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Is pulseless electrical activity a reason to refuse cardiopulmonary resuscitation with ECMO support?

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ABSTRACT

Background: Cardiopulmonary resuscitation with ECMO support (ECPR) has shown to improve outcome in patients after cardiac arrest under resuscitation. Most current recommendations for ECPR do not include patients with a non-shockable rhythm such as PEA and asystole.

Aim: The aim of this study was to investigate the outcome of 3 patient groups separated by initial rhythm at time of ECMO placement during CPR: asystole, PEA and shockable rhythm.

Methods: We made a retrospective single-center study of adults who underwent ECPR for in-hospital cardiac arrest between June 2008 and January 2017. Outcome and survival were identified in 3 groups of patients regarding to the heart rhythm at the time decision for ECMO support was made: 1. patients with asystole, 2. patients with pulseless electrical activity, 3. patients with a shockable rhythm.

Result: 63 patients underwent ECPR in the mentioned time frame. Five patients were excluded due to incomplete data. Under the 58 included patients the number of cases for asystole, PEA, shockable rhythm was 7, 21 and 30 respectively. The means of CPR-time in these groups were 37, 41 and 37 min. Survival to discharge was 0.0%, 23.8% and 40.0% respectively ($p = 0.09$). All survivors to discharge had a good neurological outcome, defined as cerebral performance category 1or 2.

Conclusion: Survival to discharge in patients with PEA as initial rhythm at the time of decision for ECPR is 23.8% while no patients with asystole as initial rhythm survived discharge. Patients with PEA should be carefully considered for ECPR.

1. Introduction

Using veno-arterial extracorporeal membrane oxygenation (VA-ECMO) during resuscitation (ECPR) improves the outcome in a certain type of patients after refractory cardiac arrest [1] and also became a possible procedure in the emergency department [2].

It remains unclear which patients benefit from this invasive and costly procedure and therefore ECPR has also significant ethical implications [3] and patient selection is important. While ECPR on patients with refractory cardiac arrest and ventricular fibrillation has shown higher survival rates comparing to conventional cardiopulmonary resuscitation (C-CPR) [4], the role of ECPR in patients with non-shockable rhythm remains unclear. Many programs exclude patients with asystole and PEA from consideration for ECPR due to very limited outcome after conventional CPR [5-6] in both of these groups, PEA and asystole. Meaney PA et al. could show in a study with more than 50,000 adult patients with cardiac arrest and mechanical CPR that survival to discharge was slightly more likely after PEA than asystole (12% vs 11%) [6]. However, data for outcome of patients with PEA and asystole who underwent ECPR are still rare and to our knowledge direct comparing of these two patient-groups has not be publicized yet.

Reasons for PEA are various include reversible diseases like hypovolemia, tachydysrhythmias, cardiomyopathy, pulmonary embolism, cardiac tamponade, tension pneumothorax, and electrolyte abnormalities [7]. The absence of mechanical contractions is caused by factors that deplete myocyte high-energy phosphate stores and inhibit myocardial fiber shortening, which include metabolic acidosis and ionic perturbations, particularly potassium and calcium changes [8]. These reversible conditions might be diagnosed and treated better by giving more time through VA-ECMO support. Therefore we hypothesize that under ECPR patients with PEA have a better outcome than patients with asystole.

We investigated in a single-center study the outcome of patients who underwent ECPR and compared 3 groups of patients regarding to

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the rhythm at the time when decision for ECPR was made: asystole, PEA and shockable rhythm (ventricular fibrillation or ventricular tachycardia).

2. Methods

2.1. Study design

This is a retrospective, single-center study.

2.2. Data collection and setting

The patients studied included 63 patients who underwent VA-ECMO placement for resuscitation after cardiac arrest between June 2008 and January 2017 in the Penn State Milton S. Hershey Medical Center. Five patients were excluded from the study due to incomplete data. Information were received through the “Cerner Health Facts® database” (Cerner Corporation, Kansas City, MO). Clinical and demographic variables included age, sex, BMI, maximal level of creatinine, lactate, LDH, bilirubin, ALT prior to ECMO, maximal and minimal level of sodium, potassium, calcium, phosphate, magnesium and maximal troponine level as well as minimum ionized calcium, and bicarbonate during the first 24 h after ECPR. Reasons for cardiogenic shock were compiled. The SOFA (Sepsis-related Organ Failure Assessment) scores were calculated 24 h after CPR was started.

2.3. Patient categories

The total of 58 patients were stratified into 3 categories by the heart rhythm at time of decision for VA-ECMO was made (asystole, PEA, shockable rhythm (ventricle fibrillation (VF) or pulseless ventricle tachycardia (VT)).

2.4. ECPR treatment and patient management

Preparation for ECPR was started when mechanical CPR did not lead to return of spontaneous circulation (ROSC) within the first 10 min. All patients were under mechanical CPR by the time ECMO was placed.

Mechanical CPR was performed in accordance to the ACLS guidelines of the American Heart Association prior and during ECMO placement.

The ECMO circuit consisted of a Quadrox® oxygenator (Maquet Cardiovascular; Wayne, NJ) and a centrifugal pump, either a Centrimag® pump (Levitronix LLC, Waltham, MA) or a Rotaflow pump (Maquet Cardiovascular, Wayne, NJ).

The ECMO cannulation was performed by the attending intensivists. A peripheral catheter placement in both the femoral artery and the femoral vein by percutaneous Seldinger technic was done in the vast majority of the patients. ECMO management and care of the patient was performed by our Heart and Vascular Institute Critical Care Unit (HVICCU) team. Epinephrine, milrinone or dobutamine were used as inotropes. ECMO flows were adjusted appropriately to maintain mean arterial pressures (MAP) of more than 65 mm Hg and arterial saturation of more than 93%.

“Target temperature management” (TTM) was used in the majority of patients after cardiac arrest and a goal temperature of 32–34 °C for 24 h was aimed.

2.5. Study endpoint

The primary endpoint was survival to discharge. The secondary endpoint was requirement for renal replacement therapy and neurological outcome.

The cerebral performance category (CPC) was used to describe the neurological status. CPC 1 and 2 were defined as good neurological outcome.

2.6. Statistical analysis

We de-identified the patients and recorded clinical and laboratory data.

We used the IBM SPSS Statistics Version 24 (IBM Corporation, Armonk, NY) for statistical analyses. The Pearson's x^2 test of independence or the Fisher's exact test and the Kruskal-Wallis test (for non-normal distributions) were used to compare data between the 3 different rhythm groups. Statistical significance was defined by a *p*-value of 0.05 or less. We established a Kaplan-Meier survival curve to show survival difference in the 3 patient groups. We reported the results as percentages, means ± standard deviations, and/or medians and interquartile ranges (IQRs).

3. Results

3.1. Patients characteristics

The characteristics of the patients divided by the initial heart rhythm at time of decision making for ECMO treatment are shown in Table 1. There was no significant difference between the 3 groups in age, gender, BMI, maximal lactate, maximal troponine, maximal LDH, bilirubin and ALT. A significant difference of the creatinine level, maximum and minimum potassium level and low magnesium level between the groups could be found, with the highest and lowest mean level respectively in the PEA group. Furthermore another significant variable was the percentage of patients with acute myocardial infarction as origin for cardiogenic shock, with the highest percentage (76.7%) within the group with shockable rhythm and the lowest percentage (38.1%) under the patients with PEA. Other reasons for cardiogenic shock were not significantly different between the groups. Duration of CPR and SOFA score also did not differ significantly.

A “target temperature management” (TTM) with a goal temperature of 32–34 °C for 24 h was performed in 30 patients (50.9%).

Table 1
Characteristics of patients after ECPR ($n = 58$).

Variables	Total cases (n = 58)	Asystole ($n = 7$)	PEA ($n = 21$)	Shockable rhythm ($n = 30$)	p-Value
Age (mean, years)	56.59 (±15.11)	52.14 (±18.05)	58.95 (±13.19)	55.97 (±15.88)	0.622
Male (n, %)	36 (62.1)	3 (42.9)	13 (65.0)	20 (66.7)	0.490
BMI	32.39(±10.75)	33.26 (±4.33)	33.43 (±14.53)	31.46 (±8.71)	0.592
Reason for shock; n(%)					
aMI	36 (62.1)	5 (71.4)	8 (38.1)	23 (76.7)	0.017
cardiomyopathy (no aMI)	2 (3.4)	0 (0)	1 (4.8)	1 (3.3)	0.835
Pulmonary embolism	4 (6.9)	0 (0)	3 (14.3)	1 (3.3)	0.235
Allograft rejection	5 (8.6)	0 (0)	3 (14.3)	2 (6.7)	0.436
Septic shock	3 (5.2)	0 (0)	3 (14.3)	0 (0)	0.062
Complication procedure	7 (12.1)	1 (14.3)	3 (14.3)	3 (10.0)	0.882
Duration of CPR (min)	38.9 (±17.9)	36.6 (±18.0)	41.1 (±15.2)	37.2 (±21.4)	0.712
SOFA	13.63 (2.51)	14.75 (2.22)	14.00 (3.04)	12.93 (1.90)	0.363

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3.2. Outcome

The results of a univariate analysis comparing the relationship between the 3 different groups and outcome are shown in Table 2. Survival to discharge rate was 0.0% for patient with asystole, 23.8% for patients with PEA, 40.0% for patients with a shockable rhythm. Fig. 1 shows a Kaplan-Meier-survival curve of the three groups. There was no significant difference in the numbers of ICU-days, days on device and days on ventilator between the 3 groups. The need for continuous renal replacement therapy (CRRT) was significantly different, with the highest number in the PEA-group and the lowest number in the patient-group with asystole.

4. Discussion

4.1. Principal finding

The study shows that although there was no significant difference in the survival rate between the groups, a remarkable better survival was seen in patients with a shockable rhythm. This was expected due to known significant differences between shockable rhythm and non-shockable rhythm in bigger studies [6]. However, we also saw a remarkable trend toward improved survival in the PEA group when compared with the asystole group.

The reason for PEA can be various acutely reversible disorders including hypovolemia, tachydysrhythmias, cardiomyopathy, pulmonary embolism, cardiac tamponade and electrolyte abnormalities [7].

We found a significant higher median level for creatinine, maximal potassium as well as minimum potassium and magnesium level in the patient group with PEA, pointing that electrolyte abnormalities might have been played an important role in this group of patients. VA-ECMO support could prolong the time for diagnostic and treatment. Especially this patient group might benefit from this time gain and give providers a better chance to resolve the electrolyte abnormalities. The need for continuous renal replacement therapy (CRRT) in the PEA group was also significantly higher.

To our knowledge this is the only study that compares outcome of ECPR patients with PEA and ECPR patients with asystole. Bigger studies are necessary to confirm or deny our hypothesis that patients with PEA have a better outcome than patients with asystole under ECPR.

If our hypothesis would be correct the outcome in patients with PEA under resuscitation with VA-ECMO should be significantly higher than in patients with asystole since this group of patients would be given more time to diagnose and treat the disorder leading to PEA. Because of the limited time of resuscitation in the pre-ECPR era patients with PEA were not given the time needed to treat these reversible disorders. Therefore patients with PEA during resuscitation should be included if considering ECPR.

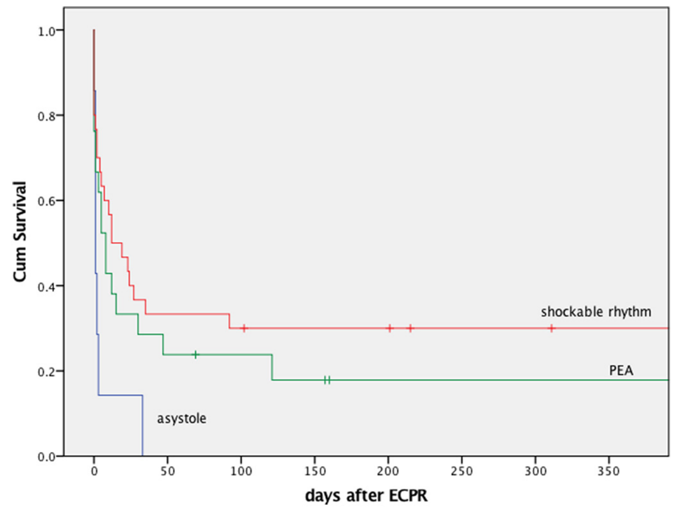

Fig. 1. Kaplan-Meier one-year survival curve of 58 ECPR patients.

In our study we even had a significantly lower amount of acute myocardial infarction in the PEA group since these patients often present with a shockable rhythm as initial rhythm in cardiac arrest.

4.2. Limitations

This study is a retrospective, single center study. The number of 58 patients might be too small to show a significant difference between the outcome of patients with asystole and patients with PEA under ECPR.

5. Conclusion

This study did show a non-significant difference in discharge to survival between patients under ECPR with asystole on the one side and patients with PEA on the other side.

Table 2
Results after ECPR (n = 58 patients).

	Total	Asystole	PEA	Shockable rhythm	*P*
Discharge n/N (%)	17 (29.3)	0 (0)	5 (23.8)	12 (40.0)	0.088
ICU days	15.31 (24.10)	7.00 (11.83)	15.90 (23.25)	16.93 (26.88)	0.274
Days on device	6.55 (7.08)	6.14 (11.87)	6.43 (6.16)	6.73 (6.56)	0.389
Ventilator days	9.61 (13.26)	7.00 (11.73)	8.72 (9.65)	10.79 (15.59)	0.267
CRRT	29 (50.0)	1 (14.3)	15 (71.4)	13 (43.3)	0.019
Creatinine	1.87 (±1.01)	1.60 (±0.71)	2.51(±1.01)	1.50 (±0.89)	0.003
Troponine	117.35(±187.47)	161.0 (±258.4)	46.6 (±97.9)	130.2 (±179.9)	0.226
Lactate	11.19 (±5.46)	13.00 (±5.49)	12.71 (±5.18)	9.59 (±5.39)	0.120
LDH	5383 (±4137)	7079 (±4375)	6667 (±5083)	3996 (±2770)	0.200
Bilirubin	1.42 (±1.15)	1.82 (±1.61)	1.61 (±1.39)	1.19 (±0.77)	0.566
Na (max level) mmol/l	146.4 (8.9)	152.0 (7.6)	144.1 (9.6)	146.7 (8.3)	0.095
Na (min level) mmol/l	135.9 (7.6)	138.6 (9.4)	134.8 (5.5)	136.0 (8.5)	0.203
K (max level) mmol/l	5.2 (1.3)	5.1 (1.2)	5.8 (1.4)	4.8 (1.0)	0.050
K (min level) mmol/l	3.3 (0.9)	3.1 (1.0)	3.8 (1.0)	3.0 (0.6)	0.005
Mg (max level) mmol/l	2.8 (1.2)	3.1 (0.8)	2.5 (0.8)	2.9 (1.5)	0.223
Mg (min level) mmol/l	2.1 (0.5)	2.5 (0.8)	2.1 (0.4)	2.0 (0.4)	0.258
Ca (min level) mmol/l	7.5 (1.1)	7.9 (0.9)	7.5 (1.2)	7.5 (1.1)	0.429
Ion Ca (min level) mmol/l	0.95 (0.24)	1.02 (0.14)	0.88 (0.27)	0.97 (0.24)	0.623
Bicarbonate (min level)	15.8 (4.6)	16.3 (3.5)	15.2 (4.0)	16.0 (5.3)	0.867
Phosphate (max) mmol/l	7.26 (3.77)	7.30 (4.94)	9.02 (3.18)	5.90 (3.44)	0.026
Phosphate (min) mmol/l	4.22 (2.59)	3.97 (4.28)	4.35 (1.29)	4.19 (2.89)	0.260

We have seen a significant higher number of patients with electrolyte abnormalities and need for CRRT in the group with PEA patients. Reversible diseases could have caused cardiac arrest in many of these cases.

Lager studies are needed to clarify if patients with PEA have a significant better outcome after resuscitation with ECPR than patients with asystole. In patients with asystole ECPR does not seem to be a reasonable option for resuscitation.

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Conflict of interest

None declared.

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