

Extra Corporeal Life Support for Cardiac ARrest patients with post-cardiac arrest syndrome: the ECCAR study

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1 Extra Corporeal Life Support for Cardiac ARrest patients with post-cardiac arrest syndrome: the
2 ECCAR study

3

4 Running Head: ECLS for Post Cardiac Arrest Syndrome

5

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1 **ABSTRACT**

2 Purpose: Post-Cardiac Arrest Shock (PCAS) occurring after resuscitated cardiac arrest (CA),
3 is a main cause of early death. Extra-Corporeal Life Support (ECLS) could be useful pending
4 recovery of myocardial failure. We aimed to describe our PCAS population, and factors
5 associated with ECLS initiation.

6 Materials and Methods: This analysis included 924 patients admitted in two intensive care
7 units (ICU) between 2005 and 2014 for CA and PCAS, and, of those patients, 43 patients for
8 whom an ECLS was initiated. Neurological and ECLS-related outcomes were gathered
9 retrospectively.

10 Results: The 43 ECLS patients were predominantly young males with evidence of myocardial
11 infarction on coronary angiography (70%). ECLS was initiated in patients suffering from
12 severe cardiovascular dysfunction (Left Ventricular Ejection Fraction: 15 [10 - 25] %), with a
13 median delay of 9 [6 - 16] hours following CA. At one year, 8 patients survived (19%) without
14 neurological disability. Blood lactate and coronary etiology were associated with neurological
15 outcomes. Logistic regression conducted using 878 PCAS controls identified age, sex,
16 current smoking, location of CA, blood lactate and creatinine levels as risk factors for
17 initiation of ECLS.

18 Conclusions: ECLS, as a salvage therapy for PCAS, could represent an acceptable
19 alternative for highly selected patients.

20

21

1 **Introduction**

2 Despite many improvements in Cardiac Arrest (CA) management, survival rate ranges from
3 11 to 17% [1,2]. Among CA patients who survived initial resuscitation, less than 30%
4 survived to hospital discharge [3–5]. Post Cardiac Arrest shock (PCAS), defined as the
5 association of a myocardial dysfunction and vasoplegia occurring after return on
6 spontaneous circulation (ROSC) [6], is globally responsible of one-third of deaths [5]. While
7 persistence of myocardial dysfunction at 24h may be associated with early death [7], no
8 differences in neurological outcomes have been shown between post-CA patients with PCAS
9 and those without PCAS [5,7].

10 Recently, two studies have described the use of Extracorporeal Life Support (ECLS) in
11 successfully resuscitated CA patients experiencing severe PCAS [8,9]. Although survival
12 benefit was not demonstrated, ECLS-assisted patients had acceptable neurological
13 prognosis. A solid understanding of key governing factors that lead those patients to die are
14 thus requested to better select the patients the most likely to benefit for this strategy.

15 Our objectives were 1/ to describe a cohort of PCAS patients treated with ECLS and 2/ to
16 identify factors that lead physicians to indicate initiation of ECLS in post-CA patients.

17

18 **Material and Methods**

19 *Population and Data collection:*

20 This retrospective observational study was conducted in two tertiary university centers in
21 Paris. We included consecutive patients admitted to intensive care unit (ICU) for CA and
22 PCAS (defined as the need for continuous norepinephrine or epinephrine infusion to maintain
23 mean arterial pressure above 60 mmHg for more than 6 hours following restoration of ROSC
24 despite adequate fluid loading [5]), and for whom an ECLS was initiated. Patients with

1 refractory CA and in-hospital CA (except those that occurred in the cath-lab and the
2 emergency ward) were not included.

3 ECLS-treated patients' data were collected retrospectively. Prospective database
4 implemented in Cochin Hospital was used to identify control group of patients experiencing
5 PCAS without ECLS [2].

6 Our local ethics committees approved the data collection and study protocol (CE SRLF N°
7 12-384).

8 *Treatment protocol*

9 Patients admitted for CA were treated according to international guidelines, and similar
10 procedures have been described elsewhere [2,10]. ECLS implantation and patient's
11 management during ECLS support, including anticoagulant treatment or weaning procedure
12 followed ELSO guidelines [12] and were previously described [11].

13 Neurological outcome was daily assessed by ICU physicians, until death or ICU discharge.
14 According to guidelines [13–16], neuroprognostication was performed daily using a
15 multimodal approach, and life-sustaining therapies withdrawal decision was taken during a
16 collegial consultation.

17 *Outcomes*

18 The primary outcome was the neurological evolution at one year, assessed by the Cerebral
19 Performance Category [17] (Favorable Outcome : CPC score = I - II ; Poor Outcome: CPC
20 score = III - V) [18] at 1 year.

21 *Analysis*

22 We performed a description of factors associated with unfavorable neurologic outcomes at
23 one year in the population of PCAS patients treated with ECLS. A logistic regression was
24 performed to assess the association between the selected variables and the neurological

1 outcome. ECLS group was compared with control group, using two-sided t test, or chi 2 test
2 when necessary. Finally, we performed a univariate and multivariate analysis, using a
3 stepwise logistic regression, to identify factors associated with the ECLS implantation.

4 Results are expressed as median (interquartiles 25-75) or number (percentage). The R
5 project software (The R Foundation for Statistical Computing, Vienna, Austria) was used for
6 statistical analysis.

7

8 **Results**

9 From January 2005 to December 2014, 46 PCAS patients treated by ECLS were included.
10 Three patients were non-included because of in-Hospital CA. Among the 3 patients non-
11 included, one was admitted for septic shock consecutive to a pulmonary infection, the CA
12 occurred 8 days after the admission, and the patient deceased. One patient was a severely
13 burned patient with ARDS. He deceased 17 days after his admission while on ECLS for CA
14 consecutive to pulmonary embolism occurring 14 days after his admission. The last non-
15 included patient was admitted for intoxication with beta-blockers, the ECLS being inserted 5
16 days after his admission, for extreme hemodynamic instability, he died while on ECLS.

17 Finally, 43 patients fulfilled the inclusion criteria. We also include a control population
18 composed by 878 PCAS patients. ECLS population was predominantly young males, with a
19 previous history of coronary events (Table 1). Sixty percent of them presented an initial
20 shockable rhythm, with No-Flow of 2 [0-10] min and a Low-Flow of 28 [14-42] min.
21 Hemodynamic parameters are described in table 2.

22 Nine patients survived (21%) at ICU discharge: myocardial recovery was observed for 7
23 patients (78%), one benefited from a heart transplantation, and one patient died at one year
24 from end stage cancer. A favorable neurological outcome at one year was observed for 8
25 (19%) of the ECLS cohort (89% of survivors).

1 Death rate during the ICU stay (79%) was mainly related to multiple organ failure (MOF)
2 (63%). Forty-five percent of death by MOF occurred in the first three days after ICU
3 admission (Figure 1). ECLS inefficacy, defined as the inability to maintain cardiac output and
4 arterial pressure despite maximal therapeutic investment, was observed in 11 of deceased
5 patients (31%). Life-sustaining therapy withdrawal was initiated for 9 of them (26%), and
6 cerebral brain death was pronounced for 2 patients (6%).

7 No statistical difference was found between centers except for the percentage of bystander
8 CPR and Low-Flow duration (Table S1).

9 ECLS-treated patients who survived without severe neurological disability were younger than
10 those with severe neurological impairment (Table 1). CPR characteristics and severity scores
11 were not different between the favorable and the poor neurological outcome group, despite
12 OHCA score showed a trend toward higher values in poor neurological group. By contrast,
13 blood lactate level at ECLS implantation discriminated the two groups (Table 2 and figure
14 S1). Coronary etiology of CA was associated with unfavorable outcome at one year, whereas
15 the arrhythmia was associated with a better prognosis (Table 1).

16 ECLS-treated patients were younger, with a longer time to ROSC and a higher proportion of
17 non-public location of CA and bystander CPR, as compared to control group (Table 3).
18 ECLS-treated patients had higher blood lactate and creatinine levels than the control.

19 In multivariate analysis (Figure 2), factors independently associated with ECLS implantation
20 were as follows: age < 62 years old, serum creatinine > 109 $\mu\text{mol/l}$, administration of
21 adrenaline < 2 mg, and public location of CA.

22 When considering the whole PCAS population, non-survivors at ICU discharge were older
23 and experienced higher blood lactate and serum creatinine levels (Table 4). Time to ROSC
24 were longer when comparing non-survivors to survivors. The etiology for CA in survivors was
25 predominantly cardiac, with higher rates of coronary angioplasty. The proportion of ECLS-
26 treated patients was not different in survivors versus non-survivors.

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Conclusions Discussion

~~Emphasizing on functional neurological outcomes, this observational study offers interesting findings.~~

The present retrospective study aimed at reporting the ten-year experience of two Parisian intensive care units in the application of ECLS for PCAS patients. Even though the death rate was high, the survivors of ECLS-treated PCAS population exerted no or minor neurological disabilities. Furthermore, the death rate in the ECLS-treated population is of a magnitude of the death rate of the PCAS population, although the severity was higher in the first population as compared to the second. The latter observation might raise the question of the potential benefit of ECLS in such a severe population. It also highlights the need for better identification of patients who could benefit of such investment. Therefore, we have identified blood lactates level at ECLS implantation and reversible cause of OHCA as potential factors associated with better outcomes.

In the survivors of ECLS-treated PCAS population, the potential for recovery of neurological function was high (89% of surviving patients were alive without severe neurological impairment). These data are consistent with previously published data [5,7], although ECLS wasn't used in those latter studies. Faster time to implantation could be a particular endpoint to achieve, as suggested by available data in the setting of refractory cardiogenic shock [19]. Well-designed studies are lacking to support this hypothesis in the setting of PCAS. On the contrary, selecting patients the most likely to benefit for such a therapy could improve functional outcomes. Indeed, despite we observed that the mortality was not significantly different in the ECLS-treated population as compared to the control, blood lactate level, as well as the etiology of CA, was associated with neurological outcomes. Initiating ECLS on patients with low blood lactate level, and suffering for PCAS consecutive to reversible cause, could improve survival rates. Indeed, even though Bougouin et al. [9] showed no association between ECLS implantation and survival, our study suggests that the coronary etiology could

1 be a potential confounding factor. Reversible causes of myocardial dysfunction could then
2 have a better prognosis in terms of myocardial recovery [20]. By contrast, in case of
3 constituted myocardial infarct, the potential for recovery could be altered [21–23]. In fact,
4 mortality observed in patients treated with ECLS for PCAS secondary to acute coronary
5 syndrome, was higher than mortality observed in patients treated with ECLS for reversible
6 causes. The mortality rates observed in our study remained high, but were comparable to
7 those reported in the two previously published studies, respectively 72 [8] and 73% [9].

8 Complications occurred frequently, but were close to those reported in a meta-analysis of 20
9 studies evaluating ECLS usage [24]. The most frequent complication in our study was acute
10 kidney injury requesting renal replacement therapy (50%), being probably more a marker of
11 the severity of the shock rather than a specific complication of ECLS. On the contrary, the
12 high rates of specific complications of ECLS observed in our cohort, as the rate of lower limb
13 ischemia (28% versus 17% in Cheng's study [24]), could worsened the prognosis of some
14 patients. However, ECLS implantation was performed by physicians trained to percutaneous
15 cannulation with previously published good results [11].

16 The retrospective design of the study limits the strength of the findings. We focused on a
17 specific subpopulation of PCAS patients, and we retrieved data from 10 years' experience of
18 two tertiary care centers. No randomized study could have been achievable in a reasonable
19 time-frame. A matched analysis designed to identify the variables associated with survival
20 would have been useful, but the low sample size of the ECLS cohort, as well as the particular
21 severity of these patients have prevented us to conduct such a matching. Moreover, we were
22 unable to collect information regarding severity at admission in the control population.

23 We limited the inclusion to the patients admitted for OHCA on purpose, even though the
24 outcomes of the 3 patients non-included could have influenced the overall results of this
25 study. Indeed, OHCA is a sudden and life-threatening pathology for whom the delay for
26 initiation of the treatments is a key aspect of the prognosis. In-Hospital CA is a more

1 heterogeneous entity, where pre-existing life-threatening pathology leads to CA. The
2 prognosis of the CA should be the combination of the pre-existing condition and the CA by
3 itself. It would have been difficult to conclude on the ECLS intervention, because of this
4 heterogeneity.

5

6 **Conclusion**

7 **Despite high rate of death in the ECLS-treated population, the neurological outcomes of the**
8 **survivors suggest a potential beneficial effect of ECLS on neurological recovery and justify its**
9 **implantation for extremely severe population, as a salvage therapy.** ~~While ECLS initiation,~~
10 ~~reported in this present work, does not impact mortality, neurologic outcomes of survivors~~
11 ~~suggest a potential beneficial effect on neurological recovery. The neurological evolution~~
12 ~~could be more likely related to the initial brain injury, rather than the PCAS by itself.~~
13 ~~Furthermore,~~ Reversible etiologies of cardiac arrest were associated with better outcomes,
14 emphasizing on selection of patients who could benefit of such a therapy. Considering the
15 assistance only for patients for whom the myocardial depression has the potential to recover
16 could be an interesting option to improve outcomes. Then, considering ECLS for a carefully
17 selected population of PCAS patients could be promising.

18

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22

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1 **TABLES**

2 **Table 1. General characteristics of the ECLS population according to outcome.** Results
 3 are expressed as median [IQR] or n (%).

4

	All N = 43	Favorable Outcome N = 8	Poor Outcome N = 35	P Value
Age (yo)	54 [46 - 59]	43 [35 - 54]	55 [49 - 61]	0.029
Male n (%)	32 (74)	5 (62)	27 (77)	0.409
Body Mass Index	26 [25 - 28]	27 [25 - 31]	26 [25 - 28]	0.736
Previous Medical Diseases				
Coronaropathy n (%)	9 (21)	1 (12)	8 (23)	0.535
Diabetes mellitus n (%)	7 (16)	0 (0)	7 (20)	0.18
Hypertension n (%)	15 (35)	1 (12)	14 (40)	0.151
Dyslipidemia n (%)	6 (14)	1 (12)	5 (14)	0.917
Active smoker n (%)	4 (9)	0 (0)	4 (11)	0.336
Severity scores on admission				
IGS II	73 [67 - 81]	70 [66 - 79]	73 [68 - 82]	0.468
SOFA score	12 [11 - 15]	12 [10 - 12]	13 [12 - 15]	0.227
SOFA cardio-vascular	4 [4 - 4]	4 [4 - 4]	4 [4 - 4]	-
OHCA score	39 [31 - 51]	32 [26 - 36]	42 [33 - 52]	0.078
Biological Data on admission				
pH	7.19 [7.05 - 7.26]	7.15 [7.11 - 7.23]	7.19 [6.97 - 7.26]	0.521
Troponin (µmol/l)	5.5 [1.32 - 63.2]	7.2 [1.86 - 20.98]	4 [1.35 - 63.7]	0.984
Blood lactate (mmol/l)	10 [6 - 13]	6 [4 - 8]	11 [7 - 14]	0.029
Serum creatinine (µmol/l)	148 [138 - 188]	150 [134 - 164]	148 [138 - 198]	0.708
Serum potassium (mmol/l)	3.7 [3.2 - 4.2]	3.3 [2.9 - 4]	3.8 [3.4 - 4.4]	0.147
Cardiac Arrest Characteristics				
No Flow (min)	2 [0 - 10]	1 [0 - 9]	3 [0 - 10]	0.734
Low Flow (min)	28 [14 - 42]	25 [11 - 30]	28 [18 - 48]	0.28
Adrenaline bolus (mg)	3 [1 - 9]	1 [0 - 3]	4 [1 - 9]	0.168
Non public location n (%)	16 (37)	2 (25)	14 (40)	0.445
Bystander CPR n (%)	32 (74)	5 (62)	27 (77)	0.414
Shockable rhythm n (%)	26 (60)	4 (50)	22 (63)	0.519
Coronary Angiogram n (%)	38 (88)	7 (88)	31 (89)	0.37
Coronary Angioplasty n (%)	15 (35)	2 (25)	13 (37)	0.414
Hypothermia n (%)	33 (77)	6 (75)	27 (77)	0.207

Cardiac Arrest Diagnoses

Atrioventricular block <i>n (%)</i>	3 (7)	1 (12)	2 (6)	0.5
Coma <i>n (%)</i>	1 (2)	0 (0)	1 (3)	0.688
Hyperkalemia <i>n (%)</i>	2 (5)	0 (0)	2 (6)	0.534
Asphyxia <i>n (%)</i>	3 (7)	1 (12)	2 (6)	0.5
ACS <i>n (%)</i>	26 (60)	2 (25)	24 (69)	0.009
Tamponnade <i>n (%)</i>	1 (2)	0 (0)	1 (3)	0.688
Arrhythmia <i>n (%)</i>	6 (14)	3 (38)	3 (9)	0.03
Drowning <i>n (%)</i>	1 (2)	0 (0)	1 (3)	0.688

Assistances

Impella <i>n (%)</i>	7 (16)	1 (12)	6 (17)	0.77
IACPB <i>n (%)</i>	8 (19)	3 (38)	5 (14)	0.139

- 1 BMI: Body Mass Index ; CA : Cardiac Arrest ; CPR : Cardio-Pulmonary Resuscitation; IACPB : Intra-
 2 Aortic Counter-Pulsation Balloon; OHCA : Out-Of-Hospital Cardiac Arrest ; SOFA : Sequential Organ
 3 Failure Assessment ; ACS : Acute Coronary Syndrome

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1 **Table 2. Hemodynamic parameters and ECLS complications in the ECLS population**
 2 **according to outcome.** Results are expressed as median [IQR] or n (%).

	All N = 43	Favorable Outcome N = 8	Poor Outcome N = 35	P Value
<i>ECLS Implantation Data</i>				
CA to ECLS delay (<i>hours</i>)	9 [6 - 16]	8 [7 - 18]	10 [6 - 15]	0.967
Hemodynamic				
MAP (<i>mmHg</i>)	58 [44 - 72]	60 [55 - 74]	57 [42 - 68]	0.553
Cardiac Index (<i>L/min/m²</i>)	1,37 [0,9 - 1,81]	1.73 [1.08 - 2.05]	1.36 [0.94 - 1.39]	0.786
Cardiac Power (<i>Watt</i>)	0,27 [0,14 - 0,44]	0.38 [0.25 - 0.49]	0.18 [0.14 - 0.35]	1
LVEF (%)	15 [10 - 25]	15 [12 - 21]	20 [10 - 25]	0.597
Inotropic Equivalent	220 [137 - 410]	160 [118 - 193]	230 [140 - 410]	0.247
<i>ECLS Efficacy</i>				
ECLS Withdrawal <i>n (%)</i>	8 (19)	7 (88)	1 (3)	< 0.001
Inefficacy <i>n (%)</i>	11 (26)	0 (0)	11 (31)	0.092
CPC ≤ 2 at D90 <i>n (%)</i>	8 (19)	7 (88)	1 (3)	< 0.001
Death at 1 year <i>n (%)</i>	35 (81)	0 (0)	35 (100)	< 0.001
<i>Potential complications ECLS-related</i>				
Complications	36 (84)	6 (75)	30 (86)	0.554
Total per patient (n = 71)	2 [1 - 3]	1 [1 - 2]	2 [1 - 2]	0.743
Hemorrhage <i>n (%)</i>	10 (23)	0 (0)	10 (29)	-
Lower Limb Ischemia <i>n (%)</i>	12 (28)	3 (38)	9 (26)	-
Coagulopathy <i>n (%)</i>	12 (28)	0 (0)	12 (34)	-
Hemolysis <i>n (%)</i>	1 (0)	0 (0)	1 (3)	-
ARDS <i>n (%)</i>	1 (0)	0 (0)	1 (3)	-
Femoral site infection <i>n (%)</i>	2 (0)	2 (25)	0 (0)	-
Renal Replacement Therapy <i>n (%)</i>	21 (50)	5 (63)	16 (46)	-
VAP <i>n (%)</i>	4 (1)	0 (0)	4 (11)	-
GastroIntestinal Bleeding <i>n (%)</i>	1 (0)	0 (0)	1 (3)	-
Mesenteric Ischemia <i>n (%)</i>	7 (16)	1 (13)	6 (17)	-

3 CA: Cardiac Arrest; LVEF: Left Ventricle Ejection Fraction; CPC : Cerebral Performance Category
 4 Score ; ARDS : Acute Respiratory Distress Syndrome ; VAP : Ventilator Associated Pneumonia

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- 1 **Table 3. Comparison between ECLS treated PCAS patients (ECLS group) and non**
- 2 **ECLS treated PCAS patients group (Control group). Results are expressed as median**
- 3 **[IQR] or n (%).**

	Overall n =921	ECLS group n = 43	Control Group n = 878	P Value
Age (yo)	62 [52 - 74]	54 [46 - 59]	63 [52 - 74]	<0.001
Male n (%)	633 (69)	32 (74)	601 (68)	0.50
Body Mass Index	25 [23 - 28]	26 [25 - 28]	25 [23 - 28]	0.19
Previous Medical History				
Coronaropathy n (%)	205 (24)	9 (21)	196 (25)	0.72
Diabete mellitus n (%)	184 (22)	7 (16)	177 (23)	0.45
Arterial Hypertension n (%)	374 (45)	15 (35)	359 (46)	0.21
Dyslipidemia n (%)	210 (26)	6 (14)	204 (26)	0.08
Active smoker n (%)	295 (40)	4 (9)	291 (42)	<0.001
Biological parameters on admission				
Blood Lactate (mmol/l)	5 [3 - 10]	10 [6 - 13]	5 [3 - 10]	0.002
Serum Creatinine (µmol/l)	109 [84 - 146]	148 [138 - 188]	108 [83 - 144]	<0.001
Potassium (mmol/l)	3.9 [3.3 - 4.5]	3.7 [3.2 - 4.2]	3.9 [3.3 - 4.5]	0.66
Characteristics of Cardiac Arrest				
No Flow (min)	3 [0 - 8]	2 [0 - 10]	3 [0 - 8]	0.33
Low Flow (min)	16 [10 - 25]	28 [14 - 42]	16 [10 - 25]	0.001
Adrenaline bolus (mg)	2 [0 - 5]	3 [1 - 9]	2 [0 - 5]	0.41
Non public location n (%)	617 (67)	16 (37)	601 (69)	<0.001
Bystander CPR n (%)	482 (52)	32 (74)	450 (51)	0.007
Shockable initial rythm n (%)	439 (48)	26 (60)	413 (47)	0.09
Coronary Angiogram n (%)	622 (68)	38 (90)	584 (67)	0.001
Coronary Angioplasty n (%)	238 (27)	15 (35)	223 (25)	0.14
Hypothermia n (%)	755 (80)	33 (77)	722 (82)	0.83

4 CPR : Cardio-Pulmonary Resuscitation;

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1 **Table 4. Factors associated with survival at ICU discharge in the whole PCAS**
 2 **population (n=921).** Results are expressed as median [IQR] or n (%)

	Survivors n = 237	Death n = 684	P Value
Age (yo)	61 [49 - 71]	63 [53 - 75]	0.01
Male n (%)	165 (70)	468 (68)	0.73
Body Mass Index	26 [22 - 28]	25 [23 - 30]	0.22
Previous Medical Diseases			
Coronaropathy n (%)	13 (6)	27 (4)	0.35
Diabetes mellitus n (%)	28 (13)	156 (26)	<0.001
Hypertension n (%)	91 (41)	283 (47)	0.18
Dyslipidemia n (%)	66 (30)	144 (24)	0.11
Active smoker n (%)	84 (40)	211 (40)	0.91
Biological Data at admission			
Blood lactate (mmol/l)	3 [2 - 5]	9 [5 - 13]	<0.001
Serum creatinine (µmol/l)	98 [76 - 124]	129 [97 - 169]	<0.001
Serum potassium (mmol/l)	3.6 [3.1 - 4.2]	4 [3.4 - 4.8]	<0.001
Cardiac Arrest Characteristics			
No Flow (min)	2 [0 - 5]	5 [0 - 10]	<0.001
Low Flow (min)	13 [7 - 20]	20 [13 - 30]	<0.001
Adrenaline (mg)	0 [0 - 3]	3 [2 - 6]	<0.001
Non public location n (%)	110 (47)	188 (28)	<0.001
Bystander CPR n (%)	140 (61)	342 (51)	0.008
Shockable rhythm n (%)	163 (69)	276 (40)	<0.001
Coronary Angiogram n (%)	187 (79)	435 (64)	<0.001
Coronary Angioplasty n (%)	85 (39)	153 (24)	<0.001
Hypothermia n (%)	216 (92)	539 (79)	<0.001
Assistances			
ECMO n (%)	9 (4)	34 (5)	0.59

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1 **FIGURE LEGENDS**

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3 **Figure 1: Mode and timing of death during ICU length of stay in the ECLS treated**
4 **population.**

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6 **Figure 2: Multivariate analysis of factors associated with ECLS initiation in the PCAS**
7 **population**

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9 **Figure S1: Serum Lactate levels according to neurological outcomes**

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