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ORIGINAL RESEARCH

Association Between Postresuscitation 12-Lead ECG Features and Early Mortality After Out-of-Hospital Cardiac Arrest: A Post Hoc Subanalysis of the PEACE Study

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BACKGROUND: Once the return of spontaneous circulation after out-of-hospital cardiac arrest is achieved, a 12-lead ECG is strongly recommended to identify candidates for urgent coronary angiography. ECG has no apparent role in mortality risk stratification. We aimed to assess whether ECG features could be associated with 30-day survival in patients with out-of-hospital cardiac arrest.

METHODS AND RESULTS: All the post-return of spontaneous circulation ECGs from January 2015 to December 2018 in 3 European centers (Pavia, Lugano, and Vienna) were collected. Prehospital data were collected according to the Utstein style. A total of 370 ECGs were collected: 287 men (77.6%) with a median age of 62 years (interquartile range, 53–70 years). After correction for the return of spontaneous circulation-to-ECG time, age >62 years (hazard ratio [HR], 1.78 [95% CI, 1.21–2.61]; *P*=0.003), female sex (HR, 1.5 [95% CI, 1.05–2.13]; *P*=0.025), QRS wider than 120 ms (HR, 1.64 [95% CI, 1.43–1.87]; *P*<0.001), the presence of a Brugada pattern (HR, 1.49 [95% CI, 1.39–1.59]; *P*<0.001), and the presence of ST-segment elevation in >1 segment (HR, 1.75 [95% CI, 1.59–1.93]; *P*<0.001) were independently associated with 30-day mortality. A score ranging from 0 to 26 was created, and by dividing the population into 3 tertiles, 3 classes of risk were found with significantly different survival rate at 30 days (score 0–4, 73%; score 5–7, 66%; score 8–26, 45%).

CONCLUSIONS: The post-return of spontaneous circulation ECG can identify patients who are at high risk of mortality after out-of-hospital cardiac arrest earlier than other forms of prognostication. This provides important risk stratification possibilities in post-cardiac arrest care that could help to direct treatments and improve outcomes in patients with out-of-hospital cardiac arrest.

Key Words: cardiac arrest ■ ECG ■ post-ROSC care

See Editorial by XXX.

Despite advances in acute and emergency medicine, only ≈20% of people experiencing an out-of-hospital cardiac arrest (OHCA) achieve a return of a spontaneous circulation (ROSC), and only 10% of those survive to hospital discharge.[1,2] ROSC probabilities can be estimated from various scores taking into account patients' and events' characteristics.[3,4] However, the risk of death after ROSC is anything but averted: mortality after ROSC has a biphasic pattern, with an early peak attributable to post–cardiac arrest circulatory failure,

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CLINICAL PERSPECTIVE

What Is New?

- The postresuscitation ECG plays a pivotal role in the diagnosis of ST-segment–elevation myocardial infarction, thus selecting patients for an urgent coronary angiography.
- With this article, the post-return of spontaneous circulation ECG acquires a prognostic role by identifying those patients at higher risk of early mortality.

What Are the Clinical Implications?

- By providing an early prognostic stratification, the post-return of spontaneous circulation ECG could help emergency medical service providers in the prehospital setting to triage care resources.
- An ECG suggesting a high early mortality risk may indicate the need for a hospital capable of providing urgent coronary angiography and circulatory support.

Nonstandard Abbreviations and Acronyms

Lombardia CARe	Cardiac Arrest Registry of the Lombardy Region
OHCA	out-of-hospital cardiac arrest
PEACE	Post-ROSC Electrocardiogram After Cardiac Arrest
ROSC	return of spontaneous circulation
TiReCa	Ticino Registry Cardiac Arrest

and a second peak attributable to postanoxic brain injury.[5] The common denominator of these 2 conditions is scarce systemic perfusion.[6]

Outcome prediction in OHCA constitutes a central component of postcardiac arrest care because the expected prognosis will help determine the extent to which resources and services are devoted, the choice of destination hospital, and the information given to families.[7] Unfortunately, there is a scarcity of early prognostic indicators of death in the postresuscitation phase, and the prognosticators available on the OHCA scene are even more rare.[8]

Current postresuscitation care guidelines[9,10] clearly recommend the acquisition of a 12-lead ECG as soon as possible after ROSC to identify those patients who experience acute coronary syndrome with persistent ST-segment elevation that would potentially benefit from urgent coronary angiography. This confers the ECG only with a diagnostic role, but it is reasonable to think that it could also provide prognostic information. A 12-lead ECG can correlate with the extent of jeopardized myocardium during an ischemic injury, and, depending on the site and the size of ST-segment elevation at presentation, it is possible to assess a patient's prognosis with regard to mortality rate.[11] Moreover, some ECG features have been described to be associated with higher mortality and higher odds of unfavorable neurological outcomes, but in general these have been derived either from ECGs acquired after hospital admission or from very small populations.[12,13] In spite of this, according to current postresuscitation care algorithms,[9,10] the ECG has no role in prognosis determination after OHCA. Indeed, its prognostic utility has rarely been investigated in this circumstance. Therefore, the aim of the current study was to assess whether a post-ROSC ECG and its features could be associated with survival at 30 days in OHCA, offering a reliable early indicator of outcome.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Type of Study and Center Selection

This is a subanalysis of the PEACE (Post-ROSC Electrocardiogram After Cardiac Arrest) study,[14] registered on Clinicaltrials.gov (NCT04096079), which was a retrospective, observational, multicenter study endorsed by the European Resuscitation Council Research-NET, aiming to assess the rate of false-positive ECG findings for ST-segment–elevation myocardial infarction (STEMI) according to the time elapsed from ROSC to ECG acquisition. The original study and the present subanalysis were approved by the ethical committee of the Fondazione IRCSS Policlinico San Matteo.

Patient Selection

All consecutive patients resuscitated from OHCA between January 1, 2015, and December 31, 2018, and admitted to 1 of the 3 participating centers (Fondazione IRCCS Policlinico San Matteo in Italy, Cardiocentro Ticino in Switzerland, and Medical University of Vienna in Austria) were considered. OHCA was defined as cessation of cardiac mechanical activity, confirmed by the absence of signs of circulation, occurring outside of a hospital setting.

OHCA with a nonmedical cause according to the 2014 Utstein[15] style were excluded.

Data Management

After being anonymized, study data were collected and managed by using the Research Electronic Data Capture[16] tool hosted at Fondazione IRCCS Policlinico San Matteo. The Research Electronic Data Capture is a secure, web-based application designed to support data capture for research studies.

Patients' Data Collection

Patients' characteristics and OHCA data elements were collected according to the 2014 Utstein style recommendations. The prehospital data relating to OHCA were obtained from prospective registries for the Fondazione IRCCS Policlinico San Matteo data (Lombardia CARe [Cardiac Arrest Registry of the Lombardy Region]) and for Cardiocentro Ticino (TiReCa [Ticino Registry Cardiac Arrest]), while for the patients admitted to the Medical University of Vienna, data were retrieved from the medical records. Survival data and time to death were also collected. Patients' mortality status at a 30-day follow-up were analyzed. For more details, please refer to the PEACE study.

ECG Data Collection

Data about the first ECG acquired after ROSC of every patient were collected. If the first ECG was not able to be evaluated because of artefacts or for technical issues and it was not recoverable, the second ECG performed was considered. The ROSC ECG time (expressed in minutes) was calculated as the time elapsed between ROSC and the acquisition of the ECG. Each center provided the evaluation of each ECG by 2 cardiologists who were, according to the PEACE study rules, blinded to both the result of the coronary angiography and the time elapsed between the ROSC and the ECG acquisition. In case of doubt, a third cardiologist was asked to solve the controversy. The rhythm, heart rate, QRS duration, QTc value, intraventricular conduction, arrhythmias, and segments with ST-segment elevation (anterior, lateral, posterior, inferior, and right) were analyzed for each ECG. The ECG was categorized as diagnostic for STEMI (or not) according to the criteria for the electrocardiographic diagnosis of STEMI recommended by the 2017 guidelines of the European Society of Cardiology.[17] Left bundle-branch block, right bundle-branch block, and Brugada pattern were defined according to the classic electrocardiographic criteria.[18–20] For the present study, the presence of Brugada pattern was annotated if present at the post-ROSC ECG, regardless of its persistence in the following hours or days.

Statistical Analysis

We performed all the analyses by using Stata 17 (StataCorp, College Station, TX). A 2-sided *P* value <0.05 was considered statistically significant. We summarized continuous variables with the median and 25th to 75th percentiles (interquartile range) and categorical variables with counts and percentages. We computed the mortality rate per 100 person-week up to 30 days after ROSC, together with its 95% CI. We used Cox regression to derive hazard ratios (HRs) and 95% CI. We verified that the proportional hazard assumption was satisfied by using a test based on Schoenfeld residuals. We included noncollinear variables with a *P*<0.1 at univariable analysis, in a multivariable Cox model. Although applying a process of variable selection is suboptimal, given the sample size and number of events, the variables were discussed between physicians and chosen accordingly to be included or not on the basis of their clinical relevance. We computed the Harrell's concordance statistic (naïve estimate) and 95% CI to assess model discrimination (the closer to 1 the better). To account for the use of covariate selection, we used a 10-fold cross validation to compute the predictive accuracy through Harrell's concordance. We assessed graphically a model calibration by comparing the predicted population average survival with the nonparametric Kaplan–Meier survival curves for each tertile of the distribution of the prognostic. We computed Huber–White robust standard errors to account for intracenter correlation of measures. We multiplied each coefficient from the model by 10 and rounded it to the nearest integer. These coefficients were then used to compute a score to predict mortality at 30 days. We used the likelihood ratio test to compare a model based on fractional polynomials of the score to a model with the score as a continuous variable and excluded the lack of a linear increase in risk. The score was then divided into the tertiles of its distribution, corresponding to low-, intermediate-, and high-risk patients; the corresponding cumulative survival Kaplan–Meier estimates were computed and plotted; HR and 95% CI with respect to the low-risk category were derived from a Cox model.

RESULTS

Patient and ECG Characteristics

Of the 586 emergency medical service (EMS)-assessed OHCAs over the study period admitted to the 3 participating centers, 216 were excluded according to the PEACE study inclusion criteria, thus resulting in 370 patients in total (121, Pavia; 38, Lugano; and 211, Vienna; Figure 1).

The population characteristics and the OHCA criteria based on Utstein style are presented in Table 1.

Most of the patients were men (77%), with a median age of 62 years (interquartile range, 53–70). Most of the OHCAs had a presumptive cardiac cause (79%) and occurred at home (50.8%) and were witnessed by bystanders (72%) or the EMS (13%). The initial rhythm was shockable in 85% of cases, and cardiopulmonary resuscitation was initiated by a bystander in 77%. Telephone cardiopulmonary resuscitation was performed in 12% of cases. Among all patients, only 10% arrived at the hospital with ongoing cardiopulmonary resuscitation, achieving ROSC in the emergency department. The percentage of patients who survived at 30 days was 66%.

The characteristics of the acquired post-ROSC ECGs are presented in Table 2. The median elapsed time from ROSC to the acquisition of the first ECG was 15.5 minutes, and the median QRS width and QTc time were 112 and 462 ms, respectively. The ECGs were performed at the site of OHCA and in the hospital with the same frequencies. Sixty percent had at least 1 mm ST-segment elevation in >1 segment, and 54% had an ECG diagnostic for STEMI.

Survival Data

Of the initially selected 370 patients, 363 had mortality data available, but it was not possible to obtain the status of 30-day survival in 7 patients. At 30-day follow-up, 106 patients (31%) had died with a mortality rate per 100 person-week of 15 (95% CI, 12–17).

At univariable Cox regression analysis, age >62 years, QRS >120 ms, the presence of >1 segment with ST-segment elevation, the presence of left or right bundle-branch blocks, and the presence of an intraventricular block were all found to be significantly associated with higher mortality at a 30-day follow-up (Table S1).

At a multivariable Cox regression analysis, age >62 years, female sex, the presence of >1 segment with ST-segment elevation, QRS >120 ms, and a Brugada pattern were found to be independently associated with a higher probability of death at 30 days in survivors of OHCA (Table 3).

The Scoring System

By summing the transformed coefficients of each 1 of the 6 variables from the multivariable Cox regression model (Table 3), we created a score ranging from 0 to 26. We observed an almost linear increase in risk of death with the increase of the score (test for linearity P=0.506, Figure 2).

The overall population was divided into 3 tertiles according to the score identifying 3 classes of risk: low risk (score 0–4), intermediate risk (score 5–7), and high risk (score 8–26), accounting for 124 (34%), 121 (33%), and 118 patients (33%), respectively. We observed a good discrimination ability of these 3 groups, with a clear separation of the survival curves (Figure 3). A 2-fold increase in 30-day mortality in

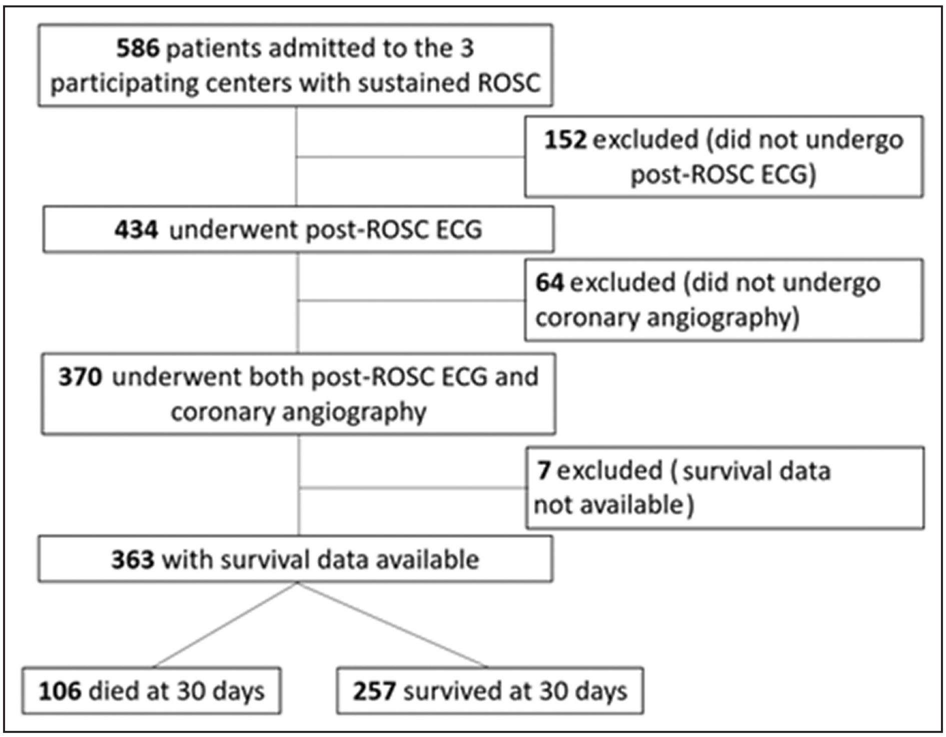

Figure 1. Flowchart of the study participants.
ROSC indicates return of spontaneous circulation.

Table 1. Characteristics of the Study Population and OHCA Events

OHCA variable	Whole population n=370
Center, n (%)	
Pavia	121 (32.7)
Lugano	38 (10.3)
Vienna	211 (57)
Sex, male, n (%)	287 (77.6)
Age, y, median (IQR)	62 (53–70)
ACS, n (%)	280 (84)
OHCA location, n (%)	
Home	187 (50.6)
Public buildings	88 (23.8)
Work/office	9 (2.4)
Street	60 (16.2)
Sport	3 (0.8)
Others	16 (4.3)
Unknown	7 (1.9)
EMS arrival time, min, median (IQR)	10 (8–12)
OHCA witnessed, n (%)	
No	53 (14.3)
Yes, by bystander	267 (72.2)
Yes, by EMS	50 (13.5)
Bystander CPR*, n (%)	233 (73.3)
First shockable rhythm, n (%)	312 (84.8)
Epinephrine administered, mg, median (IQR)	1 (0–3)
Number of shocks administered, median (IQR)]	2 (1–5)
30-d survival, n (%)	244 (65.9)
30-d survival with good neurological outcome (CPC 1 or 2)	212 (57.3)

ACS indicates acute coronary syndrome; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; IQR, interquartile range; and OHCA, out-of-hospital cardiac arrest.
*Excluding EMS witnessed.

Table 2. Specific Electrocardiographic Findings

Post-ROSC ECG items	Whole population n=370
ROSC ECG time, min (IQR)	15.5 (6–40)
Rhythm, n (%)	
Sinus rhythm	269 (72.9)
Atrial fibrillation/atrial tachycardia	80 (21.7)
Junctional or ventricular rhythm	16 (4.3)
Paced	4 (1.1)
ECG diagnostic for STEMI, n (%)	198 (53.5)
Heart rate, bpm (IQR)	98 (78–115)
QRS duration, ms (IQR)	112 (96–140)
QTc value, ms (IQR)	462 (423–500)
Intraventricular conduction, n (%)	
Normal	240 (64.9)
Left bundle-branch block	45 (12.2)
Right bundle-branch block	64 (17.3)
Bifascicular block	8 (2.2)
Others	13 (3.5)
Arrhythmias, n (%)*	
None	248 (92.5)
Ventricular ectopy	14 (5.2)
Supraventricular ectopy	6 (2.2)
Numbers of segments with ST elevation, n (%)	
0	147 (39.7)
1	104 (28.1)
2	84 (22.7)
3	28 (7.6)
4	7 (1.9)

bpm indicates beats per minute; IQR, interquartile range; ROSC, return of spontaneous circulation; and STEMI, ST myocardial infarction.
*Considering only ECG with sinus rhythm.

the intermediate risk as compared with the low-risk group and a 3-fold increase in mortality in the high-risk group were found (Table 4). The model's naïve Harrell's concordance statistic decreased from 0.66 to 0.63 after 10-fold cross validation. Finally, model's calibration, although suboptimal (particularly for the low-risk group), could be overall satisfying (Figure S1). We observed a modifying effect of different causes on the risk score (*P* for interaction <0.001), with higher mortalities in the noncardiac cause groups (Figure 4); significant differences in mortalities were observed between group comparisons in both the cardiac and noncardiac cause subgroups (Table S2).

When considering the short-term mortality at 48 hours, where 39 deaths had occurred, the risk score was still significantly associated with mortality (*P*<0.001); in particular, the high-risk group significantly differed (*P*<0.001) both from the low-risk (HR, 3.10 [95% CI, 2.28–4.22]) and the intermediate risk (HR, 3.13 [95% CI, 1.84–5.31]) groups.

DISCUSSION

This study is one of the few addressing the association between some post-ROSC ECG features and mortality. Prior studies have been published depicting a role for ECG in OHCA prognostication; however, they have either considered ECG acquired at hospital admission and not in the field as in our article, or have been collected in significantly smaller populations.[12,13] We found that ECG features can discriminate 30-day survival of patients who have survived an OHCA. In fact, in the multivariable analysis, 30-day mortality was significantly higher in patients aged >62 years, with a QRS wider than 120 ms, and with ST-segment elevation in >1 segment at the post-ROSC ECG. According to our scoring system, those patients ranking highest had a probability of 30-day mortality about 3 times higher than those in the lowest-risk group. This, if

Table 3. Multivariable Cox Regression Analysis Adjusted for Sex, Age, and ECG Findings (Model *P*<0.001; Harrell's Concordance 0.66 [95%CI, 0.57–0.76])

Variable	HR (95% CI)	*P* value	Score calculation: sum the coefficients in the table
Median age, y			
≤62	1	0.003	0
>62	1.78 (1.21–2.61)		6
Sex			
Male	1	0.025	0
Female	1.50 (1.05–2.13)		4
ROSC ECG time, min			
≥8	1	0.495	0
<8	1.16 (0.74–1.90)		1
Number segment			
≤1	1	<0.001	0
>1	1.75 (1.59–1.93)		6
QRS width, ms			
≤120	1	<0.001	0
>120	1.64 (1.43–1.87)		5
Brugada pattern			
No	1	<0.001	0
Yes	1.49 (1.39–1.59)		4

This model was not adjusted for other cardiac arrests prognostic factor. HR indicates hazard ratio; and ROSC, return of spontaneous circulation.

confirmed by prospective studies, may confer a prognostic purpose to the ECG that is beyond the already well-affirmed diagnostic one.[9,10] As opposed to the attention given to the diagnostic role of the post-ROSC ECG, its prognostic utility has rarely been investigated. A recent study found that right bundle-branch block can be an early indicator of unfavorable neurologic prognosis after OHCA.[12] Other data have suggested that postresuscitation accelerated idioventricular rhythm in the post-ROSC ECG is a prognostic factor related to higher repeated cardiopulmonary resuscitation rates within 1 hour after ROSC and lower 7-day survival rates in patients with OHCA.[13] Some authors have also focused on ECG variables both during mild induced hypothermia and after rewarming, finding that some ECG variables, including QRS upslope and QRS voltages, give a good estimation of the rate of survival.[21] However, these variables are far from being easy to assess in a prehospital setting and are often not available from routine ECGs, making their prognostic utility limited to hospitalization and more specialized clinical settings. The dispersion of QT at 24 hour after hospital admission has been proven to discriminate survival with good neurological outcome.[22] However, we could not evaluate such a finding because our observations are focused on the post-ROSC ECG taken in a prehospital setting. We were able to collect the values of QT and compute the values of QTc; however, no difference in mortality was found after dichotomizing for the median value.

Survival of patients following cardiac arrest is known to be affected by both the diagnosis of STEMI and the performance of an urgent coronary angiography.[23] In our study, being a subanalysis of the PEACE study, every patient underwent a coronary angiography with a median time of 99 minutes, and more than one-half had a diagnosis of STEMI. However, in this study, we were not focused on the difference in mortality between patients with STEMI and patients with non-STEMI with OHCA, rather in the extent of myocardial ischemia reflected by the amount of ST-segment elevation in the post-ROSC ECG. In fact, in our score, we have considered from 1 to more ST-segment elevations.

The presence of clinical characteristics such as age and sex in our score could be considered inappropriate for a study that focuses on the role of ECG features and survival. However, there is a double reason why we inserted age and sex in our model. First, it is well known that ECG criteria change according to patient's characteristics,[24,25] so all the considered ECG features needed to be corrected for these clinical characteristics. Second, the probability of death in OHCA is dependent on both age and sex, driven primarily by the presence of comorbidities, intensity of care, and cause of cardiac arrest.[26,27] In fact, in our score they account for 6 and 4 points, respectively. In addition, these are clinical data that are easy to assess and almost always identifiable. So, speaking of survival in OHCA, it is essential to include age and sex in your assessment, as otherwise ECG features would lose of much of their valuable information.

Link Between Post-ROSC ECG and Perfusion

In our study, the Kaplan–Meier curves of each risk group diverge very early within the first 48 hours and then stabilize after 10 days. This is particularly evident for the group with the highest score and is worthy of discussion because of its clinical implications. It is well known that most deaths after OHCA occur either because of circulatory collapse within the first 2 days, or later because of brain injury, with death primarily caused by the active withdrawal of life-sustaining treatment when the neurological prognosis is determined to be extremely poor.[8]

Our score is significantly associated with the high rate of mortality in the early postarrest phase, meaning that the ECG may help distinguish those patients more prone to circulatory collapse. This is the clinical phase, when intense treatment must be rapidly instituted to

SCORE	HR	95% CI	
0	1.00		
1	1.11	1.09	1.12
2	1.22	1.19	1.25
3	1.35	1.30	1.41
4	1.50	1.42	1.57
5	1.66	1.55	1.76
6	1.83	1.69	1.97
7	2.03	1.85	2.21
8	2.24	2.01	2.47
9	2.48	2.19	2.76
10	2.74	2.39	3.09
11	3.03	2.61	3.46
12	3.36	2.84	3.87
13	3.71	3.10	4.33
14	4.11	3.37	4.84
15	4.54	3.67	5.41
16	5.02	4.00	6.05
17	5.56	4.35	6.76
18	6.15	4.73	7.56
19	6.80	5.15	8.45
20	7.52	5.60	9.44
21	8.32	6.09	10.55
22	9.20	6.62	11.79
23	10.18	7.19	13.17
24	11.26	7.81	14.71
25	12.46	8.48	16.43
26	13.78	9.20	18.35

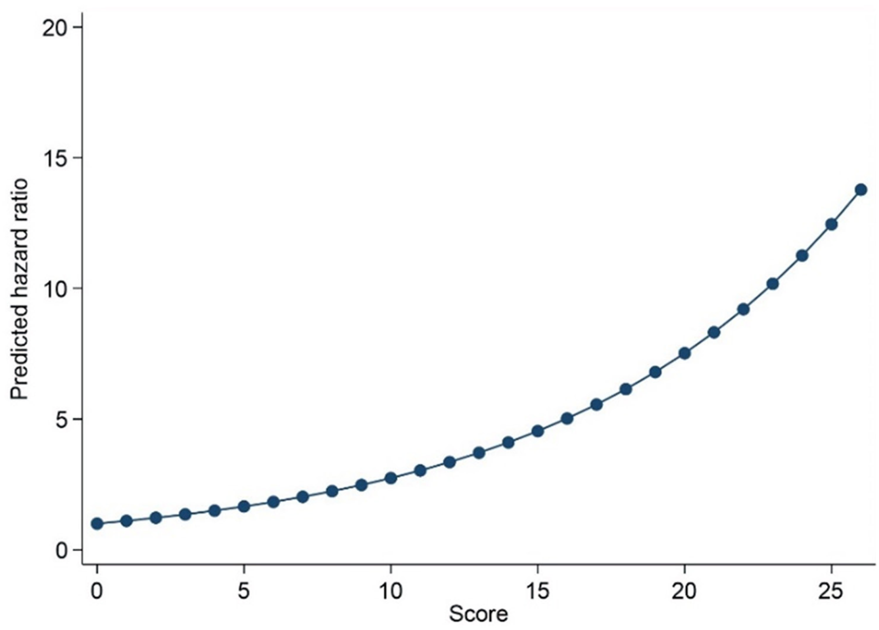

Figure 2. Plot of the predicted HR for 1-unit increase in the score.
HRs and 95% CI with respect to score 1 is tabulated to the left of the figure and plotted to the right in function of the score. HR indicates hazard ratio.

limit ongoing organ damage attributable to myocardial depression followed by superimposed inflammatory vasodilatation,[6] which cause low peripheral perfusion. In this regard, it is known from a prior study by our group[28] that low peripheral perfusion expressed by low values of the peripheral perfusion index, which is the ratio of the pulsatile blood flow to the nonpulsatile or static blood in peripheral tissue obtainable from a

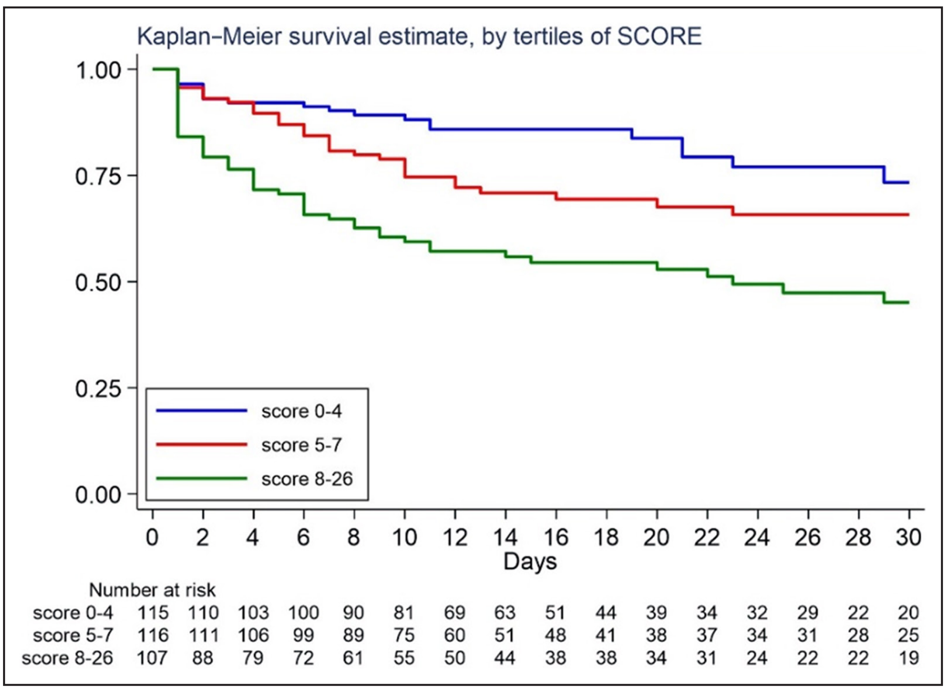

Figure 3. Kaplan–Meier survival estimates of survival (Cox *P* value <0.001).
There was a significant difference among all groups (*P*<0.001).

Table 4. Groups According to Scores and Hazard Ratios for Risk of Death at 30 days (Model *P* value=<0.001)

Groups	Score	Mortality per 100 person-week (95% CI)	HR (95% CI)	*P* value	Cumulative survival at 30 days (95% CI)
Low risk	0–4	8 (5–12)	1	1	73% (59–83)
Intermediate risk	5–7	13 (9–19)	1.72 (1.28–2.31)	<0.001	66% (55–75)
High risk	8–26	25 (1–33)	3.22 (2.40–4.31)	<0.001*	45% (34–56)

*Group 3 vs group 2: *P*<0.001. HR indicates hazard ratio.

pulse oximeter, correlates with ECG changes, such as ST-segment elevation in >1 segment, QRS widening and bundle-branch block morphology, thus affecting ECG reliability. We have also shown that low peripheral perfusion was an independent predictor of 30-day mortality and poor neurologic outcome.[29] Therefore, if poor peripheral perfusion can affect the ECG and predict survival, it is also conceivable that ECG features could predict survival, which is what we have found in the present study. Moreover, the perfusion index has been shown to predict outcome similarly to serum lactate in pediatric patients with shock,[30] and a preliminary study from our group demonstrates how prehospital values of the perfusion index are associated with those of lactate on hospital admission.[31] Given that, it is reasonable to think that the post-ROSC ECG could disclose a low perfusion state corresponding to an elevated lactate level at hospital admission outlining that a patient is more prone to an impending circulatory collapse.

Post-ROSC ECG as an Early Discriminator of Mortality Risk

We are aware that the earlier the prognostication the greater the risk for inaccuracy because, of course, greater distances from the outcome being estimated will lead to increased margins of error.[8] We are far from saying that a post-ROSC ECG acquired in the field could primarily guide the decision to withdraw any possible treatment to patients with OHCA. Such a decision must be taken after an adequate period of clinical observation and after the combination of different prognostication tools. Moreover, even those patients with the worst score show a survival of about 50% at 30 days, so it appears illogical to imagine any possible application of the present score aiming to select patients who do not deserve treatment. However, in light of these considerations, early predictors of mortality in patients with OHCA can be useful in the prehospital setting. On one hand, they can help identify patients who are at a higher risk of mortality and help EMS

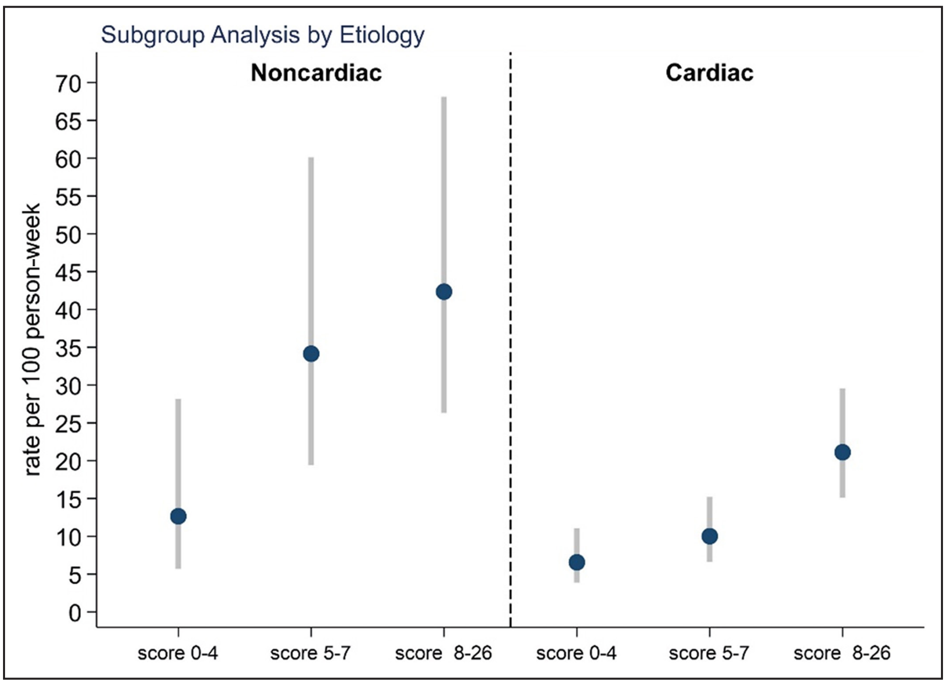

Figure 4. Rate of death per 100 person-week according to groups of risk in cardiac and noncardiac causes.

providers in the difficult process of decision making about resuscitation efforts at the OHCA scene.[32] These decisions are never simple nor clear-cut because they carry the intrinsic power to determine death.[33] On the other hand, early detection of patients at higher risk of circulatory collapse may serve as a guide to alert the receiving hospital in preparation for early advanced circulatory support systems. Whether the patient needs to be transported to a facility in which coronary artery angiography, pulmonary embolectomy, or venoarterial extracorporeal membrane oxygenation is available must be determined in a prehospital setting.[34] The problem is that the prehospital setting is a resource-limited environment, and every tool that helps the decision process is of great support. Moreover, the post-ROSC ECG is almost always performed in this setting, and its acquisition in the field has been implemented in most EMS workflows. Although we are far from affirming that post-ROSC ECG can directly predict mortality risk alone, features of the post-ROSC ECG are certainly associated with mortality occurring in the first 48 hours because of circulatory failure.

Another important topic to be discussed is that the post-ROSC ECG may have a prognostic role over the well-documented diagnostic one, which is influenced by the time passed from ROSC to ECG acquisition. As shown in the PEACE study, the diagnostic accuracy of the post-ROSC ECG increases with time from ROSC, being lower in the first 8 minutes after ROSC. The association between the post-ROSC ECG and survival, instead, is independent from the ROSC to ECG time. All the survival models in this study were corrected for ROSC to ECG time. In the very first minutes after ROSC, the post-ROSC ECG is less reliable for diagnosis but still it may be an indicator of poor survival independently from the ROSC to ECG time.

A few other early prognostication tools have been tested as predictors of mortality after ROSC, such as lactate[35] or serum potassium levels[36]; however, these are significantly limited by the fact that they are not immediately available until hospital admission. On the contrary, ECG can be done quickly and inexpensively, and it is easily assessed in the field and can readily be used to help EMS providers to personalize post-ROSC efforts.

Applicability Beyond "Cardiac Cause" Cases

It is worth noting that our results do not exclusively apply to patients whose OHCAs have a cardiac cause. In the present study, all the OHCAs with any medical cause were included, thus highlighting that the post-ROSC ECG can discriminate survival in OHCAs of presumptively noncardiac cause. Even if excluded a priori, it would be interesting to evaluate whether these findings are similar in OHCAs attributable to nonmedical causes such as trauma. This strengthens the indication of guidelines to perform an ECG after ROSC regardless of the presumptive cause of OHCA.

Limitations

This study has some potential limitations. First, even if data were prospectively collected in 2 of 3 centers, this is a retrospective analysis. The second limitation is the lack of comparison between post-ROSC ECG with prearrest ECG findings. In fact, it is not possible to exclude that some alterations recorded in the post-ROSC ECG would have already been present before the cardiac arrest. This kind of limitation is common to other studies on this topic because it is difficult to retrieve prearrest information in an acute setting. The third limitation is that our sample size is small, and our results will need validation on a larger cohort of patients for better control of confounders and better discrimination and calibration. The fourth limitation is that in the PEACE study, patients who did not undergo coronary angiography were excluded and therefore not considered in the present study. However, since the decision not to perform a coronary angiography is driven mainly by the absence of ST-segment elevation or equivalent, these patients had likely a favorable ECG pattern. The last limitation is that regression models were not run specifically for cardiogenic shock but only for survival, so, albeit plausible, we cannot demonstrate a clear relationship between ECG features and the risk of circulatory collapse.

CONCLUSIONS

The post-ROSC ECG can identify patients who are at high risk of mortality after OHCA earlier than other forms of prognostication. This provides important risk stratification possibilities in postcardiac arrest care. Early discrimination is essential to identify patients who would benefit most from further intensive care and help to improve outcomes or avoid futile treatment when unfortunate outcomes are inevitable. If our data can be confirmed on larger and prospective studies, the post-ROSC ECG should be considered an important tool in post-ROSC care after OHCA.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S2
Figure S1

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SUPPLEMENTAL MATERIAL

Table S1. Univariable Cox regression analysis.

Variable	Death (N)	Rate per 100-person week (95%CI)	HR (95%CI)	P value
Median Age (years)				**0.002**
≤ 62	42	11 (8-14)	1	
> 62	64	20 (16-26)	1.84 (1.25-2.72)	
Sex				**0.088**
Male	76	13 (11-17)	1	
Female	30	19 (14-28)	1.46 (0.96-2.23)	
ACS				**0.411**
No	12	10 (6-18)	1	
Yes	77	14 (11-17)	1.28 (0.70-2.35)	
Median ROSC ECG time (min)				**0.285**
≤ 16	58	17 (13-22)	1	
> 16	48	13 (10-17)	0.81 (0.55-1.19)	
ROSC ECG time (min)				**0.162**
≥ 8	61	13 (10-17)	1	
< 8	45	18 (13-24)	1.32 (0.9-1.94)	
Median Heart rate (bpm)				**0.643**
≤ 98	55	15 (12-20)	1	
> 98	50	14 (11-19)	0.91 (0.62-1.34)	
Median MaximumST elevation (mm)				**0.397**
≤ 5	33	16 (11-22)	1	
> 5	36	19 (14-26)	1.23 (0.76-1.97)	
Median QRS width (msec)				**0.005**
≤ 112	41	11 (8-15)	1	
> 112	65	19 (15-24)	1.73 (1.17-2.56)	
QRS width (msec)				**0.002**
≤ 120	53	11 (9-15)	1	
> 120	53	21 (16-27)	1.82 (1.24-2.66)	
Number segment				**0.004**
≤ 1	60	12 (9-15)	1	

> 1	46	22 (16-29)	1.78 (1.21-2.61)	
Median QTc (msec)				**0.387**
≤ 462	56	17 (13-22)	1	
> 462	49	13 (10-17)	0.84 (0.57-1.24)	
Rhythm				**0.844**
SR	73	14 (11-18)	1	
AT/AF	24	15 (10-22)	1.06 (0.67-1.69)	0.796
Jun/Ven	6	19 (8-42)	1.34 (0.58-3.08)	0.492
Pace	2	20 (5-81)	1.63 (0.4-6.64)	0.497
Where ECG was performed				**0.546**
OHCA location	49	18 (13-23)	1	
Hospital	43	13 (10-18)	0.86 (0.57-1.31)	0.489
Transport	14	12 (7-20)	0.73 (0.4-1.33)	0.308
Ventricular Conduction				**0.040**
Normal	57	12 (9-15)	1	
LBBB	19	24 (15-31)	2	0.009
RBBB	25	21 (14-31)	1.83	0.012
Bifascicular	2	14 (3-55)	1.13	0.862
Others	3	14 (4-42)	1.01	0.989
Ventricular Block				**0.004**
No	57	12 (9-15)	1	
Yes	49	21 (16-28)	1.75 (1.2-2.57)	
Arrhythmias				**0.044**
None	94	14 (12-18)	1	
PVC	12	24 (14-43)	1.5 (0.8-2.75)	0.182
SVEB	0	0	0	1
PVC				**0.182**
No	94	14 (12-17)	1	
Yes	12	25 (14-43)	1.54 (0.84-2.82)	
Brugada Pattern				**0.163**
No	101	14 (12-17)	1	
Yes	4	33 (12-88)	2.23 (0.82-6.06)	
ECG diagnostic for STEMI				**0.134**

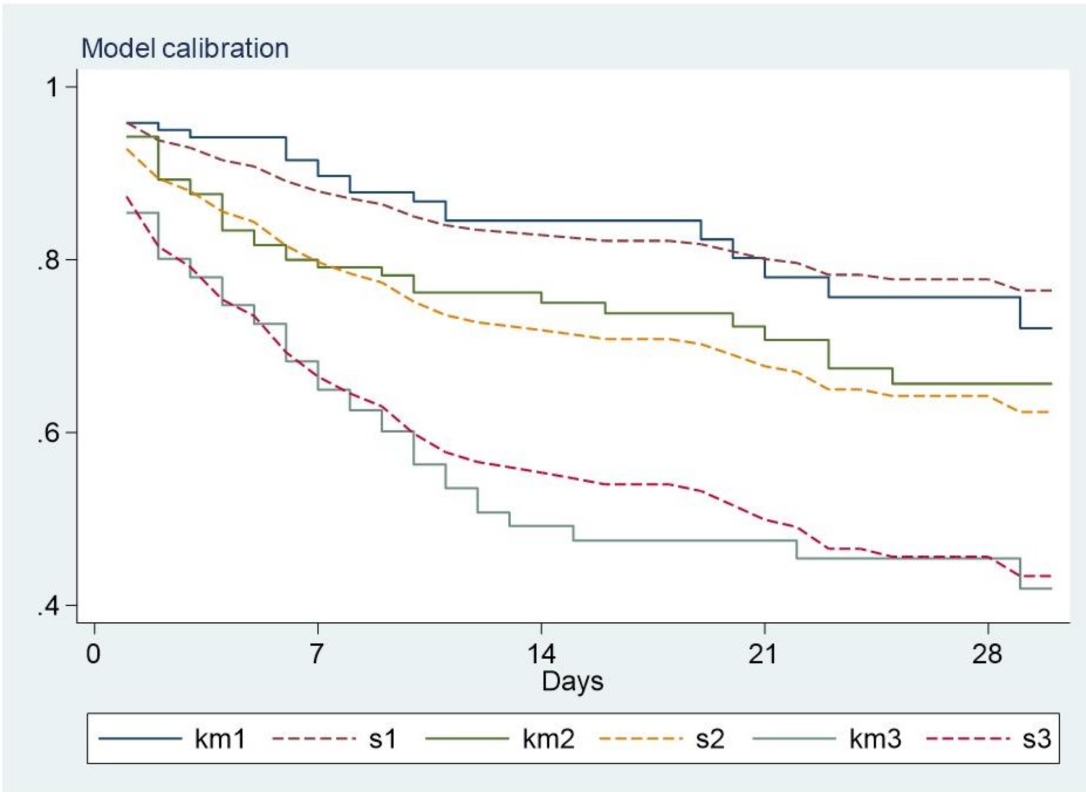
No	43	12 (9-16)	1	
Yes	63	17 (14-22)	1.34 (0.91-1.98)	
Mechanical CPR				**0.151**
No	52	14 (11-19)	1	
Yes	15	22 (13-36)	1.55 (0.87-2.76)	
Status of hospital arrival				**0.107**
ROSC	91	14 (11-17)	1	
Ongoing CPR	15	22 (13-36)	1.61 (0.93-2.78)	

HR= hazard ratio; CI= confidence interval; ROSC= return of spontaneous circulation; STEMI= ST-elevation myocardial infarction; CPR= cardiopulmonary resuscitation

Table S2. Death rate and association with the risk of death in the three score classes.

	Cardiac aetiology						Non cardiac aetiology					
Score class	**Death rate per 100-person week**	**95%CI**	**p**	**HR**	**95%CI**	**p**	**Death rate per 100-person week**	**95%CI**	**p**	**HR**	**95%CI**	**p**
0-4	6.6	3.9-11	<0.001	ref			12.6	5.7-28.1	<0.001	ref		
5-7	10	6.6-15.2		1.55	1.1-2.1	0.007	34.1	19.4-60.1		2.26	1.3-3.8	0.002
8-26	21.1	15.1-68.1		3.2	2.6-4	<0.001	42.3	26.3-68.1		3	1.8-5.1	<0.001

Figure S1. Model calibration plot comparing predicted mean population survival (S) with the observed survival (KM) for each tertile of the predictor index.



A fair, though not optimal, overlay of the predicted and observed survival is present, particularly for the second and third tertiles of the predictor index (middle and high risk patients).