

Post-Resuscitation ECG for Selection of Patients for Immediate Coronary Angiography in Out-of-Hospital Cardiac Arrest

Henrik Stær-Jensen, MD; Espen Rostrup Nakstad, MD; Eigil Fossum, MD, PhD;
Arild Mangschau, MD, PhD; Jan Eritsland, MD, PhD; Tomas Drægni, RN;
Dag Jacobsen, MD, PhD; Kjetil Sunde, MD, PhD; Geir Øystein Andersen, MD, PhD

Background—We aimed to investigate coronary angiographic findings in unselected out-of-hospital cardiac arrest patients referred to immediate coronary angiography (ICA) irrespective of their first postresuscitation ECG and to determine whether this ECG is useful to select patients with no need of ICA.

Methods and Results—All resuscitated patients admitted after out-of-hospital cardiac arrest without a clear noncardiac cause underwent ICA. Patients were retrospectively grouped according to the postresuscitation ECG blinded for ICA results: (1) ST elevation or presumably new left bundle branch block, (2) other ECG signs indicating myocardial ischemia, and (3) no ECG signs indicating myocardial ischemia. All coronary angiograms were reevaluated blinded for postresuscitation ECGs. Two hundred and ten patients were included with mean age 62±12 years. Six-months survival with good neurological outcome was 54%. Reduced Thrombolysis in Myocardial Infarction flow (0–2) was found in 55%, 34%, and 18% and a ≥90% coronary stenosis was present in 25%, 27%, and 19% of patients in group 1, 2, and 3, respectively. An acute coronary occlusion was found in 11% of patients in group 3. ST elevation/left bundle branch block identified patients with reduced Thrombolysis in Myocardial Infarction (0–2) flow with 70% sensitivity and 62% specificity. Among patients with initial nonshockable rhythms (24%), 32% had significantly reduced Thrombolysis in Myocardial Infarction flow.

Conclusions—Initial ECG findings are not reliable in detecting patients with an indication for ICA after experiencing a cardiac arrest. Even in the absence of ECG changes indicating myocardial ischemia, an acute culprit lesion may be present and patients may benefit from emergent revascularization.

Clinical Trial Registration—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT01239420.

(*Circ Cardiovasc Interv*. 2015;8:e002784. DOI: 10.1161/CIRCINTERVENTIONS.115.002784.)

Key Words: cardiac arrest ■ coronary angiography ■ coronary artery disease ■ coronary occlusion
■ post-ROSC ECG

Recent improvements in the chain of survival after out-of-hospital cardiac arrest (OHCA) have improved survival worldwide.^{1–4} Still, the majority of patients die either without return of spontaneous circulation (ROSC) or because of the severity of the post cardiac arrest syndrome.^{1,3,4} Coronary artery disease and especially acute coronary occlusion represents the most common cause of sudden cardiac arrest.⁵ Current resuscitation guidelines emphasize immediate coronary angiography (ICA) and percutaneous coronary intervention (PCI) to be considered after ROSC in patients with ST elevation or presumably new left bundle branch block (LBBB) on ECG.^{2,6,7} ICA should also be considered in the presence of life-threatening ventricular arrhythmias or hemodynamic instability.⁸ Additionally, the European Resuscitation Council

guidelines state that because chest pain and ST elevation may be poor predictors of an acute coronary occlusion in OHCA patients, it is reasonable to refer selected patients suspected of having acute myocardial ischemia for ICA.²

See Editorial by Lotun and Kern

Nonspecific ECG changes are often seen in newly resuscitated OHCA patients, and it is unclear whether post-ROSC ECG correctly identifies myocardial ischemia and to what extent ICA should be performed in the absence of ST elevation, LBBB, or life-threatening ventricular arrhythmias. Clinical data have been conflicting and consist mainly of retrospective studies, registry data, and observational studies on patients already selected for coronary angiography based

Received February 24, 2015; accepted September 6, 2015.

From the Department of Anesthesiology (H.S.-J., K.S.), Institute for Experimental Medical Research (H.S.-J.), Department of Acute Medicine (E.R.N., D.J.), Department of Cardiology (E.F., A.M., J.E., G.Ø.A.), and Department of Research and Development (T.D.), Oslo University Hospital Ullevål, Oslo, Norway; and Center for Heart Failure Research (A.M., J.E., G.Ø.A.), and Institute of Clinical Medicine (D.J., K.S.), University of Oslo, Norway.

The Data Supplement is available at <http://circinterventions.ahajournals.org/lookup/suppl/doi:10.1161/CIRCINTERVENTIONS.115.002784/-/DC1>.

Correspondence to Henrik Stær-Jensen, MD, Department of Anesthesiology, Division of Emergencies and Critical Care, Institute for Experimental Medical Research, Oslo University Hospital, PB 4956 Nydalen, N-0424 Oslo, Norway. E-mail uxshph@ous-hf.no

© 2015 American Heart Association, Inc.

Circ Cardiovasc Interv is available at <http://circinterventions.ahajournals.org>

DOI: 10.1161/CIRCINTERVENTIONS.115.002784

WHAT IS KNOWN

- Nonspecific ECG changes are often seen in newly resuscitated out-of-hospital cardiac arrest patients, and it is controversial whether the ECG after return of spontaneous circulation correctly identifies myocardial ischemia and to what extent immediate coronary angiography should be performed in the absence of ST elevation.

WHAT THE STUDY ADDS

- This prospective study presents immediate coronary angiographic findings in 210 comatose out-of-hospital cardiac arrest patients without a clear noncardiac cause transferred directly to coronary angiography irrespective of ECG findings.
- Early ECGs after return of spontaneous circulation is not a reliable method to identify patients in need of immediate coronary angiography and subsequent revascularization. Even in patients without any sign of ECG changes indicating myocardial ischemia, acute culprit lesions with an indication for emergent revascularization is indeed present, independent of initial arrest rhythm. In addition, 37% of the patients with ST elevation had normal Thrombolysis in Myocardial Infarction flow.

on ECG findings.^{9–11} The net benefit of referring all OHCA patients to ICA is therefore uncertain and under debate.¹² Important aspects are delays in optimal bundle care treatment, logistic challenges during inter- and intrahospital referral to institutions with 24/7 coronary angiography service, total outcome benefit, finances, and resources. Prospective studies on unselected OHCA patients are therefore needed to determine whether ICA should be performed after ROSC, regardless of ECG findings.

The aims of the present study were to investigate coronary angiographic findings in an unselected cohort of OHCA patients without a clear noncardiac cause referred to ICA irrespective of post-ROSC ECG and to determine whether ECG can be used to select patients with no need of ICA.

Methods

Study Population

OHCA patients of all causes in greater Oslo and rural areas of South-Eastern Norway are admitted to Oslo University Hospital-Ullevål. This observational study had prospectively defined objective and design. Between October 1, 2010, and December 31, 2013, all comatose patients (Glasgow Coma Scale ≤ 8 on admission) with maintained ROSC after OHCA were included in the study. They were transferred directly to ICA irrespective of the ECG findings if there was no clear noncardiac cause for the OHCA (Figure). Other exclusion criteria were age < 18 years and pregnancy (Figure). Patients were also excluded if they did not receive active in-hospital treatment after ROSC based on either a do-not-attempt-resuscitation order, end-stage malignancy preceding the arrest, or had minimal chances of meaningful survival (defined as not witnessed cardiac arrest with asystole, lengthy resuscitation, or advanced age).

The study complies with the Declaration of Helsinki and was part of an on-going prospective observational study (The Norwegian Cardio-Respiratory Arrest Study [NORCAST] NCT01239420) approved by the Regional Committee of Medical Ethics in South-East Norway. Written informed consent was obtained from close relatives or guardians within 24 hours after hospitalization and from all patients who regained consciousness and full decision-making capacity within 6 months. Clinical, biochemical, and outcome data were collected from clinical records and patient charts. Coronary angiography results, hemodynamic parameters, relevant ICU data, and neurological status based on cerebral performance category score¹³ were prospectively recorded, using a cross platform relational database application—Filemaker Pro version 11 (FileMaker Inc., Santa Clara, CA). Manual quality and plausibility control of individual data set were performed to exclude artifacts.

Study Procedure

In the Oslo Emergency Medical Services, OHCA patients are treated by paramedics certified in Advanced Cardiac Life Support. In addition, a physician-staffed ambulance is routinely dispatched for OHCA when available.¹⁴ A 12-lead ECG is taken prehospitally in the ambulances after achievement of stable ROSC. At hospital admission, a team with an anaesthesiologist and cardiologist take over the responsibility of the patient in the Emergency Department. Patients with a clear noncardiac cause were excluded from the study (Figure). Stable patients were transported directly to the catheterization laboratory, and unstable patients were shortly stabilized in the Emergency Department before they were transported to the catheterization laboratory. The overall goal is a short door-to-balloon time. After ICA, subsequent PCI, mainly through the femoral artery, was performed at the clinicians' discretion. The patients

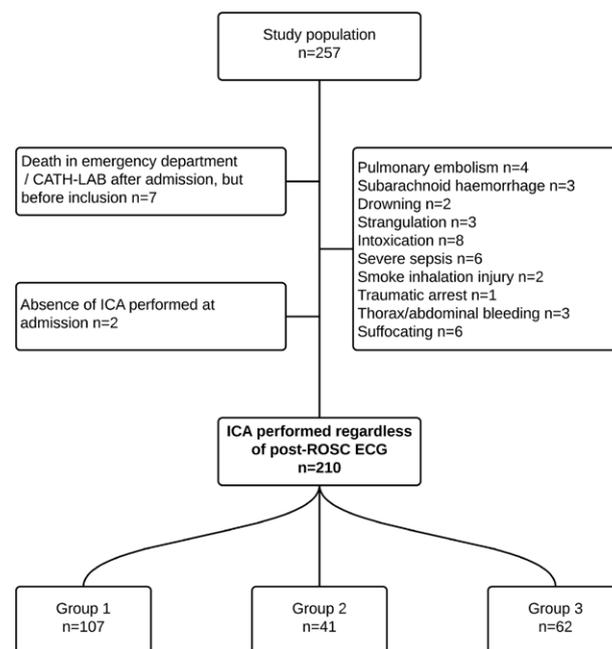


Figure. Study flow chart of patients (n=257) admitted to Oslo University Hospital-Ullevål after out-of-hospital cardiac arrest (OHCA) between October 1, 2010, and December 31, 2013. A total of 210 patients had immediate coronary angiography (ICA) performed and were included in the analyses. Reasons for exclusion of 47 patients are given. Group 1, ST elevation or presumably new left bundle branch block; Group 2, other signs of coronary ischemia (a) marked horizontal ST depression (> 0.2 mV) in > 2 leads or T inversion ≥ 0.1 mV in 2 contiguous leads with prominent R wave or R/S ratio > 1 . (b) Ventricular tachycardia or (c) atypical, intraventricular conduction disturbance with QRS duration ≥ 0.15 ms; Group 3, No signs of myocardial ischemia. CATH-LAB indicates catheterization laboratory; and ICA, immediate coronary angiography.

received 300 mg aspirin before the procedure and either 600 mg clopidogrel or 60 mg prasugrel after the procedure if PCI was performed subsequently. Heparin was administered if a radial access was used (<5% of the patients) or if PCI was performed. Patients treated with prehospital thrombolysis (3%) received clopidogrel 300 mg. Adjunctive treatment was given according to European guidelines for management of ST-segment-elevation myocardial infarction^{7,8} Clopidogrel was replaced by prasugrel during the first 48 hours in patients without contraindications if PCI was performed. After the procedures, patients were admitted to the ICU for standardized post-resuscitation care.^{15,16}

Evaluation of Outcomes

ECG Evaluation

The first 12-lead ECG obtained after establishing stable ROSC was separately, individually, and retrospectively evaluated by 2 experienced cardiologists blinded from all other patient information. The ECGs were evaluated with regard to heart rhythm, possible ischemic findings (see below), and whether indication for ICA was present based on the current European Society of Cardiology guidelines.^{7,8} If disagreement occurred, a third independent cardiologist participated in the final evaluation (in 20% of patients). According to the ECG findings, the patients were categorized into 3 groups.

Group 1

Patients with ECG findings in line with current guidelines recommendation for ICA defined as ischemic findings suspected of an ST-segment-elevation myocardial infarction: new ST elevation at the J-point in 2 contiguous leads with the cut-off points, 0.2 mV in men or 0.15 mV in women in leads V2–V3 or 0.1 mV in other leads or presumably new LBBB.

Group 2

Patients without ST elevation or LBBB but with ECG findings where it was reasonable to suspect myocardial ischemia with indication for ICA, based on the following:

1. Marked horizontal or down-sloping ST depression (>0.2 mV) in >2 contiguous leads and T inversion ≥ 0.1 mV in 2 contiguous leads with prominent R wave or R/S ratio >1¹⁷
2. Ventricular tachycardia (heart rate >100 with QRS duration >0.12 ms and atrioventricular dissociation)¹⁸
3. Atypical, intraventricular conductance disturbance with QRS duration ≥ 0.15 ms

Group 3

Patients with no significant ECG changes indicating acute myocardial ischemia.

Coronary Angiography Evaluation

All coronary angiography recordings were reevaluated by a single experienced interventional cardiologist blinded from the first post-ROSC ECG. If disagreement with the primary evaluation occurred, a third independent cardiologist participated in the final evaluation of the ICA (in 18% of patients).

Significant coronary artery disease was defined as lesions with $\geq 50\%$ lumen reduction compared with reference segment and further classified into lesions with $\geq 50\%$ or $\geq 90\%$ stenoses. Coronary flow was assessed using the Thrombolysis in Myocardial Infarction (TIMI) classification.¹⁹ A coronary occlusion was defined as TIMI grade 0 to 1 flow and considered acute or recent if there was angiographic evidence of thrombus at the site of occlusion or through the ability of opening the occluded artery by passing a guidewire easily through the lesion.^{20,21} Reduced coronary flow was defined as TIMI grade 0 to 2 flow. Patients with chronic occlusions were categorized according to TIMI flow (0–3) in the remaining coronary arteries. PCI was defined successful when TIMI grade 2 or 3 flow was obtained after reperfusion. Outcome data were assessed 6 months after hospital discharge, and the neurological outcome was defined as good with cerebral performance category scores of 1 and 2. Coronary angiographic findings related to initial cardiac arrest rhythms were also evaluated in detail.

Statistics

Statistical analyses were performed using SPSS 20 for Windows (SPSS, Inc, Chicago, IL). Continuous data are presented as mean \pm SD or median (quartiles) depending on the data distribution. Categorical data are presented as number of total (%). Continuous data were compared using Student's *t* test, one-way analysis of variance, Mann–Whitney U-test, or the Kruskal–Wallis Test according to the data distribution and the number of output categories. Levenes test for homogeneity of variances was used. If the assumption of homogeneity of variance was not met, the Welch test was used. Categorical data were compared using Chi-square with continuity correction. A 2-sided *P* value <0.05 was considered to be statistically significant. Because of the exploratory study design, there were no adjustments for multiple comparison when comparing the groups in Tables 1 and 2. Comparisons of the ICA results in Table 2 were performed between group 1 versus group 2+3 only. A manual backward stepwise elimination procedure using a multivariate logistic regression model was performed to study the association between clinical variables present at admission, in addition to ECG classification and TIMI 0 to 1 flow on coronary angiography. Covariates were included in the model based on an association with TIMI flow 0 to 1 with a *P* value <0.25 in univariate analyses.

Results

Over the 3-year study period, 257 comatose OHCA patients with ROSC were admitted to Oslo University Hospital-UIH-eval and screened for inclusion. Forty-seven (18%) patients were excluded (Figure), leaving 210 patients for final study inclusion. Average door-to-balloon time was 44 minutes. Overall, 121 patients (58%) survived to 6 months, and 114 patients (54%) had good neurological outcome, with no differences between the 3 different ECG groups (Table 1). There was a difference in initial cardiac arrest rhythms, with more patients in ventricular fibrillation in group 1 and more with nonshockable rhythms in group 3 (Table 1). Clinical and biochemical characteristics were similar in the 3 groups, but patients with ST elevation or presumably new LBBB (group 1) had higher peak troponin T values than the 2 other groups ($P < 0.001$; Table 1). A total of 192 (91%) of the patients were treated with therapeutic hypothermia at 33°C after hospital admission (Table 1).

After blinded reevaluation of the first post-ROSC ECG, 107 (51%), 41 (20%), and 62 (30%) patients were classified into groups 1, 2, and 3, respectively (Table 1). The respective coronary angiographic findings are summarized in Table 2. Reduced TIMI flow was found in 84 (40%) of the patients, and 60 (29%) had an acute or recent occlusion. Only 55 (26%) of the patients had no significant coronary disease. More patients in group 1 had reduced TIMI flow and higher frequency of significant coronary stenosis (Table 2), with 45 (42%) having an acute coronary occlusion (TIMI 0–1) and 91 (88%) with significant coronary lesions. Only 5 group 1 patients received prehospital thrombolysis (4 in the ST elevation subgroup and 1 in the LBBB subgroup). After excluding these, 57 (56%) patients in group 1 had reduced coronary flow (TIMI 0–2). Group 1 patients with presumed new LBBB had less frequently acutely occluded coronary arteries than patients with ST elevation ($P < 0.001$; Table 2). ST elevation or LBBB identified patients with an acute coronary lesion with reduced TIMI (0–2) flow with 70% sensitivity and 62% specificity. Similarly, ST elevation alone identified patients with reduced TIMI (0–2) flow with less sensitivity (64%), but higher

Table 1. Clinical and Biochemical Characteristics of Patients With Out-of-Hospital Cardiac Arrest According to Classification Based on First Post-ROSC ECG

	Overall, N=210	Group 1, N=107	Group 2, N=41	Group 3, N=62
Female sex	36 (17)	16 (15)	8 (20)	12 (19)
Age, y	62±12	61±13	61±8	63±14
Prior CAD	66 (31)	30 (28)	13 (32)	23 (37)
Prior heart failure	65 (31)	33 (31)	13 (32)	19 (31)
Prior stroke	13 (6)	6 (6)	2 (5)	5 (8)
Current smoking	78 (37)	41 (38)	16 (39)	21 (34)
Treated hypertension	75 (36)	36 (34)	15 (37)	24 (39)
Treated diabetes mellitus	32 (15)	19 (18)	4 (10)	9 (15)
Witnessed arrest	177 (84)	90 (84)	35 (85)	52 (84)
Bystander CPR	165 (79)	79 (74)	34 (83)	52 (84)
Initial VF/VT	160 (76)	88 (82)*	32 (78)	40 (65)
Time to ROSC, min	27±16	27±19	29±17	24±15
Time, door to balloon, min	44 (31–55)	48 (33–61)†	36 (28–50)	37 (30–48)
Epinephrine during CPR	127 (60)	68 (64)	26 (63)	33 (53)
Lactate at admission, mmol/L	5.1 (3–10)	5.5 (4–10)	5.3 (2–9)	4.7 (3–10)
Base deficit at admission, mEq/L	−8.5±5.2	−9.1±5.0	−8.3±4.4	−7.4±5.8
Peak troponin T, ng/L	1405 (469–4127)	2437 (711–6712)‡	1743 (472–3578)	715 (290–1724)
Se-Creatinine at admission, μmol/L	114±57	115±62	117±50	111±54
Therapeutic hypothermia	192 (91)	96 (90)	37 (90)	59 (95)
Survival (6-months follow up)	121 (58)	59 (55)	24 (59)	38 (61)
CPC 1+2 (good neurological outcome)§	114 (54)	55 (51)	23 (56)	36 (58)

Continuous data are presented as mean±SD or median (quartiles) depending on the distribution of the data. Categorical data presented as number of total, N (%). Group 1, ST elevation or presumed new left bundle branch block; Group 2, other signs of myocardial ischemia; and Group 3, no signs of myocardial ischemia. CAD indicates coronary artery disease; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

* $P=0.03$ Group 1 vs Group (2+3).

† $P=0.04$ Group 1 vs Group (2+3).

‡ $P<0.001$ Group 1 vs Group (2+3).

§Best CPC score after discharge from intensive care unit was used in 2 patients who suffered new fatal cardiac arrest within 6 months.

specificity (75%). Nine patients in group 2 had ventricular tachycardia according to our definition. In group 3, an acute coronary lesion with reduced flow (TIMI 0–2) was found in 11 patients (18%). Acute PCI was performed in 56%, 41%, and 24% of the patients in groups 1, 2, and 3, respectively (Table 2). Significant coronary stenoses and reduced coronary flow were found to a similar degree, regardless of initial cardiac arrest rhythm. Sixteen (32%) patients with pulseless electric activity or asystole had significantly reduced TIMI flow (Table 3), with 12 (24%) having >90% stenosis (with clinical and biochemical characteristics presented in Table I in the Data Supplement).

Univariate analyses of possible associations between clinical variables available at hospital admission and TIMI 0 to 1 flow at coronary angiography are shown in Table 4. The multivariate logistic regression analysis is shown in Table II in the Data Supplement. ECG changes classified into group 1 were associated with an ≈6-fold increase in the odds of finding a coronary artery with TIMI 0 to 1 flow (crude odds ratio 5.7 [2.4,13.7]; $P<0.001$). Univariate analysis of ECG group 2 and TIMI flow revealed a nonsignificant odds ratio of 1.9

(0.6, 5.7); $P=0.3$. After adjustment for clinical and biochemical covariates available at admission in a multivariate model (Table II in the Data Supplement), ECG group 1 remained a strong, independent predictor of TIMI 0 to 1 flow with an adjusted odds ratio of 6.0 (2.5, 14.5); $P<0.0001$. There was a nonsignificant trend against an inverse association between age and TIMI 0 to 1 flow (Table II in the Data Supplement). No other clinical or biochemical variables were associated with TIMI flow in the multivariate analyses.

Discussion

The principal finding of this prospective clinical study in unselected OHCA patients admitted after ROSC is that early post-ROSC ECGs is not a reliable method to identify patients in need of immediate ICA and subsequent revascularization. Even in the absence of ST-segment-elevation, presumably new LBBB, or other signs suspect of ischemia on post-ROSC ECG, a culprit coronary lesion with an indication for emergent revascularization may indeed be present, independent of initial rhythm. Noteworthy, 37% of the patients with ST elevation had normal TIMI flow.

Table 2. Immediate Coronary Angiographic Findings in Resuscitated Out-of-Hospital Cardiac Arrest Patients Related to Evaluation of First Post-ROSC ECG

Coronary Angiography and PCI Finding	Total, N=210	Classification Based on Post-ROSC ECG			
		Group 1, N=107		Group 2, N=41	Group 3, N=62
		ST Elevation, N=86	LBBB, N=21		
Evaluation of coronary flow					
TIMI flow 0–1*	60 (29)	42 (49)†	3 (14)‡	8 (20)	7 (11)
TIMI flow 2*	24 (11)	12 (14)	2 (10)	6 (15)	4 (6)
TIMI flow 3	126 (60)	32 (37)†	16 (76)§	27 (66)	51 (82)
Evaluation of coronary stenosis					
>90% stenosis	50 (24)	22 (26)†	5 (24)	11 (27)	12 (19)
50% to 90% stenosis	105 (50)	53 (63)†	11 (52)	22 (54)	19 (31)
<50% stenosis	55 (26)	11 (12)†	5 (24)	8 (20)	31 (50)
1-vessel disease	60 (28)	30 (35)	4 (19)	12 (29)	14 (23)
2-vessel disease	46 (22)	22 (26)	5 (24)	11 (27)	8 (13)
3-vessel disease	44 (22)	20 (23)	6 (29)	10 (24)	8 (13)
Identified culprit lesions					
Right coronary artery	20 (10)	10 (12)	1 (5)	5 (12)	4 (6)
Left descending coronary artery	61 (29)	40 (47)†	3 (14)	9 (22)	9 (15)
Left circumflex coronary artery	19 (9)	9 (10)	2 (10)	4 (10)	4 (6)
Left main coronary artery	2 (1)	1 (1)	0	0	1 (2)
PCI performed during ICA	92 (44)	55 (64)¶	5 (24)	17 (41)	15 (24)
Time from ROSC to balloon, min	111±48	111±41	111±48	115±44	102±49

Continuous data presented as mean±SD. Categorical data is presented as number of total, N (%). Statistical comparisons between ST elevation and LBBB were only performed on TIMI flows. Group 1, ST elevation or presumably new left bundle branch block (LBBB); Group 2, other signs of myocardial ischemia; and Group 3, no signs of myocardial ischemia. ICA indicates immediate coronary angiography; PCI, percutaneous coronary interventions; ROSC, return of spontaneous circulation; and TIMI, Thrombolysis in Myocardial Infarction.

*Only acute or recent reduction in TIMI flow.

† $P<0.01$ Group 1 vs Group (2+3).

‡ $P<0.001$ ST elevation vs LBBB.

§ $P=0.004$ ST elevation vs LBBB.

¶ $P<0.001$ Group 1 vs Group (2+3).

We found reduced TIMI flow (0–2) in 24% of the patients with no ST-segment-elevation or LBBB pattern on their post-ROSC ECG and in 18% of the patients without any ECG suspicion of ischemia. Moreover, a $\geq 90\%$ stenosis was present in 19% of patients with no significant ECG changes, indicating potential myocardial ischemia. Although some have reported high positive and negative predictive values of ST elevation on post-ROSC ECG in selected patients,²⁰ our study on more unselected patients confirm findings from the Parisian Regional Out-of-Hospital Cardiac Arrest Trial (PROCAT) registry. They found at least one significant lesion in 58% of patients without ST elevation on the post-ROSC ECG.¹¹ Similarly, Radsel et al demonstrated acute culprit coronary lesions in 24% of patients without ST-segment-elevation.²¹ This confirms the difficulty in selecting OHCA patients for ICA based on post-ROSC ECG with the risk of neglecting the existence of acute coronary lesions in patients without ST-segment-elevations. Interestingly, we found significant coronary disease and presumably acute coronary lesions in 32% of patients with initial nonshockable rhythms (pulseless electric activity, asystole) and in patients of all age groups, again demonstrating the difficulty to exclude selected patient groups from ICA.

Reduced coronary flow (TIMI 0–2) was present in only 5 (24%) patients presenting with a possible new-onset LBBB, probably reflecting the clinical impression that the majority of these patients have undetected, not new-onset LBBB. Interestingly, the proportion of patients with TIMI 0 to 2 flow was identical in patients with LBBB and patients without any ischemic ECG changes (group 3). Contrary to previous studies, although 88% of the patients in group 1 had significant coronary lesions, less than half of the patients with ST elevation on post-ROSC ECG had an acute coronary occlusion, demonstrating further the limited specificity of ECGs obtained early after ROSC. This finding was consistent even after excluding patients receiving prehospital thrombolysis.

The present study adds additional information to the use of ECG changes other than ST-segment-elevation in selecting cardiac arrest patients for ICA. Even if ST-segment depression and other ECG findings compatible with myocardial ischemia are included as indicators for ICA, patients with normal post-ROSC ECGs (with regard to ischemia) may still have a culprit lesion, which may benefit from emergent revascularization. Our study differs from previous ones based on the prospective design without selection, bringing all patients without a clear noncardiac cause to ICA, regardless of the ECG pattern.

Table 3. Immediate Coronary Angiographic Findings in Resuscitated Out-of-Hospital Cardiac Arrest Patients Related to Initial Heart Rhythm

Coronary Angiography Findings	Initial Heart Rhythm (N=210)	
	VF/VT, N=160	PEA/Asystole, N=50
Evaluation of coronary flow		
TIMI flow 0–1	49 (31)	11 (22)
TIMI flow 2	19 (11)	5 (12)
TIMI flow 3	92 (58)	34 (68)
Evaluation of coronary stenoses		
>90% stenosis	38 (24)	12 (24)
50% to 90% stenosis	92 (58)*	13 (26)
<50% stenosis	30 (19)*	25 (50)
1-vessel disease	50 (31)	10 (20)
2-vessel disease	37 (23)	9 (18)
3-vessel disease	37 (23)	7 (14)
Identified culprit lesions		
Right coronary artery	14 (10)	6 (12)
Left descending coronary artery	50 (31)	11 (22)
Left circumflex coronary artery	17 (11)	2 (4)
Left main coronary artery	1 (1)	1 (2)

Categorical data is presented as number of total, N (%). PEA indicates pulseless electric activity; TIMI, Thrombolysis in Myocardial Infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia.

* $P=0.001$.

The retrospective blinded ECG assessment and coronary angiography reevaluation further strengthens the quality. Finally, our study outcome was not successful versus unsuccessful PCI as in previous studies, but the association between post-ROSC ECG patterns and ICA findings. Studies using PCI as study outcome may be hampered by a high degree of variation between PCI operators and PCI centers with regard to the indication for PCI when significant, but not flow-limiting coronary lesions are present. Thus, the present data support a recent consensus statement from the European Association for Percutaneous Cardiovascular Interventions recommending ICA in OHCA patients independently of the presence of ST elevation when an obvious noncardiac cause is absent.²² They emphasize that ICA should be performed immediately in the presence of ST elevation and as soon as possible (<2 hours) in other patients if no noncardiac cause of arrest is found. ICA should be followed by immediate PCI directed toward the culprit lesion particularly in hemodynamically unstable patients.²²

The survival benefit of early invasive treatment in OHCA patients presenting ST elevation or presumably new LBBB on post-ROSC ECG is well documented in retrospective and prospective registries,^{23–25} and this strategy is therefore recommended in the recent guidelines.² Controversy, however, still exist on whether all patients surviving OHCA should be referred for ICA and especially about the timing of coronary angiography in the absence of ST-segment-elevation.^{9,11,12,22} The net benefit of emergent revascularization after OHCA on cardiac function (ie, infarct size and left ventricular ejection fraction) after OHCA, and thereby quality of life, is difficult

Table 4. Possible Associations Between Clinical Variables Available at Admission and TIMI Flow Grade at Immediate Coronary Angiography

	TIMI 0–1, N=60	TIMI 2–3, N=150	P Value
Female sex	9 (15)	27 (18)	0.60
Age, y	60±13	63±12	0.09
Prior CAD	13 (22)	53 (35)	0.10
Prior heart failure	16 (27)	49 (32)	0.46
Prior stroke	2 (3)	11 (7)	0.47
Current smoking	27 (45)	51 (34)	0.54
Treated hypertension	19 (32)	56 (37)	0.72
Treated diabetes mellitus	10 (17)	22 (15)	0.72
Witnessed arrest	50 (83)	127 (85)	0.81
Bystander CPR	46 (77)	119 (79)	0.67
Initial VF/VT	49 (82)	111 (74)	0.24
Time to ROSC, min	28±21	26±16	0.42
Epinephrine during CPR	42 (70)	85 (57)	0.09
Lactate at admission, mmol/L	7.1±4.3	6.3±4.4	0.21
Base deficit at admission, mEq/L	−9.0±4.8	−8.2±5.4	0.32

Continuous data presented as mean±SD. Categorical data presented as number of total, N (%). CAD indicates coronary artery disease; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; TIMI, Thrombolysis in Myocardial Infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia.

to explore because >50% of the patients die. Only a large randomized trial can answer the question if an all-referral-policy to ICA after OHCA carries significant survival and other outcome benefits. With the present survival of 58% (54% with good neurological outcomes), we clearly show that the potential for good outcome after OHCA is present.

Limitations

Several potential limitations must be addressed. Our study was a single-center, prospective, observational nonrandomized study, and we acknowledge that the total study population was relatively small. No information about coronary artery lesions in the 18% excluded patients was available and may limit the conclusions, but we would not expect patients with clear noncardiac causes to have acute coronary lesions. Further, the ECGs used for group allocation were recorded by the ambulance crew after ROSC and before coronary angiography, but the time from cardiac arrest to first post-ROSC ECG differed between patients. This reflects real-world clinical practice, and a more accurate timing could not be obtained. We recognize that a single post-ROSC ECG may not reflect myocardial ischemia because ischemia-induced ECG changes can be dynamic and change over time. ST elevation and depression may be absent on one ECG but appear over time on another. However, we emphasize that our goal is to allocate patients with reversible ischemia to a hospital with 24/7 PCI service and to reduce the door-to-balloon time whenever possible. Another limitation is the heterogeneity of ECG findings in group 2. Because of the relatively small number, subgroup analyses of different entities, such as ST depression, T-wave inversions, broad-complex tachycardia, and intraventricular conduction disturbances, could not be performed. Finally, in

the majority of patients, no prearrest ECG was available, and we could therefore not categorize LBBB as new onset or not.

Conclusions

Initial ECG findings are not reliable in detecting patients with an indication for ICA after experiencing a cardiac arrest. Even in the absence of ECG changes indicating myocardial ischemia and independent of initial arrest rhythm, an acute culprit lesion may be present and patients may benefit from emergent revascularization.

Acknowledgments

The Norwegian Cardio-Respiratory Arrest Study is approved by the Regional Committee of Medical Ethics in South-East Norway.

Sources of Funding

This work was supported by East Norway Regional Health Authority [2011138] and Laerdal Foundation [Centre of Excellence grant] and by Oslo University Hospital.

Disclosures

None.

References

- Eisenberg MS, Mengert TJ. Cardiac resuscitation. *N Engl J Med*. 2001;344:1304–1313. doi: 10.1056/NEJM200104263441707.
- Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, Koster RW, Wyllie J, Böttiger B; ERC Guidelines Writing Group. European Resuscitation Council Guidelines for Resuscitation 2010 Section 1. Executive summary. *Resuscitation*. 2010;81:1219–1276. doi: 10.1016/j.resuscitation.2010.08.021.
- Lund-Kordahl I, Olasveengen TM, Lorem T, Samdal M, Wik L, Sunde K. Improving outcome after out-of-hospital cardiac arrest by strengthening weak links of the local Chain of Survival; quality of advanced life support and post-resuscitation care. *Resuscitation*. 2010;81:422–426. doi: 10.1016/j.resuscitation.2009.12.020.
- Wissenberg M, Lippert FK, Folke F, Weeke P, Hansen CM, Christensen EF, Jans H, Hansen PA, Lang-Jensen T, Olesen JB, Lindhardsen J, Fosbol EL, Nielsen SL, Gislason GH, Kober L, Torp-Pedersen C. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA*. 2013;310:1377–1384. doi: 10.1001/jama.2013.278483.
- Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JF, Carli P. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med*. 1997;336:1629–1633. doi: 10.1056/NEJM199706053362302.
- Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Juni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J*. 2014; 35:2541–2619.
- Steg PG, James SK, Atar D, Badano LP, Blomstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van 't Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33:2569–2619. doi: 10.1093/eurheartj/ehs215.
- Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, Wijns W, Zahger D; ESC Committee for Practice Guidelines. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32:2999–3054. doi: 10.1093/eurheartj/ehr236.
- Bro-Jeppesen J, Kjaergaard J, Wanscher M, Pedersen F, Holmvang L, Lippert FK, Møller JE, Køber L, Hassager C. Emergency coronary angiography in comatose cardiac arrest patients: do real-life experiences support the guidelines? *Eur Heart J Acute Cardiovasc Care*. 2012;1:291–301. doi: 10.1177/2048872612465588.
- Zanuttini D, Armellini I, Nucifora G, Grillo MT, Morocutti G, Carchietti E, Trillò G, Spedicato L, Bernardi G, Proclemer A. Predictive value of electrocardiogram in diagnosing acute coronary artery lesions among patients with out-of-hospital-cardiac-arrest. *Resuscitation*. 2013;84:1250–1254. doi: 10.1016/j.resuscitation.2013.04.023.
- Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, Empana JP, Carli P, Mira JP, Jouven X, Spaulding C. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac Arrest) registry. *Circ Cardiovasc Interv*. 2010;3:200–207. doi: 10.1161/CIRCINTERVENTIONS.109.913665.
- Nolan JP, Cariou A. Therapeutic hypothermia and coronary angiography are mandatory after out-of-hospital cardiac arrest: Yes. *Intensive Care Med*. 2014;40:1027–1029. doi: 10.1007/s00134-014-3327-3.
- Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, Halperin H, Handley A, Herlitz J, Hickey R, Idris A, Kloeck W, Larkin GL, Mancini ME, Mason P, Mears G, Monsieurs K, Montgomery W, Morley P, Nichol G, Nolan J, Okada K, Perlman J, Shuster M, Steen PA, Sterz F, Tibballs J, Timerman S, Truitt T, Zideman D; International Liaison Committee on Resuscitation; American Heart Association; European Resuscitation Council; Australian Resuscitation Council; New Zealand Resuscitation Council; Heart and Stroke Foundation of Canada; InterAmerican Heart Foundation; Resuscitation Councils of Southern Africa; ILCOR Task Force on Cardiac Arrest and Cardiopulmonary Resuscitation Outcomes. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for health-care professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110:3385–3397. doi: 10.1161/01.CIR.0000147236.85306.15.
- Olasveengen TM, Sunde K, Brunborg C, Thowsen J, Steen PA, Wik L. Intravenous drug administration during out-of-hospital cardiac arrest: a randomized trial. *JAMA*. 2009;302:2222–2229. doi: 10.1001/jama.2009.1729.
- Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, Drægni T, Steen PA. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73:29–39. doi: 10.1016/j.resuscitation.2006.08.016.
- Tømte O, Andersen GØ, Jacobsen D, Drægni T, Auestad B, Sunde K. Strong and weak aspects of an established post-resuscitation treatment protocol-A five-year observational study. *Resuscitation*. 2011;82:1186–1193. doi: 10.1016/j.resuscitation.2011.05.003.
- Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction; ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33:2551–2567. doi: 10.1093/eurheartj/ehs184.
- Harkness JR, Morrow DA, Braunwald E, Ren F, Lopez-Sendon J, Bode C, Budaj A, Scirica BM. Myocardial ischemia and ventricular tachycardia on continuous electrocardiographic monitoring and risk of cardiovascular outcomes after non-ST-segment elevation acute coronary syndrome (from the MERLIN-TIMI 36 Trial). *Am J Cardiol*. 2011;108:1373–1381. doi: 10.1016/j.amjcard.2011.06.058.

19. Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, Dodge HT, Francis CK, Hillis D, Ludbrook P. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. *Circulation*. 1987;76:142–154. doi: 10.1161/01.CIR.76.1.142.
20. Anyfantakis ZA, Baron G, Aubry P, Himbert D, Feldman LJ, Juliard JM, Ricard-Hibon A, Burnod A, Cokkinos DV, Steg PG. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. *Am Heart J*. 2009;157:312–318. doi: 10.1016/j.ahj.2008.09.016.
21. Radsel P, Knafelj R, Kocjancic S, Noc M. Angiographic characteristics of coronary disease and postresuscitation electrocardiograms in patients with aborted cardiac arrest outside a hospital. *Am J Cardiol*. 2011;108:634–638. doi: 10.1016/j.amjcard.2011.04.008.
22. Noc M, Fajadet J, Lassen JF, Kala P, MacCarthy P, Olivecrona GK, Windecker S, Spaulding C; European Association for Percutaneous Cardiovascular Interventions (EAPCI); Stent for Life (SFL) Group. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/stent for life (SFL) groups. *EuroIntervention*. 2014;10:31–37. doi: 10.4244/EIJV10I1A7.
23. Garot P, Lefevre T, Eltchaninoff H, Morice MC, Tamion F, Abry B, Lesault PF, Le Tarnec JY, Pougès C, Margenet A, Monchi M, Laurent I, Dumas P, Garot J, Louvard Y. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. *Circulation*. 2007;115:1354–1362. doi: 10.1161/CIRCULATIONAHA.106.657619.
24. Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation*. 2007;74:227–234. doi: 10.1016/j.resuscitation.2007.01.016.
25. Larsen JM, Ravkilde J. Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—a systematic review and meta-analysis. *Resuscitation*. 2012;83:1427–1433. doi: 10.1016/j.resuscitation.2012.08.337.

Post-Resuscitation ECG for Selection of Patients for Immediate Coronary Angiography in Out-of-Hospital Cardiac Arrest

Henrik Stær-Jensen, Espen Rostrup Nakstad, Eigil Fossum, Arild Mangschau, Jan Eritsland, Tomas Drægner, Dag Jacobsen, Kjetil Sunde and Geir Øystein Andersen

Circ Cardiovasc Interv. 2015;8:

doi: 10.1161/CIRCINTERVENTIONS.115.002784

Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2015 American Heart Association, Inc. All rights reserved.

Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circinterventions.ahajournals.org/content/8/10/e002784>

Data Supplement (unedited) at:

<http://circinterventions.ahajournals.org/content/suppl/2015/10/13/CIRCINTERVENTIONS.115.002784.DC1>

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation: Cardiovascular Interventions* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

Reprints: Information about reprints can be found online at:
<http://www.lww.com/reprints>

Subscriptions: Information about subscribing to *Circulation: Cardiovascular Interventions* is online at:
<http://circinterventions.ahajournals.org/subscriptions/>

Supplemental Material

Supplemental Table 1. Clinical and biochemical characteristics of patients with out-of-hospital cardiac arrest according to initial rhythm.

	VF/VT N=160	PEA/asystole N=50	<i>p</i>-value
Female gender	23(14)	13(26)	0.09
Age (years)	62 ± 12	62 ±12	0.93
Prior CAD	50(31)	16(32)	1.0
Prior heart failure	45(28)	20(40)	0.24
Prior stroke	6(4)	7(14)	0.02
Current smoking	58(36)	20(40)	0.81
Treated hypertension	58(36)	17(34)	0.49
Treated diabetes	21(13)	11(22)	0.19
Witnessed arrest	137(86)	40(80)	0.47
Bystander CPR	127(79)	38(76)	0.76
Time to ROSC (min)	26±18	27±18	0.63
Epinephrine during CPR	89(56)	38(76)	0.04
Lactate at admission (mmol/L)	6.2±4.3	7.5±4.5	0.05
Base deficit at admission (mEq/L)	-8.1 ±5.1	-9.5±5.5	0.13
Se-Creatinine at admission (μmol/L)	113±60	117±49	0.66
Peak Troponin T (ng/L)	3855 (587-4786)	679 (228-3450)	0.03

Continuous data presented as mean ± SD or or median (quartiles) depending on the distribution of the data.

Categorical data presented as number of total, N (%).

VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity; CAD, coronary artery disease; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation.

Supplemental Table 2. Crude and multivariable adjusted odds ratios for having TIMI 0-1 flow in any coronary arteries after out-of-hospital cardiac arrest according to ECG classification.

Model	Variable	β	OR	95 % C. I.	<i>p</i> -value
<i>Crude</i>	ECG group 1*	1.74	5.7	[2.4, 13.7]	0.000
	ECG group 2	0.64	1.9	[0.6, 5.7]	0.25
<i>Model 1</i>	ECG group 1	1.54	4.6	[1.8, 11.7]	0.001
	ECG group 2	0.77	2.2	[0.7, 6.8]	0.2
	Age	-0.03	0.97	[0.95, 1.00]	0.08
	Prior CAD	0.16	1.2	[0.5, 2.6]	0.7
	Initial VF/VT	-0.44	0.6	[0.3, 1.5]	0.3
	Epinephrine during CPR	-0.46	0.6	[0.3, 1.3]	0.2
	Lactate at admission	0.03	1.0	[0.96, 1.12]	0.4
<i>Model 2</i>	ECG group 1	1.66	5.3	[2.1, 13.0]	0.000
	ECG group 2	0.70	2.0	[0.6, 6.2]	0.2
	Age	-0.03	0.97	[0.95, 1.0]	0.05
	Initial VF/VT	-0.35	0.7	[0.3, 1.6]	0.4
	Epinephrine during CPR	-0.48	0.6	[0.3, 1.2]	0.2
<i>Model 3</i>	ECG group 1	1.80	6.0	[2.5, 14.5]	0.000
	ECG group 2	0.64	1.9	[0.6, 5.7]	0.3
	Age	-0.03	0.98	[0.95, 1.00]	0.06

TIMI, Thrombolysis in Myocardial Infarction (TIMI) classification; OR, Odds ratio; CAD, coronary artery disease; VF, ventricular fibrillation; VT, ventricular tachycardia; CPR, cardiopulmonary resuscitation.

*ECG class 3 as reference.