Title: The impact of on-site cardiac rhythm on mortality in patients supported with extracorporeal cardiopulmonary resuscitation: A retrospective cohort study.

Running title: Cardiac rhythm before ECPR and mortality.

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Abstract

Background: Extracorporeal cardiopulmonary resuscitation (ECPR) is increasingly used in patients with out-of-hospital or in-hospital cardiac arrest in whom conventional cardiopulmonary resuscitation remains unsuccessful. The aim of this study was to analyze the impact of initial cardiac rhythm - detected on-site of the cardiac arrest - on mortality.

Methods: We performed a retrospective cohort study of patients who received ECPR in our tertiary care cardiac arrest center. Patients were divided into three groups depending on their cardiac rhythm: shockable rhythm, pulseless electrical activity, and asystole. The primary endpoint was mortality within the first 7 days after ECPR deployment. Secondary endpoints were mortality within 28 days and impact of pre-ECPR potassium, serum lactate, pH and pCO2 on mortality. The association of the initial cardiac rhythm and the location of arrhythmia detection (patient monitored in hospital [category: *monitored*], not monitored but hospitalized [*in-hospital*], not monitored, not hospitalized [*out-of hospital*]) with the primary and secondary outcome was examined by means of univariable and multivariable logistic regression.

Results: Sixty-five patients could be included in the final analysis. Thirty-two patients (49.2%, 95%CI 36.6% - 61.9%) died within the first 7 days. In terms of 7-day-mortality patients differed in the initial cardiac rhythm (p=0.040) and with respect of the location of arrhythmia detection (p=0.002). Shockable cardiac rhythm (crude OR 0.21; 95%CI 0.03 - 0.98) and pulseless electrical activity (0.13; 0.02 - 0.61) as the initial rhythm on-site showed better odds for survival compared to asystole. However, this association did neither persist in adjusted analysis nor in pairwise comparison.

Discussion: The study could not demonstrate a better outcome with shockable rhythm after ECPR. More homogeneous and adequately powered cohorts are needed to better understand the impact of cardiac rhythm on patient outcome after ECPR.

Keywords

Cardiac rhythm; extracorporeal cardiopulmonary resuscitation; cardiac arrest, mortality

Background

Sudden cardiac arrest is a leading cause of death in Europe, affecting up to 700,000 individuals per year.[1,2] In recent years, survival following sudden cardiac arrest has been improved by broad implementation of first-responder systems - especially in rural areas where more time is needed for emergency rescue services to reach the patient, but also in some urban areas which have a greater proportion of knowledgeable lay rescuers prepared to assist in the initial resuscitation of cardiac arrest.[3] Despite all these efforts, the probability of survival after sudden cardiac arrest, at 10–20%, is low, regardless of whether cardiac arrest occurred out of hospital (OHCA) or in hospital (IHCA).[4-6] Even the introduction of mechanical resuscitation aids has not significantly improved prognosis, although these aids have shown advantages in selected situations.[7]

Technological progress has led to the development of extracorporeal cardiopulmonary resuscitation (ECPR), a technique derived from cardiopulmonary bypass which is increasingly being used as an extension of conventional cardiopulmonary resuscitation.[8,9] Data on ECPR promise better outcomes of OHCA patients due to a reduction in low-flow time, and subsequently better organ perfusion.[10] The most recent guidelines for resuscitation note that the use of ECPR should be considered in patients in whom advanced resuscitation is unsuccessful or in the facilitation of specific interventions.[2] ECPR is increasingly being applied in the in-hospital setting, as well as in individual pilot studies outside the hospital. However, the evidence from available studies does not allow to clearly determine which patients might benefit from the use of ECPR. In this retrospective, single-center cohort analysis, we aimed to analyse the effect of the initial cardiac rhythm - detected on-site of cardiac arrest - on mortality.

Methods

ECPR cases at our tertiary referral center between May 1, 2013, and September 30, 2017, were retrospectively identified from different data sources. Exclusion criteria for the current analysis were age <18 years and ECPR for rewarming in cases of profound accidental hypothermia. The following data were collected: demographics (age, sex, height, weight, and body mass index), data on cardiac arrest (cause, on-site cardiac rhythm, the location of arrhythmia detection (definition please see under statistical analysis), resuscitation time before ECPR deployment, cumulative days in intensive care, survival within 7 and 28 days after ECPR deployment, hospital discharge, time to and cause of death and ECPR-associated complications. Vital parameters were taken from the electronic anaesthesia protocol and the electronic patient protocol of the intensive care unit. ECPR-specific parameters such

as information on cannulation, maximum blood flow and the duration of extracorporeal support were taken from the perfusionist's protocol. ECPR was performed in accordance with our local guidelines.[11] Each ECPR deployment took place in our hospital. The cornerstone of our routine clinical care of post cardiac arrest patients consists of initial normothermic treatment. This is followed by prognostication after withdrawal of sedatives and clinical assessment of the neurological status thereafter if hemodynamic stability allows, further bedside electroencephalography, biomarkers (neuron specific enolase) and neuroimaging (computed tomography and magnetic resonance imaging) are routinely employed. Prognostication is routinely performed after 96 hours.

Patients were divided into three groups depending on their cardiac rhythm on-site: 1. shockable rhythm (ventricular fibrillation, pulseless ventricular tachycardia, VF/PVT), 2. pulseless electrical activity (PEA) and 3. asystole. As the primary endpoint, mortality within the first 7 days after ECPR deployment was analyzed with regards to the cardiac rhythm. As secondary endpoints, mortality after 28 days was assessed. Further, as an exploratory analysis, laboratory values from blood gas analysis before ECPR were evaluated with regards to their impact on mortality. The aim was to identify possible predictors with significant differences in mortality vs. survival within the first 7 days, thus possibly facilitating a decision for or against the use of ECPR. For this purpose, potassium, serum lactate, pH and $paCO_2$ were analyzed for statistically significant differences between the groups "alive" (survivors 7 days after ECPR) and "death" (death within 7 days of ECPR). The study was reviewed and approved by the local Ethical Committee (ID: 2018-01684).

Statistical analysis

Continuous variables were examined for normality using the Shapiro-Wilk test and are presented with mean and standard deviation for normally distributed data and with median and interquartile range (IQR) otherwise. Categorical variables are presented with counts and percentages. Group comparisons for normally distributed data is based on Student's t-test, for skewed continuous data on the Wilcoxon rank sum test and for categorical data on the chi-square and on the exact Fisher test when the expected count in some cells is lower than 5. The association of the initial cardiac rhythm and the location of arrhythmia detection (patient monitored in hospital [category: *monitored*], not monitored but hospitalized [*in-hospital*], not monitored, not hospitalized [*out-of hospital*]) with the primary and secondary outcome was examined by means of univariable and multivariable logistic regression. The statistical significance of the above-mentioned two categorical predictors was examined by the drop in deviance and its

associated p-value. Using the estimated marginal means framework for the multivariable logistic regression models (R package emmeans),[12] we illustrated both crude and adjusted predictions plot of the probability of death for 7-days and 28-days. Pre-ECPR laboratory values of potassium, lactate, $paCO_2$ and pH were compared between surviving and deceased patients and a generalized additive model (GAM) was used to visualize the non-linear relationship between pre-ECPR laboratory values and the primary outcome. As the comparisons of laboratory values are purely explorative in nature, no p-value adjustment for multiple comparisons were performed. A p-value<0.05 was considered statistically significant and all analyses were performed using R version 4.0.2.[13]

Results

Eighty-eight patients were identified during the study period. One patient was excluded due to age (<18 years). Six patients received veno-arterial extracorporeal cardiac life support (ECLS) in severe shock without cardiac arrest and five patients received ECPR but were not transferred to our hospital. In two patients, ECPR could not be established. Nine patients had to be excluded from the analysis due to missing data relevant to the study purposes. Of the 88 initially identified patients, 65 were included in the final analysis. Patients` demographics are shown in Table 1, ECPR-related data in Table 2. In all groups, the proportion of male patients was higher than that of female patients (69.2% vs. 30.8%). The groups did not differ in terms of age (p=0.25), or body mass index (p=0.08). Most patients who were resuscitated out-of-hospital or in-hospital had VF/PVT as initial rhythm on-site of cardiac arrest (41.4% and 24.1%, respectively). Groups did differ in cardiac arrest location, initial serum lactate level, subsequent lactate levels, and ECPR duration.

Primary endpoint

Mortality within 7 days

Overall, thirty-two patients (49.2%, 95%CI 36.6% - 61.9%) died within the first 7 days after ECPR. The most common causes of mortality were refractory cardiogenic shock in 15 patients (46.9%) and severe neurologic injury in 9 patients (28.1%) (Supplement 1.). In terms of 7-day-mortality patients differed in the initial cardiac rhythm on-site of cardiac arrest (p=0.040) and with respect of the location of arrhythmia detection (p=0.002). VF/PVT (crude OR 0.21; 95%CI 0.03 - 0.98) and PEA (0.13; 0.02 - 0.61) as the initial rhythm showed better odds for survival compared to asystole (Table 3). However, adjusting for the location of arrhythmia detection, the effect of VF/PVT and PEA for survival was less pronounced

and more statistically uncertain. Overall, the location of arrhythmia detection was a significant predictor for 7-day-survival in the multivariable logistic regression model (p=0.011) in contrast to the initial cardiac rhythm (p=0.286). The estimated probability of death for each initial cardiac rhythm and their pairwise comparisons are illustrated in Figure 1 highlighting the impact of the adjustment for the location of arrhythmia detection. No pairwise adjusted comparisons were statistically significant (Supplement 2).

Secondary endpoints

Mortality within 28 days

Within 28 days after ECPR, 34 patients died and 31 survived (47.7%; 95%CI 35.1% - 60.5%). Similarly to the primary outcome, VF/PVT (0.21; 95%CI 0.03 - 0.98) and PEA (0.17; 0.02 - 0.85) as the initial rhythm showed better odds for survival compared to asystole (Table 4). Again, the location of arrhythmia detection in the multivariable model was a significant predictor for 28-days-survival (p=0.018) in contrast to initial cardiac rhythm (p=0.239).

Impact of pre-ECPR potassium, serum lactate, pH and pCO_2 on mortality

The potassium levels of the two groups showed no significant differences (p=0.70). Lactate levels were significantly higher in the group of patients who died within 7 days (p=0.048, Table 5). Regarding the last $paCO_2$ measured before ECPR deployment, no significant effect on survival after ECPR could be demonstrated (p=0.178). Likewise, the pH values before ECPR deployment showed no significant difference between the survivors and decedents (p=0.058). Figure 2 illustrates the estimated non-linear relationship between pre-ECPR laboratory values and the primary outcome.

Discussion

Sixty-five cardiac arrest patients with a known initial cardiac rhythm on-site (before ECPR deployment) were included in the calculation of the primary endpoint (mortality within the first 7 days), and almost half of those (32 patients; 49%) died within the first 7 days. The group with a shockable rhythm showed a trend towards an increased probability for survival in comparison to the asystole group in the crude analysis. These observations reflect the situation encountered in Advanced Cardiac Life Support (ACLS) efforts without ECPR, with poor outcomes after resuscitation in patients with asystole. However, this trend did not persist in adjusted analysis. The demographic variables do not show strong imbalances (Table 1). We examined the pre-ECPR values in Table 2, and the strongest imbalance was found in the

ECPR location (P<0.001). Assuming that the location of the cardiac arrest might strongly impact the survival chance (i.e. the closer to the hospital the more likely the survival), we found that this imbalance could have impact on the analysis. The finding that after adjustment no difference between rhythms was obvious is in line with a retrospective cohort study that investigated mortality as primary outcome after ECPR in a similar cohort as ours.[14] The authors, could not demonstrate an association of the initial cardiac rhythm to mortality and concluded that a non-shockable rhythm should not be considered as an exclusion criterion for ECPR. It can be assumed that the low number of survivors with shockable rhythm (3/16), together with a high portion of intoxicated patients with non-shockable rhythm is responsible for this result. Another publication with a comparable population found the strongest association of mortality after ECPR was ongoing CPR time and time from cardiac arrest to start of ECPR, initial cardiac rhythm was not significant.[15] Likewise the latest consensus statement from the extracorporeal life support organization does not give recommendations regarding initial rhythm and decision for or against the initiation of ECPR.[9] However, valuable data indicate that the use of ECPR in patients with out-of-hospital cardiac arrest and an initial cardiac rhythm of asystole should be viewed critically.[16-18] Lastly, whether early deployment of ECPR in asystole patients can significantly reduce mortality compared to conventional cardiopulmonary resuscitation remains questionable and requires further investigation.

No significant difference in mortality could be observed within 7 days after ECPR for patients with PEA and patients with a shockable initial rhythm. In both groups, 7-day survival was almost 50% and did not decrease significantly by 28 days after ECPR. Only two more patients died between 8 and 28 days after ECPR. On average, those who died within the first 7 days did so on the 2nd day after receipt of ECPR. This is interesting from a prognostic point of view, since the probability of survival increases significantly after a few critical days. However, the probability of survival does not describe neurological outcome of the surviving patients any further. With 7-day survival of 50.8% and 28-day survival of 47.7% after ECPR, the probability of survival in this retrospective study is in the upper range of comparable studies.[19-23] This could be related to the hospital's internal guidelines and international consensus statements for ECPR.[9] There is debate over whether the exclusion criteria are too restrictive, especially regarding patient age.[24]

The success of ECPR depends to a large extent on the duration of the "no flow time". Therefore, when discussing prognostic factors, it is important to consider the location of cardiac arrest (in-hospital vs. out-of-hospital) in addition to factors such as initial rhythm. In our study, the impact of the location of arrhythmia detection was significant, with better 7- and 28-day survival, respectively, when

cardiopulmonary resuscitation performed in-hospital or even in a patient under already existing hemodynamic monitoring. This result is obvious and can certainly be explained by the shorter time required to re-establish organ perfusion, but also by better and more quickly available logistics.[25]

Considering 7-day survival in dependence on potassium level after ECPR, there is no significant difference between patients who died and those who survived in the first 7 days. As with arterial pCO2, no substantial change in mortality could be proven before ECPR. As a result, neither parameter is acceptable for estimating mortality under ECPR or deciding whether ECPR should be performed. In a retrospective analysis a pH <6.8 was associated with a poor outcome.[26] In a meta-analysis different risk factors were examined regarding their prognostic value in OHCA patients.[27] The primary outcome was significantly improved in patients with OHCA in the presence of an initially shockable cardiac rhythm, a higher pH, and low serum lactate, analogous to the results of this retrospective analysis, and to a prospective study.[28] The pH seems to be a better predictor of the neurological outcome than the serum lactate, at least in OHCA patients with conventional cardiopulmonary resuscitation.[29] Individual values, however, should be interpreted with caution and should not be used in the sole context of decision-making for or against ECPR. To date, there are no well-validated cut-off values for serum lactate and pH that should be independently used for an ECPR decision.[30] It is far more crucial to consider the data overall; pathological laboratory findings can aid in the decision-making process, but they should not be used as a predictor.

Study strengths

Our study population is a well-documented cohort from a well-described catchment area (urban and rural) of our university center. This increases the validity and interpretability of our results. Another strength is the evaluation of mortality at two different time points after ECPR (7d and 28d) and additional factors (e.g. lactate, potassium level, the location of arrhythmia detection) on the outcome after ECPR. In our opinion, the publication of results from 2013 to 2017 does not limit the validity of the study. Although there are already some well-designed studies on this topic, the influence of cardiac rhythm has so far found its way into the current guidelines only to a limited extent. Our study and the conclusions is not new in this regard, but highlights the relevance of consistent patient assessment prior to ECPR, which is a costly and personnel-intensive intervention with a high mortality rate.[31]

Study limitations

A major limitation of this study is the reporting of a small cohort with data until 2017. Due to the retrospective study design, the group sizes vary considerably. For example, the group of patients with asystole as the initial rhythm is significantly smaller than the other two groups. It should also be noted that a bias exists regarding patient selection which was dependent of the rescue team on- site and thus, included sometimes patients with an initial bad prognosis. Also, due to the study design, not all laboratory values required for the evaluation of the secondary endpoints were available from all patients. Given the sample size we decided only to choose one covariate (location of arrest) for the logistic regression, classical approaches like propensity score matching would not be feasible given the sample size. There are other studies pointing towards our finding also. Nevertheless, we think that every publication of single (ECPR) center experience can add important information to the body of evidence and also serve as data basis for possible future analyses. Guidelines may even be stronger if they are based on a broad, growing, basis of evidence.

Conclusion

In conclusion, this study could not demonstrate a difference in outcome depending on initial (on-site) cardiac rhythm after cardiac arrest. The relevance of on-site cardiac rhythm to the early management of cardiac arrest with ECPR requires, in our opinion, more homogeneous and adequately powered cohorts to better understand its impact on patient outcome after ECPR.

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Tables

Table 1: Patients' demographics stratified according to on-site cardiac rhythm.

	All ***N=65***	**Asystole** ***N=11***	**PEA** ***N=25***	**VF/PVT** ***N=29***	***P***
Age (yr)	53.8 (15.3)	51.3 (11.3)	57.8 (15.0)	51.3 (16.5)	0.253
Sex:					0.771
Male	45 (69.2%)	8 (72.7%)	16 (64.0%)	21 (72.4%)	
Female	20 (30.8%)	3 (27.3%)	9 (36.0%)	8 (27.6%)	
Height (cm)†	172 (9.12)	171 (6.95)	172 (9.33)	172 (9.80)	0.965
Weight (kg)‡	76.7 (18.6)	76.4 (15.3)	81.1 (18.9)	73.1 (19.0)	0.290
BMI (kg/m^2)†	25.6 (5.01)	26.0 (4.49)	27.2 (4.87)	24.1 (5.01)	0.082

† 3 values missing; ‡ 2 values missing
PEA indicates pulseless electrical activity; VF/PVT, ventricular fibrillation, or pulseless ventricular tachycardia; BMI, body mass index; yr, years. Values are mean (standard deviation) or number (percentage, %).

Table 2: ECPR-related data stratified according to on-site cardiac rhythm.

	All *N=65*	**Asystole** *N=11*	**PEA** *N=25*	**VF/PVT** *N=29*	***P***
Pre-ECPR					
Group:					<0.001
out-of-hospital	20 (30.8%)	7 (63.6%)	1 (4.00%)	12 (41.4%)	
in-hospital	14 (21.5%)	2 (18.2%)	5 (20.0%)	7 (24.1%)	
monitored	31 (47.7%)	2 (18.2%)	19 (76.0%)	10 (34.5%)	
l-CPR, min	0.00 [0.00;0.00]	3.00 [0.00;10.0]†	0.00 [0.00;0.00]‡	0.00 [0.00;0.00]*	0.001
p-CPR, min	35.0 [18.0;52.0]	45.0 [27.8;57.2]	27.0 [10.0;41.2]	41.0 [25.0;59.0]	0.083
CPR cumulative, min	35.0 [17.5;51.8]	45.0 [39.5;57.0]	27.0 [10.0;41.2]	38.0 [22.0;55.0]	0.044
K+, mmol/l	4.60 [4.00;5.30]	4.75 [4.15;5.80]	4.70 [4.15;5.30]	4.50 [3.65;5.25]	0.516
a-pH	7.05 (0.23)	7.00 (0.34)	7.14 (0.22)	6.99 (0.16)	0.130
a-pCO2, mmHg	50.0 (19.4)	46.9 (24.6)	46.0 (14.6)	54.9 (20.6)	0.376
a-BE, mmol/l	-15.25 [-18.08;-9.80]	-17.10 [-19.75;-9.75]	-11.95 [-17.92;-4.75]	-16.40 [-17.45;-14.10]	0.240
a-pO2, mmHg	91.0 [69.0;206]	158 [89.0;296]	93.4 [67.0;228]	84.5 [70.0;116]	0.314
Hb, g/l	117 (26.3)	110 (34.0)	117 (27.0)	122 (20.7)	0.507
Lactate, mmol/l	11.9 (6.53)	16.2 (8.15)	9.97 (5.37)	11.1 (5.54)	0.045
ECPR					
Cannulae:					1.000
Peripheral	56 (96.6%)	10 (100%)	20 (95.2%)	26 (96.3%)	
Central	2 (3.45%)	0 (0.00%)	1 (4.76%)	1 (3.70%)	
ECPR Type: VA-	65 (100%)	11 (100%)	25 (100%)	29 (100%)	.
Pacemaker					0.741
No	45 (80.4%)	8 (88.9%)	18 (81.8%)	19 (76.0%)	
Yes	11 (19.6%)	1 (11.1%)	4 (18.2%)	6 (24.0%)	
Perfusion cannulae					0.864
No	19 (29.2%)	2 (18.2%)	7 (28.0%)	10 (34.5%)	
Other	27 (41.5%)	6 (54.5%)	10 (40.0%)	11 (37.9%)	
Yes	19 (29.2%)	3 (27.3%)	8 (32.0%)	8 (27.6%)	
ECPR flow, l/min	4.00 [3.35;4.50]	3.50 [3.00;4.32]	4.20 [3.40;4.70]	4.00 [3.44;4.34]	0.307
best SvO2, %	79.1 (8.54)	75.9 (8.57)	81.3 (9.73)	78.2 (7.11)	0.220
worst SvO2, %	56.1 [48.1;62.9]	58.6 [42.6;61.0]	52.0 [48.5;60.5]	58.7 [48.4;63.5]	0.798
K+, mmol/l	4.15 [3.60;5.12]	3.90 [3.65;5.50]	4.55 [3.58;5.25]	4.00 [3.50;4.45]	0.454
a-pH	7.15 [7.05;7.30]	7.13 [7.04;7.26]	7.16 [7.04;7.33]	7.16 [7.09;7.29]	0.755
a-pCO2, mmHg	37.4 (12.2)	36.2 (14.9)	36.7 (11.6)	38.4 (12.1)	0.851
a-BE, mmol/l	-13.15 (6.67)	-15.42 (6.66)	-13.09 (7.55)	-12.29 (5.83)	0.428
a-pO, mmHg	316 [178;408]	386 [348;422]	311 [178;445]	216 [132;344]	0.088
Hb, g/l	103 (22.0)	87.5 (21.0)	101 (21.2)	110 (20.5)	0.017
Lactate, mmol/l	12.5 (5.41)	15.9 (5.86)	12.9 (5.82)	10.9 (4.27)	0.034
Post-ECPR					
ECPR cumulative, hrs	44.0 [12.0;73.0]	9.50 [5.62;29.0]	52.0 [23.0;110]	47.0 [16.0;73.0]	0.024

PEA indicates pulseless electrical activity; VF/PVT, ventricular fibrillation or pulseless ventricular tachycardia; ECPR, extracorporeal cardiopulmonary resuscitation; CPR, cardiopulmonary resuscitation before ECPR deployment; monitored CPR, patient on a monitoring unit before CPR; l-CPR, lay resuscitation in minutes (min); p-CPR, professional resuscitation; K+, potassium level; a-, arterial blood gas; pCO2, partial pressure of carbon dioxide; BE, base excess; pO2, partial pressure of oxygen; Hb, hemoglobin level; VA-, veno-arterial; Perfusion cannulae, distal perfusion cannulae (shunt) to prevent limb ischemia; SVO2, venous oxygen saturation; hrs, hours. Values are number (percentage, %), mean (standard deviation) or median [interquartile range].

Table 3: Summary statistics of mortality (and survival) within 7 days. Coefficients of a logistic regression model are shown for the unadjusted case (where only the on-site cardiac rhythm is a predictor) and the adjusted case including the location of arrhythmia detection as a predictor.

	Summary Measures			Unadjusted Regresion			Adjusted Regression		
	Alive (N=33)	**Death (N=32)**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Cardiac Rhythm			0.040						
Asystole	2 (6.06%)	9 (28.1%)		—	—		—	—	
PEA	16 (48.5%)	9 (28.1%)		0.13	0.02, 0.61	0.019	0.36	0.04, 2.33	0.3
VF/PVT	15 (45.5%)	14 (43.8%)		0.21	0.03, 0.98	0.069	0.25	0.03, 1.38	0.14
Location of arrhythmia detection			0.002						
Out of hospital	4 (12.1%)	16 (50.0%)		—	—		—	—	
In hospital	7 (21.2%)	7 (21.9%)					0.27	0.05, 1.28	0.11
Monitored	22 (66.7%)	9 (28.1%)					0.11	0.02, 0.47	0.005

OR indicates Odds Ratio; CI, confidence interval; PEA, pulseless electrical activity; VF/PVT, ventricular fibrillation or pulseless ventricular tachycardia; ECPR, extracorporeal cardiopulmonary resuscitation. Values are number (percentage, %) or OR with 95% CI.

Table 4: Summary statistics of mortality (and survival) within 28 days. Coefficients of a logistic regression model are shown for the unadjusted case (where only the initial cardiac rhythm is a predictor) and the adjusted case including ECPR location included as a predictor.

	Summary Measures			Unadjusted Regresion			Adjusted Regression		
	Alive (N=31)	**Death (N=34)**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Cardiac rhythm			0.094						
Asystole	2 (6.45%)	9 (26.5%)		—	—		—	—	
PEA	14 (45.2%)	11 (32.4%)		0.17	0.02, 0.85	0.047	0.48	0.06, 3.08	0.5
VF/PVT	15 (48.4%)	14 (41.2%)		0.21	0.03, 0.98	0.069	0.25	0.03, 1.37	0.14
Location of arrhythmia detection			0.008						
Out of hospital	4 (12.9%)	16 (47.1%)		—	—		—	—	
In hospital	7 (22.6%)	7 (20.6%)					0.24	0.04, 1.17	0.085
Monitored	20 (64.5%)	11 (32.4%)					0.12	0.02, 0.54	0.008

OR indicates odds ratio; CI, confidence interval; VF/PVT, ventricular fibrillation or pulseless ventricular tachycardia; ECPR, extracorporeal cardiopulmonary resuscitation. Values are number (percentage, %) or OR with 95% CI.

Table 5: Laboratory measurements pre-ECPR stratified according to the primary outcome (survival 7 days).

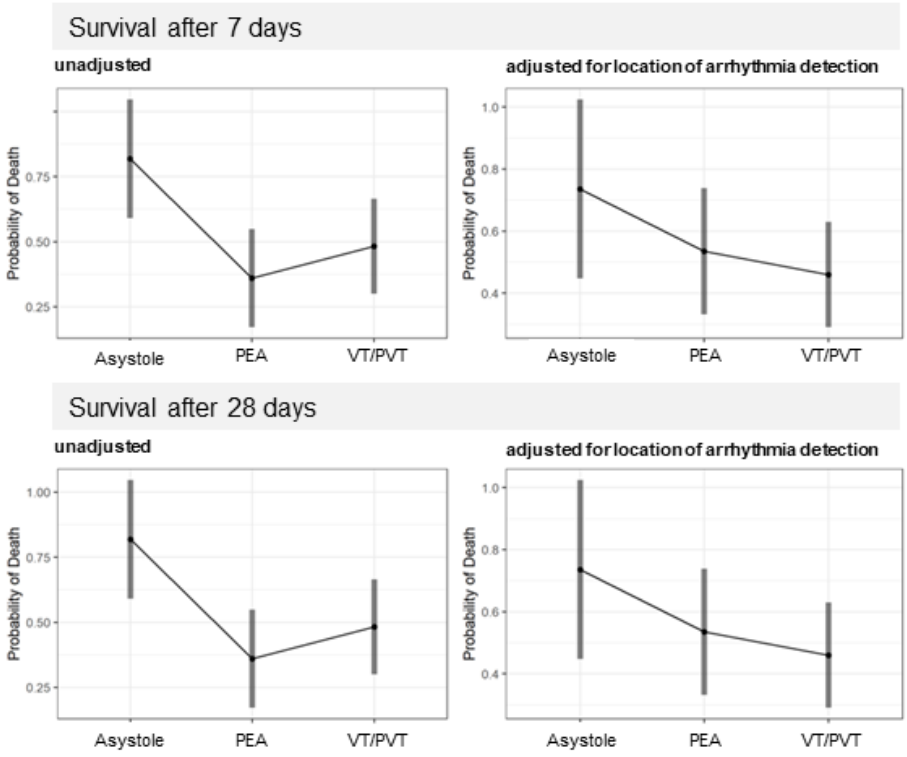
	All patients ***N=65***	**Alive** ***N=33***	**Death** ***N=32***	***P***
Potassium	4.60 [4.00;5.30]	4.60 [4.00;5.30]	4.70 [4.05;5.47]	0.704
Lactate	11.9 (6.53)	9.68 (5.00)	13.5 (7.13)	0.048
paCO2	50.0 (19.4)	45.6 (17.1)	53.6 (20.7)	0.178
pH	7.05 (0.23)	7.12 (0.18)	6.99 (0.25)	0.058

Values are mean (standard deviation) or median [interquartile range].

Figure legends

Figure 1. Estimated probability of death for each initial cardiac rhythm for the primary outcome (top panel) and secondary outcome (bottom panel). The probabilities are based on the logistic regression models shown in Table 4. Mean and the 95% confidence intervals (shaded bands) are shown.

Figure 2. Non-linear relationship estimated by a generalized additive model (GAM) between Pre-ECPR laboratory values and the primary outcome (survival 7 days). Mean values and 95% confidence intervals are shown.



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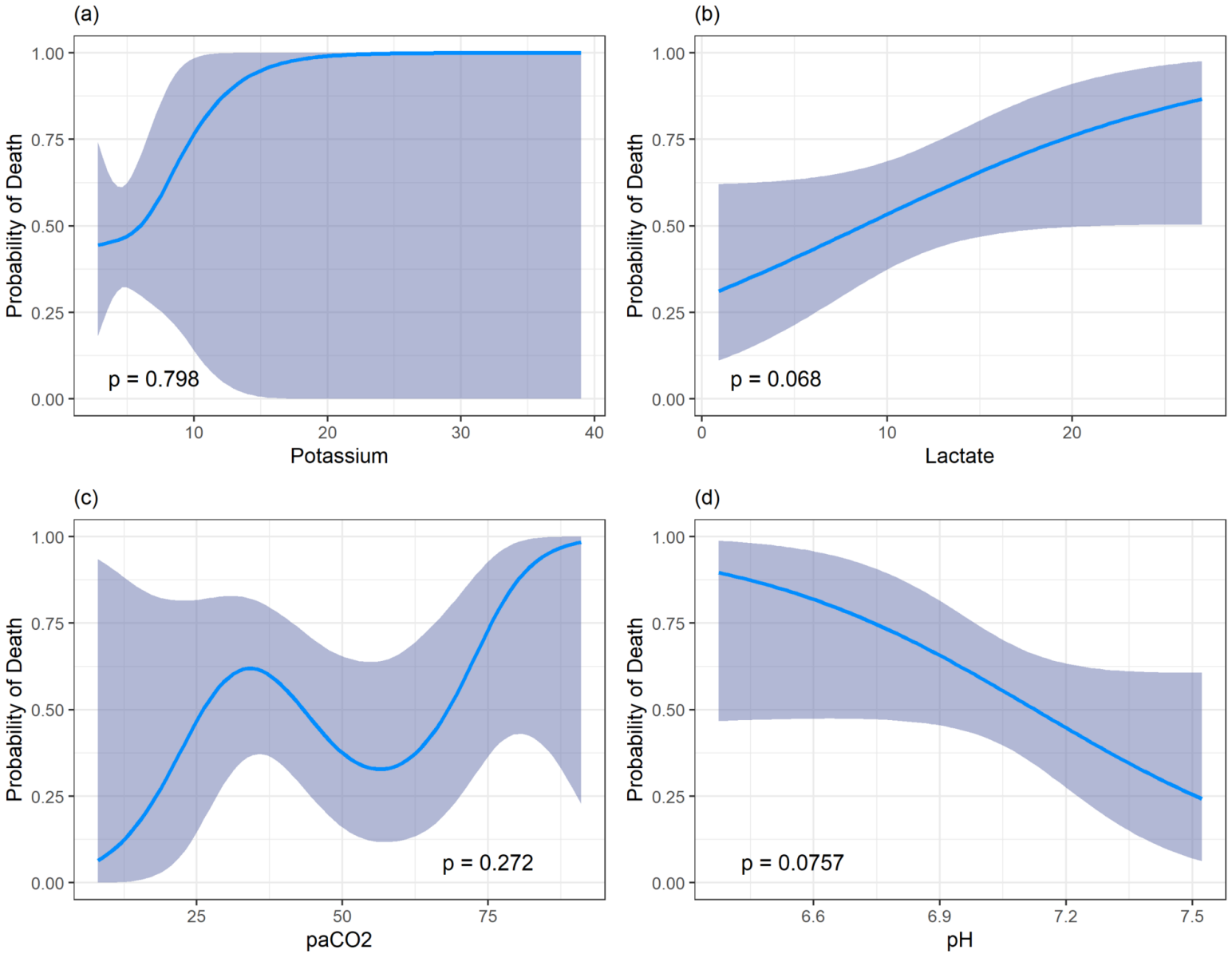

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