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ORIGINAL SCIENTIFIC PAPER
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Ischaemic electrocardiogram patterns and its association with survival in out-of-hospital cardiac arrest patients without ST-segment elevation myocardial infarction: a COACT trials' post-hoc subgroup analysis

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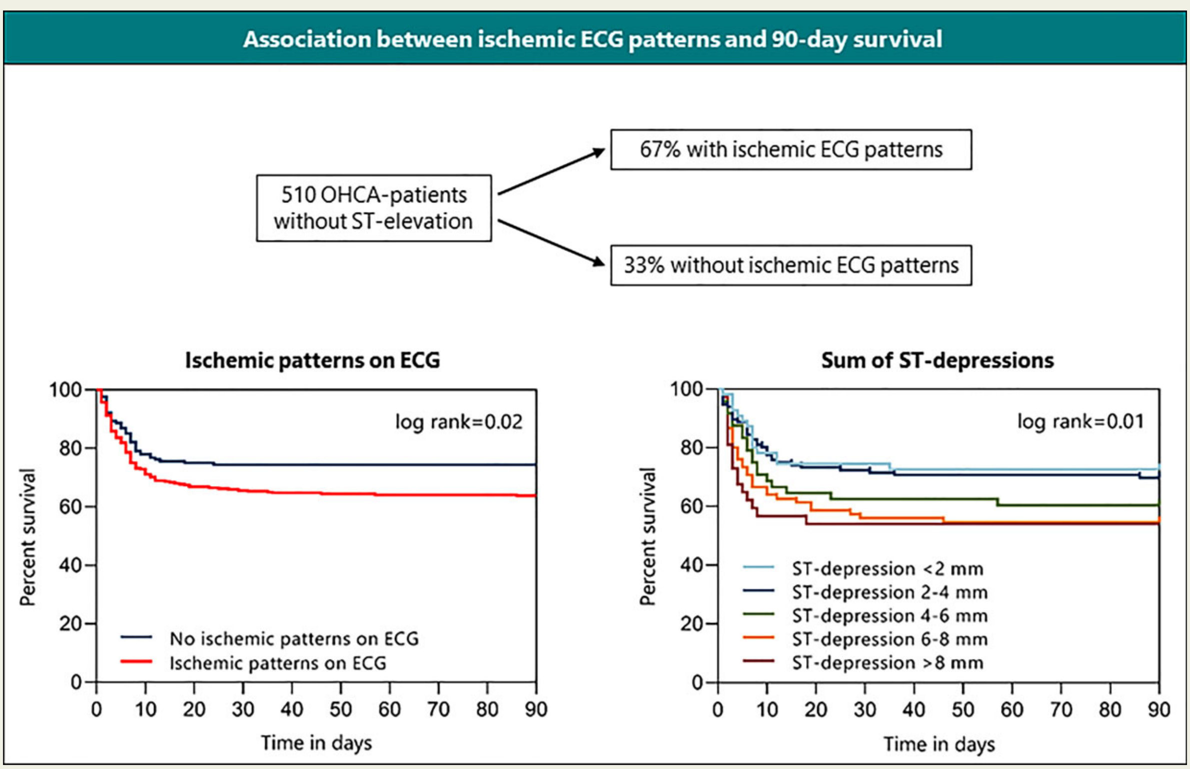
Aims ST-depression and T-wave inversion are frequently present on the post-resuscitation electrocardiogram (ECG). However, the prognostic value of ischaemic ECG patterns is unknown.

Methods and results In this post-hoc subgroup analysis of the Coronary Angiography after Cardiac arrest (COACT) trial, the first in-hospital post-resuscitation ECG in out-of-hospital cardiac arrest patients with a shockable rhythm was analysed for ischaemic ECG patterns. Ischaemia was defined as ST-depression of $\geq$0.1 mV, T-wave inversion in $\geq$2 contiguous leads, or both. The primary endpoint was 90-day survival. Secondary endpoints were rate of acute unstable lesions, levels of serum troponin-T, and left ventricular function. Of the 510 out-of-hospital cardiac arrest patients, 340 (66.7%) patients had ischaemic ECG patterns. Patients with ischaemic ECG patterns had a worse 90-day survival compared with those without [hazard ratio 1.51; 95% confidence interval (CI) 1.08–2.12; $P = 0.02$]. A higher sum of ST-depression was associated with lower survival (log-rank = 0.01). The rate of acute unstable lesions (14.5 vs. 15.8%; odds ratio 0.90; 95% CI 0.51–1.59) did not differ between the groups. In patients with ischaemic ECG patterns, maximum levels of serum troponin-T (µg/L) were higher [0.595 (interquartile range 0.243–1.430) vs. 0.359 (0.159–0.845); ratio of geometric means 1.58; 1.13–2.20] and left ventricular function (%) was worse (44.7 $\pm$ 12.5 vs. 49.9 $\pm$ 13.3; mean difference −5.13; 95% CI −8.84 to −1.42). Adjusted for age and time to return of spontaneous circulation, ischaemic ECG patterns were no longer associated with survival.

Conclusion Post-arrest ischaemic ECG patterns were associated with worse 90-day survival. A higher sum of ST-depression was associated with lower survival. Adjusted for age and time to return of spontaneous circulation, ischaemic ECG patterns were no longer associated with survival.

Graphical Abstract



Keywords Cardiac arrest • Shockable rhythm • ECG • Ischaemia • Left ventricular function

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death.[1] In patients with return of spontaneous circulation (ROSC), vital organ support and treatment of the underlying aetiology are paramount to improve survival. Ischaemic heart disease is the most common cause of cardiac arrest[2] and accounts for approximately 70% of cases.[3]

The ST-segment elevation myocardial infarction (STEMI) on the post-resuscitation electrocardiogram (ECG) has shown to be a useful predictive marker for acute thrombotic occlusions, with a positive predictive value of >85%.[3–6] In those presenting with STEMI, immediate reperfusion has demonstrated improved survival and thus this is advocated in the current guidelines.[7]

The recently published Coronary Angiography after Cardiac arrest (COACT) trial and the Immediate Unselected Coronary Angiography vs. Delayed Triage in Survivors of Out-of-hospital Cardiac Arrest Without ST-segment Elevation (TOMAHAWK) trial found that urgent coronary angiography was not beneficial in OHCA patients without STEMI.[8–10] The results of the COACT trial were incorporated in the European Society of Cardiology guidelines.[11]

Repolarization abnormalities such as ST-depression and T-wave inversion on the post-resuscitation ECG are frequently encountered.[12–14] In patients presenting with non-STEMI (NSTEMI) who are not resuscitated, ST-depression has shown to be an independent predictor for comorbidity and mortality.[15,16] However, data on the prognostic value of ST-repolarization abnormalities on the post-resuscitation ECG in the absence of STEMI is scarce. So far, cardiac arrest studies have mainly focused on the presence of STEMI.[6,17,18] Whether post-ROSC ST-repolarization disorders in the absence of STEMI are a predictor for mortality is yet to be determined.

In the present study, we compared angiographic outcomes, myocardial damage, left ventricular function, and survival in patients presenting with or without ischaemic ECG patterns on the first post-resuscitation ECG recorded in-hospital.

Methods

Study population

This is a post-hoc analysis of the COACT trial.[8,9] The COACT trial was a multicentre, randomized controlled trial that investigated the benefit of immediate coronary angiography compared with delayed coronary angiography in successfully resuscitated patients without STEMI on the post-resuscitation ECG. This study found no benefit of immediate coronary angiography on 90-day survival and 1-year survival.[8,9] All patients with an initial shockable rhythm, absence of STEMI, and no obvious non-coronary cause of the arrest were eligible for enrolment. Important exclusion criteria were shock and signs of STEMI (including new left-bundle branch block or isolated ST-depression in V1–V3 due to a posterior infarction). Further in- and exclusion criteria are described previously.[8] For the current study, patients who had an ECG recorded in the emergency department were included in the analysis. The primary outcome was the overall survival rate at 90 days and the secondary endpoint overall survival at 1 year. Other secondary outcomes were maximum levels of cardiac biomarkers, rate of acute unstable lesions and acute thrombotic occlusions, and left ventricular function. The trial design of the main COACT trial was reviewed and approved by the VUmc ethics committee, and is registered at The Netherlands Trial Register, number NTR4973.

Electrocardiogram analysis

All initial ECGs recorded at the emergency department were assessed for ischaemic ECG patterns by two experienced physicians blinded to the patients' history, angiographic findings, previous ECG manifestations, and the time elapsed between arrest and ECG recording. The assessment of a third professional assessor was requested when consensus was not reached. Ischaemia was defined as ST-depression of $\geq$0.1 mV in $\geq$2 contiguous leads or T-wave inversion in $\geq$2 contiguous leads, or both. According to the post-resuscitation ECG, patients were categorized into two groups: those with ischaemic ECG patterns, and those without ischaemic ECG patterns. The primary analysis of this post-hoc analysis concerns the comparison of these two groups.

Coronary angiography evaluation

As part of the COACT trial protocol, all patients were randomized to immediate or delayed coronary angiography.[8] An independent core laboratory performed an evaluation of coronary angiography, by personnel that was blinded to the timing of angiography, patients' history and ECG findings. Angiographic definitions are described in the Supplementary Appendix.

Statistical analysis

Continuous variables were summarized by mean $\pm$ standard deviation or median (interquartile range). Categorical variables were summarized by numbers and percentages. Differences between the two groups were tested using independent *T*-test, or Mann–Whitney *U*, Pearson's χ^2 test, or Fisher's exact test. Effect sizes are expressed in hazard ratios (HRs), odds ratios (ORs), mean differences, or ratio of geometric means with 95% confidence intervals (CIs). Survival curves were derived using Kaplan–Meier method and compared between patients with and without ischaemic ECG patterns using the log-rank test. Hazard ratios and their 95% CIs were derived using Cox regression. Cox regression was used to separately adjust the HR for ischaemic ECG patterns on survival for the following potential confounders; age, sex, history of myocardial infarction, percutaneous coronary intervention (PCI) or coronary artery disease (CAD), and time from OHCA to ROSC. For each potential confounder, an adjusted HR and *P*-value were calculated. Additionally, we performed a multivariable analysis identifying predictive factors for survival including ischaemic ECG patterns, age, sex, history of myocardial infarction, PCI and CAD, and time from arrest to ROSC. A two-tailed *P*-value of $<$0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics, version 26 (IBM, Armonk, NY, USA).

Results

Between January 2015 and July 2018, 552 successfully resuscitated OHCA patients without signs of ST-segment elevation were included in the COACT trial. Fourteen patients that withdrew informed consent and 28 patients in whom ST-depression or *T*-wave inversion could not be determined were excluded from analysis (see Supplementary material online, *Figure S1*). Of the 510 patients eligible for this analysis, 340 (66.7%) patients had ischaemic ECG patterns on the post-ROSC ECG. Of the patients with ischaemic ECG patterns, 151 (44.4%) patients had ST-segment depression, 175 (51.5%) patients had T-wave inversion, and 14 (4.1%) patients had both. The median time from arrest to the first recorded ECG

Table 1 Baseline characteristics

	Ischaemia on ECG ($N = 340$)	No ischaemia on ECG ($N = 170$)	*P*-value
Age (years)	66 ± 12	63 ± 15	0.003
Sex (male)	274 (80.6)	126 (74.1)	0.09
Medical history			
Hypertension	163 (48.4)	78 (46.2)	0.64
Myocardial infarction	101 (29.7)	35 (20.6)	0.03
CABG	46 (13.6)	15 (8.8)	0.12
PCI	74 (21.9)	25 (14.7)	0.054
Coronary artery disease	134 (39.4)	47 (27.6)	0.009
CVA	23 (6.8)	8 (4.7)	0.36
Diabetes mellitus	64 (18.9)	29 (17.1)	0.62
Smoker	75 (24.0)	36 (22.8)	0.78
Hypercholesterolaemia	95 (28.1)	38 (22.6)	0.19
Peripheral artery disease	24 (7.1)	10 (5.9)	0.61
Arrest characteristics			
Witnessed arrest	269 (79.1)	129 (75.9)	0.41
Time from arrest to BLS (min)	2 (1–5)	2 (1–5)	0.20
Time from arrest to ROSC (min)	15 (10–21)	13 (7–20)	0.07
Time from arrest to ECG at ED (min)	53 (39–71)	49 (27–70)	0.20
Glasgow Coma Scale at admission	3 (3–3)	3 (3–3)	0.97
Laboratory results			
pH	7.21 ± 0.14	7.23 ± 0.12	0.07
Bicarbonate (mmol/L)	19.1 ± 4.5	19.5 ± 4.2	0.45
Base excess	−7.8 ± 6.4	−7.2 ± 5.4	0.30
Troponin-T (μg/L)	0.058 (0.032–0.111)	0.034 (0.022–0.075)	<0.001
Creatinine-MB (μg/L)	6.9 (4.1–22.9)	4.9 (3.0–8.7)	0.001
Creatinine kinase (IU/L)	164 (119–243)	162 (105–284)	0.85
Lactate (mmol/L)	5.2 (3.2–8.8)	4.5 (2.8–8.2)	0.20
Creatinine (μmol/L)	103 (88–118)	99 (86–115)	0.10
Randomization to immediate CAG	168 (49.4)	94 (55.3)	0.21

BLS, basic life support; CABG, coronary artery bypass grafting; CAG, coronary angiography; CVA, cerebrovascular accident; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation.

at the emergency department was 53 (39–71) min for patients with ischaemic ECG patterns and 49 (27–70) min for patients without ischaemic ECG patterns ($P = 0.20$).

Most patients were men (78.4%; *Table 1*). Patients with ischaemic ECG patterns were older than patients without (66 ± 11 vs. 62 ± 14 years; $P = 0.003$). A history of myocardial infarction or CAD was found more frequently in patients with ischaemic ECG patterns than in patients without ischaemia (history of myocardial infarction 29.7 vs. 20.6%; $P = 0.03$, history of CAD 39.4 vs. 27.6%; $P = 0.009$). Furthermore, serum troponin-T at baseline was 0.058 (0.032–0.111) μg/L in patients with ischaemic ECG patterns and 0.034 (0.022–0.075) μg/L for patients without ($P < 0.001$). The median baseline Creatinine Kinase Myocardial Binding (CK-MB) value for patients with ischaemic ECG patterns was 6.9 (4.1–22.9) and 4.9 (3.0–8.7) μg/L for patients without ischaemic ECG patterns ($P = 0.001$). Arrest characteristics such as the number of patients with witnessed arrest, time to basic life support, or time to ROSC did not differ between the two groups. In addition, the proportion of patients who were randomized to immediate coronary angiography was balanced ($P = 0.21$).

Coronary angiography was performed in 81.2% of patients with ischaemic ECG patterns, and 81.8% in patients without (OR 0.96; 95% CI 0.60–1.55; *Table 2*). In 35 patients allocated to a delayed angiography strategy until neurological recovery, urgent angiography was performed due to cardiac deterioration. This was performed more often in the patients with an initial ischaemic ECG (9.1 vs. 2.4%, OR 4.16; 95% CI 1.45–12.00). Significant CAD was found in 67.4% in the ischaemic ECG group and 57.6% in the non-ischaemic ECG group (OR 1.52; 95% CI 1.01–2.32). Patients with ischaemic ECG patterns more frequently had multivessel disease compared with those without. In addition, chronic total occlusions (CTOs) were found more frequently in patients with ischaemic signs (OR 1.71; 95% CI 1.10–2.67). The proportion of patients with unstable lesions did not differ between the two groups (14.5 vs. 15.8%, OR 0.90; 95% CI 0.51–1.59).

Table 2 Angiographic outcomes

	Ischaemia on ECG ($N = 340$)	No ischaemia on ECG ($N = 170$)	Odds ratio (95% CI)[a]
Coronary angiography performed	276 (81.2)	139 (81.8)	0.96 (0.60–1.55)
Urgent coronary angiography due to deterioration (in the delayed group)	31 (9.1)	4 (2.4)	4.16 (1.45–12.00)
STEMI	12/324 (3.7)	1/167 (0.6)	6.39 (0.82–49.53)
Cardiogenic shock	1/324 (0.3)	0 (0.0)	N.A.
Recurrent ventricular arrhythmias	7/324 (2.2)	3/166 (1.8)	1.20 (0.31–4.70)
Other	11/324 (3.4)	3/167 (1.8)	1.92 (0.53–6.98)
Significant coronary artery disease (>70%)	186 (67.4)	80 (57.6)	1.52 (1.01–2.32)
Coronary artery disease severity			
One-vessel disease	70 (25.4)	44 (31.7)	Reference
Two-vessel disease	60 (21.7)	22 (15.8)	1.71 (0.93–3.18)
Three-vessel disease	56 (20.3)	14 (10.1)	2.51 (1.28–5.04)
Acute unstable lesion	40 (14.5)	22 (15.8)	0.90 (0.51–1.59)
Acute thrombotic occlusion	16 (5.8)	5 (3.6)	1.65 (0.59–4.60)
Chronic total occlusion	108 (39.1)	38 (27.3)	1.71 (1.10–2.67)
PCI	95 (27.9)	49 (28.8)	0.96 (0.63–1.48)
CABG	25 (7.4)	13 (7.6)	0.96 (0.48–1.92)
Conservative treatment	222 (65.3)	109 (64.1)	1.05 (0.71–1.55)

CABG, coronary artery bypass grafting; CI, confidence interval; NA, not applicable; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.
[a]Odds ratios are reported as effect estimates with 95% confidence intervals. No ischaemia was used as the reference group.

Also, the proportion of patients with acute thrombotic occlusions was not found to differ between the groups (5.8 and 3.6%; OR 1.65; 95% CI 0.59–4.60). The proportion of patients that underwent revascularization such as PCI or CABG did not differ between patients with and without ECG ischaemic ECG patterns.

Almost all patients were treated with targeted temperature management (92.4 and 95.3%), with a median temperature in both groups of 34°C (33–36°C; *Table 3*). Maximum levels of serum troponin were higher in patients with ischaemic ECG patterns [0.595 (0.243–1.430) µg/L] compared with patients without ischaemic ECG patterns [0.359 (0.159–0.845) µg/L; ratio of geometric means 1.58; 95% CI 1.13–2.20]. Maximum levels of CK-MB were also higher in patients with ischaemic ECG patterns [39.1 (18.8–122.9) vs. 21.8 (12.7–47.5) µg/L; ratio of geometric means 1.80; 95% CI 1.39–2.32]. Left ventricular ejection fraction (%), assessed by cardiac magnetic resonance (CMR) imaging or echocardiography during hospitalization, was worse in patients with ischaemic ECG patterns (44.7 ± 12.5) than in patients without ischaemic ECG patterns (49.9 ± 13.3%; mean difference −5.13; 95% CI −8.84 to −1.42). Patients without ischaemic ECG patterns more frequently had an implantable cardioverter defibrillator (ICD) implanted (OR 0.63; 95% CI 0.43–0.92).

At 90 days, 212 (62.4%) patients with ischaemic ECG patterns survived, and 125 (73.5%) patients without ischaemic ECG patterns survived (HR for death 1.51; 95% CI 1.08–2.12; $P = 0.02$; *Figure 1*). Causes of death did not differ between the groups (see Supplementary material online, *Table S1*). At 1 year, 195 (59.3%) patients with ischaemic ECG patterns survived and 115 (69.7%) patients without ischaemic ECG patterns survived (HR for death 1.44; 95% CI 1.04–2.00; $P = 0.02$). A higher sum of ST-depression was associated with worse survival (log-rank = 0.01). In multivariate Cox analysis, ischaemic ECG patterns were not an independent predictor for survival (see Supplementary material online, *Table S2*). Predictors' age (HR 1.06; 95% CI 1.04–1.08; $P < 0.001$) and time to ROSC (HR 1.03; 95% CI 1.02–1.04; $P < 0.001$) were strongly correlated with 90-day survival. When the impact of potential confounders was examined in separate analyses, we found that after adjustment for age (HR 1.33; 95% CI 0.94–1.86; $P = 0.10$) and time from arrest to ROSC (per minute; HR 1.36; 95% CI 0.93–2.00; $P = 0.12$), the association between ischaemic ECG patterns and 90-day survival was no longer significant (*Table 4*, Supplementary material online, *Figure S2*). Among all patients that had an ICD implanted, the association between ischaemic ECG patterns and survival was not significant (HR 1.30; 95% CI 0.12–14.33; $P = 0.83$; see Supplementary material online, *Table S3*). In the same way, in all patients in whom an ICD was not implanted, the association between ischaemic ECG patterns and survival was again not significant (HR 1.25; 95% CI 0.89–1.76; $P = 0.21$). At 1 year, there were no differences in revascularization, ICD implantation, or rate of ICD shocks between the groups (see Supplementary material online, *Table S4*).

Discussion

Our study has shown that patients with ischaemic ECG patterns in the absence of STEMI on the post-resuscitation ECG had more CAD, higher levels of myocardial injury, worse left ventricular

Table 3 Clinical outcomes

	Ischaemia on ECG ($N = 340$)	No ischaemia on ECG ($N = 170$)	Effect size (+95% CI)[a]
Survival at 90 days follow-up	212 (62.4)	125 (73.5)	1.51 (1.08–2.12)
Targeted temperature management	314 (92.4)	162 (95.3)	0.60 (0.26–1.35)
Median target temperature	34 (33–36)	34 (33–36)	
Geometric mean (95% CI)	34 (34–34)	34 (34–34)	1.00 (0.99–1.01)
Left ventricular ejection fraction[b]	44.7 ± 12.5	49.9 ± 13.3	−5.13 (−8.84 to −1.42)
Noradrenaline administered	303 (89.1)	137 (80.6)	1.97 (1.18–3.29)
Duration of administration (days)	1.9 (1.2–2.9)	1.6 (1.1–2.3)	
Geometric mean (95% CI)	1.7 (1.5–1.9)	1.5 (1.3–1.8)	1.09 (0.90–1.32)
Dobutamine administered	93 (27.4)	42 (24.7)	1.15 (0.75–1.75)
Duration of administration (days)	1.2 (0.7–1.6)	1.3 (0.8–1.8)	
Geometric mean (95% CI)	1.0 (0.8–1.2)	1.1 (0.8–1.5)	0.91 (0.63–1.30)
Use of assist device	4 (1.2)	3 (1.8)	0.66 (0.15–3.00)
Acute kidney injury[c]			
Stage 0			Reference
Stage 1	16/307 (5.2)	4/156 (2.6)	2.06 (0.68–6.28)
Stage 2	5/307 (1.6)	4/156 (2.6)	0.64 (0.17–2.43)
Stage 3	14/307 (4.6)	8/156 (5.1)	0.90 (0.37–2.20)
Need for renal replacement therapy	11 (3.2)	5 (2.9)	1.10 (0.38–3.23)
Recurrence of ventricular tachycardia needing defibrillation	20 (5.9)	13 (7.6)	0.76 (0.37–1.56)
ICD implanted	124 (36.5)	81 (47.6)	0.63 (0.43–0.92)
Maximum troponin value (μg/L)	0.595 (0.243–1.430)	0.359 (0.159–0.845)	
Geometric mean (95% CI)	0.863 (0.660–1.129)	0.413 (0.296–0.574)	1.58 (1.13–2.20)
Maximum creatinine kinase MB (μg/L)	39.1 (18.8–122.9)	21.8 (12.7–47.5)	
Geometric mean (95% CI)	46.4 (38.2–56.3)	26.4 (21.1–33.1)	1.80 (1.39–2.32)
Maximum creatinine kinase (IU/L)	800 (379–2087)	899 (361–1555)	
Geometric mean (95% CI)	917 (773–1088)	876 (690–1111)	1.06 (0.86–1.31)
Maximum lactate (mmol/L)	4.9 (2.8–8.4)	4.5 (2.8–8.0)	
Geometric mean (95% CI)	5.0 (4.51–5.50)	4.5 (3.9–5.2)	1.05 (0.92–1.19)
Duration of ICU hospitalization	4 (2–6)	3 (2–6)	
Geometric mean (95% CI)	4 (4–5)	4 (3–4)	1.11 (0.97–1.29)
Duration of hospital admission	12 (6–19)	16 (7–22)	
Geometric mean (95% CI)	11 (9–12)	13 (11–15)	0.83 (0.69–0.99)

CI, confidence intervals; ICD, implantable cardioverter defibrillator; ICU, intensive care unit.
[a]Effect sizes are expressed in hazard ratios for death, odds ratios, mean differences, and ratio of geometric means with 95% confidence intervals. No signs ischaemia on the ECG is used as the reference group.
[b]Left ventricular function was assessed using CMR or echocardiography in 122 patients with ischaemic ECG patterns and in 75 patients that were without ischaemic ECG patterns.
[c]Acute kidney injury classification ranges from 0 to 3, higher score indicating a higher stage of injury.

function, and lower survival compared with patients without ischaemic ECG patterns. In addition, a higher sum of ST-depression was associated with worse survival outcomes. After adjustment for either age or time to ROSC, the association between ischaemic ECG patterns and survival was no longer significant. In patients without STEMI, this is the first study that compared post-ROSC ischaemic ECG patterns to non-ischaemic ECG patterns and its association with outcome.

The association between ischaemic ECG patterns and survival persisted after 1-year follow-up. The majority of deaths occurred in the first months after cardiac arrest, as reflected by a 2% mortality rate in both patient groups between 90 days and 1-year follow-up. During the index hospitalization, patients without ischaemic ECG patterns more frequently received an ICD compared with patients with ischaemic ECG patterns. This might be the result of a lower rate of CAD in patients without ischaemic ECG patterns, and revascularization of CAD in these patients might have abrogated the ICD indication. Another possible explanation is that a higher number of patients with ischaemic ECG patterns died during hospitalization, before an ICD could be implanted. Although patients without ischaemic

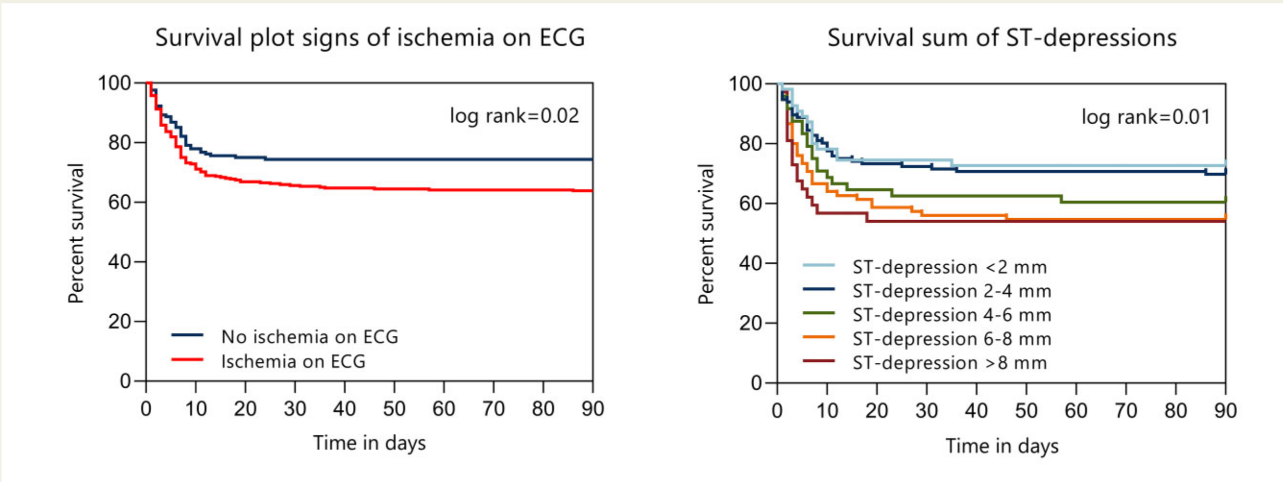


Figure 1 Kaplan–Meier estimates on 90-day survival. Patients with ischaemic electrocardiogram patterns had worse survival compared with patients without.

Table 4 Assessment of potential confounders for association between ischaemic electrocardiogram and 90-day survival

	(Adjusted) HR for ischaemic ECG	95% CI for (adjusted) HR for ischaemic ECG	*P*-value for (adjusted) HR for ischaemic ECG
Ischaemic ECG (unadjusted HR)	1.51	1.08–2.12	0.02
Adjusted for single confounder			
Age	1.33	0.94–1.86	0.10
Male sex	1.53	1.09–2.16	0.01
History of myocardial infarction	1.45	1.03–2.04	0.03
History of PCI	1.46	1.04–2.05	0.03
History of coronary artery disease	1.45	1.03–2.04	0.03
Time from OHCA to ROSC (min)	1.36	0.93–2.00	0.12

Hazard ratios and adjusted hazard ratios for ischaemic ECG and 90-day survival.
HR, hazard ratio; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation.

ECG patterns more frequently had an ICD implanted, the rate of ICD shocks during 1 year did not differ between the groups.

In our study, higher rates of significant CAD were found in patients with ischaemic ECG patterns compared with patients without ischaemic ECG patterns (67.4 and 57.6%). The higher rate in significant CAD was previously observed in OHCA patients presenting with ST-depression (63–75%).[18,19] However, in the study of Leclercq *et al.*,[18] the rate of significant CAD was lower in patients without ischaemic ECG patterns (33.4%) compared with our study and the rate of acute coronary lesions and acute coronary occlusions was higher among patients with ischaemic ECG patterns compared with patients without ischaemic ECG patterns (23.3 vs. 6.7% and 3.3 vs. 0%). We found no such difference; the rate of acute unstable lesions was 14.5% in patients with ischaemic ECG patterns vs. 15.8% in patients without. Acute thrombotic occlusions were present in 5.8% of patients with ischaemic ECG patterns vs. 3.6% in patients without. However, we found a significant difference in CTO rate, 39.1% in patients with ischaemic ECG patterns, compared with 27.3% in patients without ischaemic ECG patterns. In these patients, the cardiac arrest might be scar related as a result of previous myocardial infarction. The presence of CTO lesions might add myocardial territories which are susceptible to contribute to ECG changes. Remarkably, 32.6% of patients with ischaemic ECG patterns did not have any significant CAD. In these patients, it has been suggested that an abnormal metabolic milieu due to global cardiac ischaemia as a result of the arrest itself may also play a part in causing these ECG findings.[4] Further research is needed to address the mechanism of ischaemia after cardiac arrest and its outcome.

In our study, we found that patients with ischaemia on the ECG in the delayed angiography group were more likely to undergo urgent coronary angiography due to cardiac deterioration, emphasizing the higher risk of this patient group.

We observed that patients with post-ROSC ischaemic ECG patterns had worse left ventricular function than patients without. Whether this is attributable to myocardial injury during the cardiac arrest or whether the worse left ventricular fraction was pre-existent and might have been the substrate of the arrest in these patients remains unknown since no data on pre-arrest left ventricular function was available. However, patients with ischaemic ECG patterns were found to have higher troponin and CK-MB values than patients without ischaemic ECG patterns in our study. Nonetheless, immediate or delayed coronary angiography did not seem to affect left ventricular function in post-arrest patients without STEMI.[20]

Compared with OHCA patients with STEMI, survival rates for patients without STEMI are known to be lower.[12,18,21,22] Previous research showed that ST-depression is present in approximately 20% of successfully resuscitated patients.[12,13] In non-resuscitated NSTEMI patients, ST-depression is considered an independent predictor of mortality.[15,16] Our study found that baseline characteristics in patients with ischaemic ECG patterns on the ECG differed from patients not having ischaemic ECG patterns. They were older and more frequently had a history of myocardial infarction or CAD. These differences in patient characteristics were previously described.[18] However, the previous study focused on patients with STEMI. When adjusted for confounders' age and time to ROSC, ischaemic ECG patterns were no longer found to be associated with 90-day survival. Age is a known predictor of survival as well as a risk factor for CAD, resulting in ischaemic ECG changes. Time to ROSC is also a known predictor of survival, and a longer time from arrest to ROSC will increase ischaemic myocardium, resulting in ischaemic ECG patterns on the ECG.

In the acute phase, the underlying aetiology of the arrest is often unclear, and to what extent urgent coronary angiography should be performed has been debated.[8,23,24] The post-resuscitation ECG alone is a poor predictor for acute coronary occlusions.[13,17,25] Since ischaemic ECG patterns are associated with worse survival in our study, one might argue that urgent coronary angiography and PCI, if indicated, may improve survival in these patients. However, in a subgroup analysis of the COACT trial, immediate coronary angiography did not improve 90-day survival in patients with ischaemic ECG patterns.[8] These findings suggest that ischaemic ECG patterns are not an expression of an acute coronary syndrome in the majority of these patients. Hence, no benefit of an early invasive strategy can be expected.

Predicated on the findings of COACT, current guidelines on the management of patients with ACS without ST-segment elevation recommend a delayed as opposed to immediate coronary angiography in patients successfully resuscitated after an OHCA.[11,26] An unsolved question is the striking difference between registry data and the results of randomized studies in survivors of OHCA without ST-segment elevation.[8,10,14,27] A possible explanation for these opposite findings is that the decision to perform early coronary angiography in retrospective studies depended on clinical judgement of individual physicians, and hereby increasing the risk of indication bias. One important challenge that clinicians face is to appropriately select patients who would benefit from immediate coronary angiography. Our findings suggest that ischaemic ECG changes cannot identify these patients. Ascertain predictors for acute coronary lesions in OHCA survivors without ST-segment elevation is an important issue for further research. Prognostication tools such as Cardiac Arrest Hospital Prognosis (CAHP) score or MIRACLE2 may add incremental value; however, this is yet to be demonstrated.

Limitations

Few limitations related to this study should be noted. This a post-hoc analysis dealing with a non-randomized comparison and in its nature inherent to risk of bias and especially bias due to confounders. Pre-arrest ECGs were not available and therefore it was not known whether ECG abnormalities were pre-existent. The COACT trial excluded patients with haemodynamic instability; therefore, the results cannot be extrapolated to patients with shock.

Conclusion

In successfully resuscitated patients without signs of STEMI, ischaemic ECG patterns such as ST-depression and/or T-wave inversion were found to be associated with worse 90-day survival. Moreover, a higher sum of ST-depression was associated with worse survival. Adjusted for age and time to ROSC, ischaemic ECG patterns were no longer associated with survival. These findings suggest that ischaemic ECG patterns in survivors of OHCA with no ST-segment elevation are mostly due to myocardial ischaemia caused by prolonged resuscitation.

Supplementary material

Supplementary material is available at *European Heart Journal: Acute Cardiovascular Care*.

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Data availability

The data underlying this article cannot be shared publicly. The data will be shared on reasonable request to the corresponding author.

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