of pediatric cannulae were not available. Conversely, patients older than 70 years were considered not eligible due to the poor expected neurological recovery.

Protocol

Prehospital emergency medical service (EMS) team performed CPR according to the American Heart Association guidelines [2]. In case of refractory cardiac arrest, CPR was pursued in the prehospital phase using an automated device (Autopulse®, Zoll Inc,

Chemlsford, MA) [19]. In the Paris area, all prehospital physician-staffed emergency units have been equipped with an automated chest compression device because France has developed a nationwide program of organ harvesting in non-heart beating donors. As soon as the EMS team considered that initial CPR had failed, they immediately alerted our ICU through the emergency unit regulating center to organize the patient admission and to ensure of the availability of the mobile cardiothoracic surgery team. This unit works in our hospital and includes a surgeon, a resident in surgery, and a technician, together with full equipment required to set up emergency ECLS anywhere. This mobile cardiothoracic surgery team has had extensive experience in our hospital and in our city [12,20,21]. During transfer to the hospital, resuscitation was continued without stopping at any moment.

At the admission to the ICU, absence of ROSC and absence of heart beat were checked before engaging the procedure. Then mechanical ventilation and automated chest compression device were continued until the start of ECLS. ECLS was established surgically with a peripheral femoro-femoral cannulation. The equipment included heparinized polyvinyl chloride tubing, a membrane oxygenator (Quadrox Bioline, Jostra-Maquet®, Orleans, France) and venous and arterial femoral cannulae (Biomedicus Carmed, Medtronic®, Boulogne-Billancourt, France) inserted using a surgical approach. An oxygen/air blender (Sechrist®, Sechrist Industries, Anaheim, CA) was used to supply the membrane oxygenator. Pump flow was initially set at 3–4 $L.min^{-1}$ and then, arterial and central venous catheters were inserted to continuously measure arterial blood pressure and allow frequent blood sampling. To avoid limb ischemia, an anterograde reperfusion catheter for distal limb perfusion was inserted. Objectives to optimize organ perfusion were PaO2 > 100 mmHg, normocapnia and arterial blood pressure > 60 mmHg with administration of fluids, blood transfusion to achieve a hematocrit > 35%, or vasopressive drugs (norepinephrine or epinephrine). Mild hypothermia (target body temperature 33-35 °C) was maintained during the first 24h using external cooling

(pulsed-air blanket) and neuromuscular blocking agents with sedatives were administered [22]. Minimum lung ventilation was maintained to avoid pulmonary collapse during ECLS with a tidal volume of 4-5 $ml.kg^{-1}$, respiratory rate 6 min^{-1}, and positive end-expiratory pressure of 5 cmH_2O. To avoid coagulation in the membrane oxygenator, non fractioned heparin was intravenously administered during ECLS with repeated control to maintain the activated clotting time ratio over 2.0, but this administration was postponed in most patients because of major coagulation abnormalities. An inhibitor of the proton pump was systematically given to prevent upper gastrointestinal bleeding. The possible cause of cardiac arrest was immediately investigated with regular and repeated troponin Ic assays, trans-thoracic or trans-oesophageal echocardiography and electrocardiogram as soon as an electric activity was present. In this context, patients with strong indications of acute myocardial infarction were transported to the catheter laboratory with ECLS to perform a percutaneous coronary angiography and any appropriate invasive treatment [23]. Sedation was stopped after a 24 hour period of mild hypothermia and then neurological (clinical examination and eventually electroencephalogram) and infectious status were checked. Withdrawal from ECLS required an echocardiography assessment of myocardial function (left ventricular ejection fraction >50%) and an arterial blood PaO2/FiO2 ratio >150 mmHg. The pump flow was progressively reduced to check for the absence of any deterioration in hemodynamic status. The possibility of the use of a ventricular assistance device or heart transplantation was examined if irreversible damage in myocardium function was diagnosed with an unsuccessful weaning from ECLS despite a favourable neurological outcome. Discontinuation of ECLS was based upon evidence of multiple organ failure (MOF), massive bleeding, or brain death. Any ECLS-associated complications were carefully monitored.

Measurements

The following variables were recorded according to the Utstein style [24]: age, sex, cardiovascular risk factors, delays from collapse to basic CPR, advanced CPR, installation of automated chest compression device, arrival into ICU, and installation of ECLS, initial cardiac rhythm, use of vasopressor and defibrillation during initial CPR, supposed cause of cardiac arrest. End-tidal CO_2 during CPR before ECLS was also recorded [25]. During CPR, signs of life (respiratory gasps, movements) were noted.

The following biological measurements were performed before ECLS: arterial blood gas analysis, blood lactate (normal range <1.8 $mmol.L^{-1}$), serum creatinine, blood potassium, fibrinogen, and prothrombin activity. Troponin Ic (normal range <0.15 $\mu g.L^{-1,}$ Stratus autoanalyser, Dade-Behring, Paris La Défense, France) and protein S100β (normal range <0.10 $\mu g.L^{-1}$, LIA-mat 300 analyzer, Byk-Sangtec France Laboratories, Le Mée sur Seine, France) were also measured [26]. The evolution of arterial pH and blood lactate levels were recorded after 1-2 hours of ECLS, and the following variables calculated: delta arterial pH, blood lactate clearance expressed as percent of initial values, number of patients with blood lactate clearance ≤-10%, as previously described [27].

The final outcome was determined at day 28 and the Glasgow coma outcome scale was determined at 6 months. The Glasgow outcome scale defines the following categories: 1, death; 2, persistent vegetative state; 3, severe disability (minimally conscious state, severe motor deficit, aphasia, and need for continuous help); 4, moderate disability; 5, good recovery.

Since the start of the study (January 2009), French guidelines of the indications for the use of ECLS in refractory cardiac arrest have been published [28]. These guidelines considered the following variables to determine whether or not ECLS is indicated following out-of-hospital cardiac arrest: duration of no flow (≤ 5 min), duration of low flow (≤100 min), end-tidal CO_2 (≥10 mmHg), at least in non-hypothermic patients and in patients without life

signs during on-going CPR (Additional file 1) [28]. Thus we assessed if the main criteriae (no-flow, low-flow, $ETCO_2$) recommended in these guidelines were followed during our study and if the whole algorithm was respected.

Statistical analysis

Data are expressed as means ± SD or median [25-75 interquartile] for non-Gaussian variables (Kolmogorov test). Categorical variables are given as percentages and their 95% confidence interval. Comparison between two groups was performed using the Student t test, Mann-Whitney U test, or Fisher's exact method as appropriate. Correlation between two variables was performed using the least square linear regression. All P values were two-tailed and a p value of less than 0.05 was considered significant. Statistical analysis was performed using NCSS 6.0 software (Statistical Solutions Ltd, Cork, Ireland).

Results

During the study period, we performed ECLS in 59 patients who had experienced a refractory cardiac arrest. Three patients who had suffered IH cardiac arrest were excluded as well as 5 patients with severe hypothermia (24.5 ± 1.8 °C) before cardiac arrest. Thus, 51 patients were finally included in the study. The main characteristics of our population are shown in table 1. The supposed causes of cardiac arrest were cardiac (n=44, 86%), trauma (n=3, 6%), drug overdose (n=2, 4%), respiratory (n=1, 2%), and electrocution (n=1, 2%). Only one patient had signs of life during CPR before ECLS.

ECLS flow could not be established in 9 (18%) patients. These patients had a more prolonged no flow duration (2.5 [1-6] vs 3 [0.5-6.5] min, P=0.04) and a lower $ETCO_2$ (9 ± 3 vs 12 ± 2 min, P=0.046) than the remaining patients. In one case, the failure was the consequence of an impossible cannulation of femoral artery, probably related to an aortic dissection. The remaining failures of ECLS were related to an insufficient pump flow despite massive fluid challenge and transfusion. In the remaining 42 patients the initial ECLS output was 3.6 ± 1.8 L.min-1 providing an arterial blood pressure of 67 ± 39 mmHg. During the ECLS procedure, 30 (59%) patients required blood transfusion (4 [2-6] packed red blood cell units). Body temperature was 34.1 ± 0.9 °C.

Twenty of the 42 patients in whom ECLS was installed (48%) patients underwent coronary angiography because of clinical or electrical signs suggesting myocardial infarction but significant coronary abnormalities were noted in only 10 of these patients (50%). Angioplasty without stenting was performed in 1 patients and coronary stent following percutaneous transluminal angioplasty was inserted in 7 patients. Coronary spasm was diagnosed in 2 of these patients.

Arterial blood gas samples at the admission showed severe lactic acidosis (Table 1) Initial blood lactate level was significantly correlated with the OH duration of cardiac arrest

until ECLS (p=0.02) (Figure 1). In contrast, the correlations between arterial pH (R=0.05) or blood potassium levels (R=0.23) were non significant. After 1 hour of ECLS, blood lactate levels slightly but significantly decreased whereas arterial pH markedly increased (Figure 2).

Seventeen of the 42 patients in whom ECLS was installed (40%) survived after 24 hours of ECLS, but only 5 (12%) after 48 hours. At day 28, only two patients were alive, providing a global survival rate of 4% (95% confidence interval 1-13%). The cause of death was refractory MOF (n=23, 45%), brain death (n=10, 20%), and severe hemorrhage (n=7, 14%), and failure of ECLS in the remaining patients (n=9, 18%).

In the first survivor (cardiac cause, ventricular fibrillation, no flow 1 min, low flow 132 min, protein S100 1.5 $\mu g.L^{-1}$), withdrawal from ECLS was possible only at day 36 because of severe and prolonged heart failure (left ventricular ejection volume estimated to 30%) and an implantable automatic defibrillator was inserted. His length of stay in the ICU was 58 days, and 187 days in the hospital. Follow-up at six month showed only minor cognitive dysfunction (Glasgow outcome scale of 5) but a persistent altered left ventricular ejection fraction (35%). In the second survivor (cardiac cause, ventricular fibrillation, no flow 0 min, low flow 170 min, protein S100 4.5 $\mu g.L^{-1}$), withdrawal from ECLS was possible at day 5. His length of stay in the ICU was 25 days and 77 days in the hospital, with a Glasgow outcome score of 4 at 6 months.

Conformity of the cases considering a no-flow period $\leq$ 5 min was noted in 36 (71%) patients, a low-flow period $\leq$ 100 min in 14 (27%) patients, and an end-tidal $CO_2 \geq$ 10 mmHg in 32 (63%) patients. Conformity to the whole algorithm of the French guidelines was seen in 8 (16 %) patients. Figure 3 shows the distribution of values of no-flow, low-flow, arterial pH, blood lactate and potassium, in patients who died and survivors. Although the two survivors fulfilled the criteria of a no-flow of less than 5 min, they did not fulfil that of a low flow of less than 100 min (Figure 3). In an attempt to identified futile ECLS, we compared patients

who survived less than 24 hours and those who survived more than 24 hours (post hoc comparison). Only $ETCO_2$ (18 $\pm$ 10 vs 29 $\pm$ 12 mmHg, P=0.006) and blood lactate clearance during ECLS (+11% [-24;+26] vs -22% [-26;-1], P=0.045) were significantly different between patients who survived less or more than 24 hours.

Discussion

Our primary objective was to assess the use of ECLS following OH refractory cardiac arrest. In a selected population, we observed a 4% survival with a good neurological outcome. Although this survival rate is close to that observed in France in the general population who undergo non refractory OH cardiac arrest [29], it represents a low survival rate compared to previous studies of ECLS in IH cardiac arrest.

Refractory cardiac arrest is defined by the lack of ROSC within a period of at least 30 min of CPR in the absence of pre-existing hypothermia [1,28]. Because this condition is associated with no survival, it is an indication for stopping CPR and declaring the patient dead. It indicates both the absence of the likelihood of restoring cardiac activity and a poor chance of obtaining good neurological outcome. The introduction of ECLS has created a new paradigm since a refractory cardiac arrest might be now defined only as a function of the possibility of obtaining a good neurological recovery since ECLS support cardiac function [27]. Recent publications have shown very encouraging results with 17 to 30% survivors with good neurological outcome [12-14,16,30]. Several studies and a meta-analysis have also reported favourable outcome in children [29,31,32]. However, most of these patients experienced IH cardiac arrests. The marked difference in prognosis between IH and OH cardiac arrest has been well-recognized but is only partly explained by a shorter treatment delay [18]. Kagawa et al. [15] compared IH and OH refractory cardiac arrest treated with ECLS and reported a lower survival rate in OH cardiac arrest (10 vs 26%). Our results cannot be extrapolated to patients with recurrent cardiac arrest [33] and those with circulatory failure after ROSC, in whom ECLS might be a therapeutic option. ECLS has also been successfully used in patients with cardiogenic shock before cardiac arrest, particularly in severe drug intoxication [34].

Several factors may explain the low survival rate in OH refractory arrest treated with ECLS. The most important one is probably the delay required to start ECLS (i.e. low-flow), the minimum being 75 min in our study whereas ECLS was started within 50 min in 50 % of patients in a previous study [14]. Some studies reported a relationship between the probability of survival and the low-flow duration [14] but some other did not [32]. Part of this delay is unavoidable but some time could probably be saved by earlier alerting of the system before reaching the 30 min delay to diagnose a refractory cardiac arrest [28]. The no-flow duration may also be crucial and the best candidates remain those patients who benefit from immediate CPR (i.e., 0 no-flow). The role of the delay to initiate advanced CPR may be far less important, was not considered in the French guidelines [28], and the essential role of immediate CPR even without ventilation has been largely confirmed [35]. However, other important factors should be considered, particularly the quality of CPR during ground transportation. The limited number of persons available to perform CPR during the prehospital phase and the difficulties associated to transportation were strong arguments to use an automated chest compression device. However, the quality of CPR provided may not be optimal since this device failed to improve survival in a randomized study [19] and may be more heterogeneous between patients than standard CPR.

Victims of refractory cardiac arrest are widely considered as potential non-heart beating organ donors [36]. From an ethical point of view, and beyond the dead organ donor rule [37], it is essential that a clear separation exists between those patients who should be considered for organ donation and whose death is declared and those patients who might benefit from a therapeutic option like ECLS. The French guidelines tried to help the physician by explaining the contra-indications for ECLS in refractory cardiac arrest [28]. Our study suggests that the criteria of a no-flow $\leq$ 5 min and an $ETCO_2 \geq 10$ mmHg remains appropriate, although this last criteria could be considered as too liberal taken into account the

lower $ETCO_2$ in patients who survived less than 24 hours. In contrast, a low-flow ≤ 100 min might be too restrictive since a survivor was observed after a no-flow of 132 min (Figure 3), as previously reported [12]. However, because of the low global survival rate, extension of the criteria may not be suitable and most studies performed in IH cardiac arrest only considered patients with a low flow ≤ 100 min [13,14]. Thus, although the low-flow criteria may remain a matter of debate, further criteria are warranted.

Prolonged CPR leads to severe lactic acidosis and hyperkalemia and we observed a more severe decrease in pH as that observed in IH cardiac arrest [30]. Müllner et al. [38] have demonstrated a significant correlation between total duration of cardiac arrest and admission levels of arterial lactate concentration and observed that a lactate level >16.3 $mmol.L^{-1}$ was systematically associated with impaired neurological recovery. However, this result may not apply to patients undergoing ECLS and, although we observed a significant correlation between duration of low-flow and blood lactates (Figure 1), no precise threshold could be used to decide or not ECLS (Figure 3), as previously noted [12]. Arterial pH and blood potassium are also potential biological candidates. Nevertheless, the lack of significant relationship between low-flow duration and these biological variables is not encouraging. The troponin Ic values is probably not useful since it reflects cardiac injury related to both CPR and the cause of cardiac arrest. The value of protein S100 might be helpful although our survivors have elevated values. Although most of early deaths were related to MOF and massive hemorrhage, biological variables exploring hemostasis abnormalities also do not seem very interesting for that purpose. We consider that a large multicenter study with an increased number of survivors and using multivariate analysis is mandatory to improve the decision to perform or not ECLS in these patients.

There is a growing interest in measuring lactate clearance [26,39]. We observed that ECLS induced a rapid and marked increase in pH but a slight decrease in blood lactate during

the first hours (Figure 2). Although there was no significant difference in arterial pH change during ECLS between patients who survived more than 24 hours and those who did not, the blood lactate clearance was significantly greater, suggesting that blood lactate clearance may help to decide an earlier interruption of futile ECLS.

A potential limitation of a wider use of ECLS in refractory cardiac arrest was the fear that it may lead to the survival of patients with poor neurological recovery and the associated use of costly resources and considerable suffering for the patient and its relatives [28]. Our study confirms that, in non-survivors, death rapidly occurs due to irreversible MOF or massive hemorrhage. Moreover, most patients with isolated brain injury evolved to brain death and not to a vegetative state. As compared to previous studies [12-15,30], we observed a higher incidence of MOF and massive hemorrhage, probably because of the longer CPR duration, and this is reflected by the major hemostasis abnormalities observed before ECLS.

Some limitations in our study deserve consideration. First, the sample size was relatively low. Nevertheless our study enables us to alert medical community about the risk of futile resuscitation in most OH refractory cardiac arrest. Second, the absence of a control population of victims of cardiac arrest was ethically justified because natural evolution of these refractory cardiac arrests remains death. Our results may not apply to a pediatric population since the cause of OH cardiac arrest in children markedly differs from adults. Because the respiratory causes are predominant in children, a refractory cardiac arrest may indicate that the heart suffered from prolonged anoxia and thus that severe brain damage has occurred.

Conclusions

ECLS may be an appropriate therapeutic option in patients following OH refractory cardiac arrest cardiac since survival with good neurological outcome can be observed.

However, because the survival rate remains markedly lower (4%) than that in IH refractory cardiac arrest, indication of ECLS should be restricted to a highly selected population. Further prospective multicenter studies are needed to define population with OH refractory cardiac arrest that would benefit from ECLS.

Key messages

- Extracorporeal life support (ECLS) has shown encouraging results in resuscitation of in-hospital refractory cardiac arrest.
- We assessed the use of ECLS following out-hospital refractory cardiac arrest in 51 patients and observed a low survival rate (4%).
- Further prospective multicenter studies are needed to define population with out-of-hospital refractory cardiac arrest that would benefit from ECLS.

Abbreviations

CPR, cardiopulmonary resuscitation; ECLS, extracorporeal life support; EMS, emergency medical service; $ETCO_2$, end-tidal carbon dioxide; IN, in hospital; MOF, multiple organ failure; OH, out-of-hospital; ROSC: return of spontaneous circulation.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MLG and ANR conceived the study, performed acquisition, analysis, and interpretation of the data. SC and MR made substantial contributions to acquisition and interpretation of the data, and helped to draft the manuscript; PL conceived the study and was responsible for the ECLS mobile team; BR conceived the study, performed the statistical analysis, and wrote the manuscript; OL conceived the study and participated in its design and coordination. All authors read and approved the final manuscript.

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Additional files

Additional file 1:

Algorithm to decide whether extracorporeal life support in treating refractory cardiac arrest (CA) is indicated or not. From Riou et al. [28].

A suggested algorithm to decide whether extracorporeal life support in treating refractory cardiac arrest (CA) is indicated or not. CPR: cardiopulmonary resuscitation ; VT : ventricular tachycardia; VF : ventricular fibrillation; TP : torsades de pointes ; $ETCO_2$: end-tidal CO_2 (measured 20 min after the onset of medical CPR). *: a CPR duration > 100 min could be accepted in case of poisoning with cardiac drugs. †: indications accepted by ILCOR. Co-morbidities are those which should contra-indicated invasive care (admission into ICU, major surgery, coronary angioplasty for example). The low-flow duration encompasses basic CPR (witness and/or paramedics) and medical CPR.

Table 1 Main characteristics of the patients (n=51).

Variable	Values	Range
Age (year)	42 ± 15	13-70
Men	46 (90%)	
Women	5 (10%)	
Comorbidity		
- Hypertension	6 (12%)	
- Diabetes mellitus	3 (6%)	
- Ischemic heart disease	11 (20%)	
- Other cardiac disease	10 (20)	
Site of cardiac arrest		
- home	19 (37%)	
- work	6 (12%)	
- public	20 (39%)	
- sport	6 (12)	
Initial rhythm		
- ventricular fibrillation	32 (63%)	
- asystole	15 (29%)	
- pulseless rhythm	4 (8%)	
Defibrillation		
- patients receiving shock	37 (72%)	
- number of shocks	4 [2;6]	1-20
Epinephrine		
- patients receiving epinephrine	51 (100%)	
- dose (mg)	13 [10;20]	2-100
End tidal CO_2 (mmHg)	22 ± 12	0-50
Delay		
- fall to basic CPR (min)	3 [1;7]	1-22
- fall to advanced CPR (min)	12 [5;23]	0-40
- fall to automated CPR (min)	41 [30;55]	15-110
- fall to ICU admission (min)	90 [65;115]	48-175
- fall to ECLS onset (min)	120 [102;149]	75-195
Biological measurement		
-Arterial pH	6.93 ± 0.17	6.56-7.25
-Blood lactate ($mmol.L^{-1}$)	19.9 ± 6.7	7.7-40.8
-Arterial bicarbonate ($mmol.L^{-1}$)	16.5 ± 12.1	1.9-58.7
-PaO2 (mmHg)	135 ± 129	6-489
-PaCO2 (mmHg)	69 ± 25	19-128
-Blood potassium ($mmol.L^{-1}$) *	5.1 ± 1.7	2.7-10.5
-Serum creatinine ($\mu mol.L^{-1}$)	129 ± 30	51-275
-Prothrombin time (%)	39 ± 16	11-66
- Fibrinogene ($g.L^{-1}$)	1.3 [<0.6;1.6]	<0.6-3.6
-Hemoglobin ($g.L^{-1}$)	109 ± 25	59-169
-Troponin Ic ($\mu g.L^{-1}$)	3.98 [0.93;85.5]	0-669.0
-Protein S100 ($\mu g.L^{-1}$) †	4.2 [2.4;10.4]	0-36.0

Values are mean ± SD, median [25;75 interquartile], or number (percentages). CPR: cardiopulmonary resuscitation; ECLS: extracorporeal life support. *: blood potassium could not be measured in 4 patients because of hemolysis.†: Protein S100 was measured in only 27 patients.

Legends for figures

Figure 1. Relationship between initial blood lactate level and delay between fall and onset of extracorporeal life support (ECLS) (n=48).

Figure 2. Kinetic of arterial pH (Panel A) and arterial blood lactate (Panel B) during the first hour following extracorporeal life support (ECLS) (n=38). Box plot represents median, 25-75 interquartile, and extreme values.

Figure 3. Distribution of the values of no-flow, low-flow, end-tidal CO_2 ($ETCO_2$) initial arterial pH, blood lactate, and kaliemia in the studied population (n=51). The grey zones and vertical bars indicate the threshold considered in the French guidelines for no-flow (≤ 5 min), low flow (≤ 100 min), and $ETCO_2$ (≥ 10 mmHg).

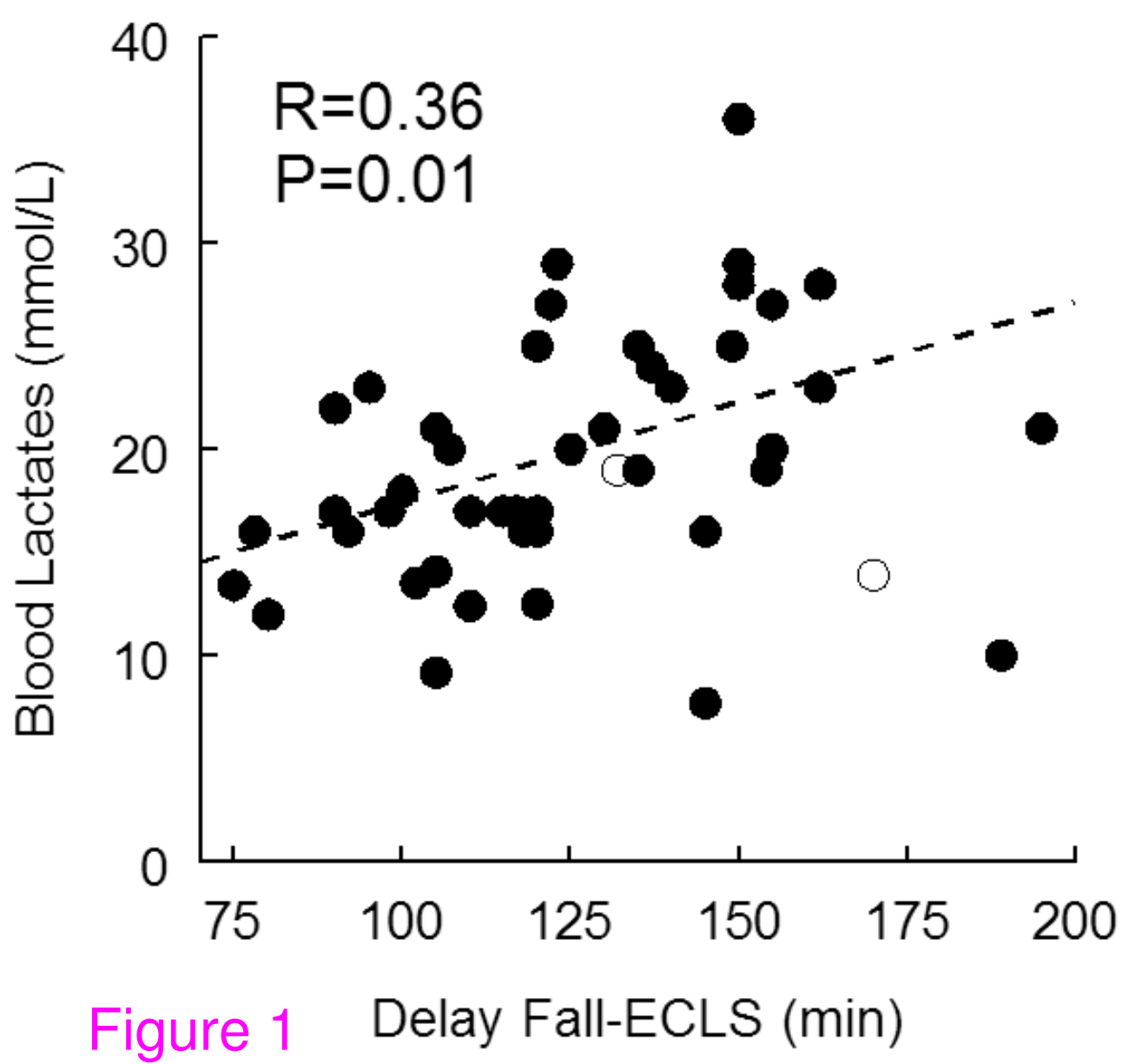
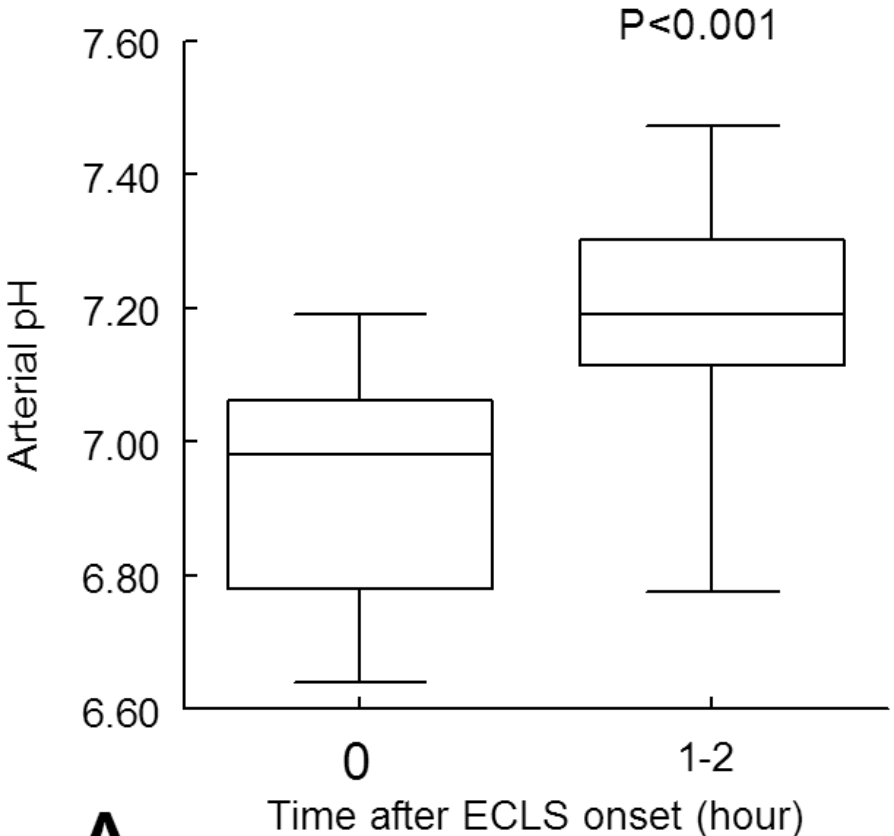

R=0.36
P=0.01
Blood Lactates (mmol/L)
40
30
20
10
0
75
100
125
150
175
200
Delay Fall-ECLS (min)

Figure 1


P<0.001
7.60
7.40
7.20
7.00
6.80
6.60
Arterial pH
0
1-2
Time after ECLS onset (hour)
A

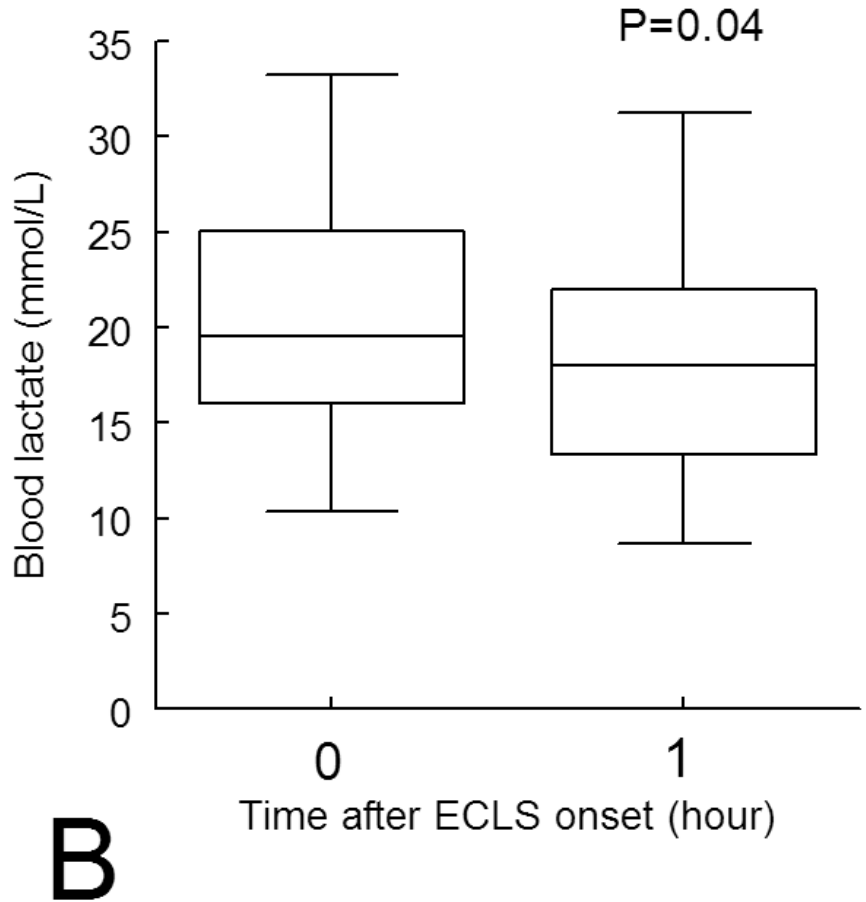

P=0.04
35
30
25
20
15
10
5
0
Blood lactate (mmol/L)
0
1
Time after ECLS onset (hour)
B

Figure 2

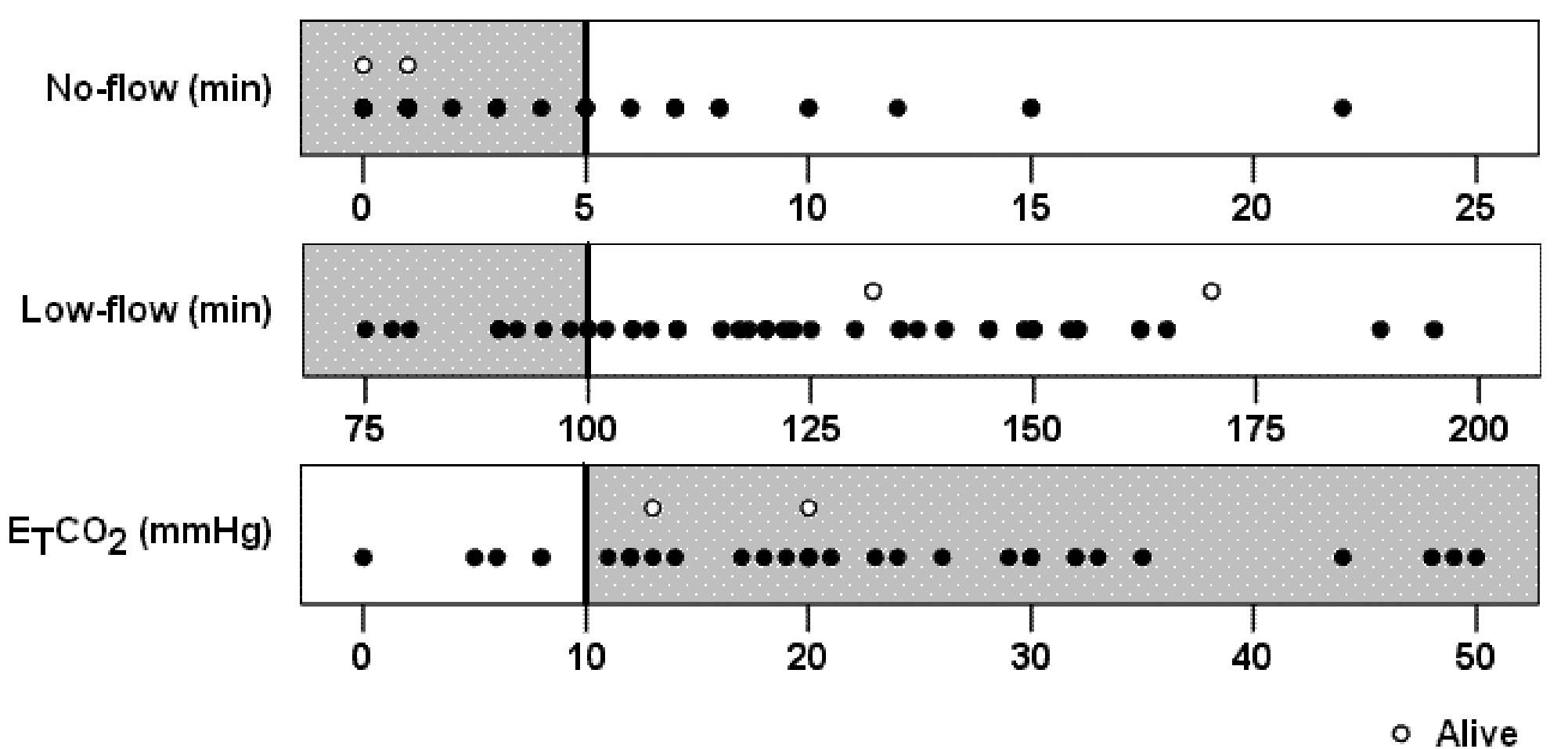

No-flow (min)
0
5
10
15
20
25
Low-flow (min)
75
100
125
150
175
200
E_TCO_2 (mmHg)
0
10
20
30
40
50
Alive
Dead

Figure 3

Additional files provided with this submission:

Additional file 1: AdditionalFile1.doc, 36K
http://ccforum.com/imedia/1002590825069768/supp1.doc