Emergency coronary angiography in comatose cardiac arrest patients: do real-life experiences support the guidelines?

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Abstract

Aims: To describe the use of emergency coronary angiography (CAG) and primary percutaneous coronary intervention (PCI) and the association with short- and long-term survival in consecutive comatose survivors after out-of-hospital cardiac arrest (OHCA).

Methods: In the period 2004–10, a total of 479 consecutive patients with OHCA of suspected cardiac cause were referred to a tertiary cardiac centre, 360 patients were comatose and admitted to the ICU for post-resuscitative care. The population was stratified in two groups according to the pattern of the first ECG obtained after re-established circulation; ST-segment elevation (STEMI, $n=116$) and ECG without STEMI pattern (No-STEMI, $n=244$). Emergency CAG (≤ 12 hours after OHCA) was performed at the discretion of the attending cardiologist. Primary outcome was 30-day and 1-year survival.

Results: Emergency CAG was performed in all patients in the STEMI group compared to 82 (34%) in the group without STEMI pattern ($p<0.0001$) with significant coronary lesions found in 108 (93%) compared to 43 (52%) patients, respectively ($p<0.0001$). Survival at 30 day according to emergency CAG vs. no emergency CAG was 65% in the STEMI group compared to 66% and 54% in the group without STEMI pattern ($p_{\log\text{-rank}}=0.11$). The use of emergency CAG in the group without STEMI pattern was not associated with reduced mortality ($HR_{\text{adjusted}}=0.69$, 95% CI 0.4–1.2, $p=0.18$).

Conclusions: In comatose survivors of OHCA presenting with STEMI, a high prevalence of coronary disease and culprit lesions suitable for emergency PCI was found, whereas in patients without STEMI pattern, significant coronary stenosis was less frequent. Clinical benefits of emergency CAG/PCI in comatose survivors of OHCA presenting without STEMI could not be identified.

Keywords

Cardiac arrest, coronary angiography, coronary intervention, hypothermia, outcome, survival

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Introduction

The treatment of comatose survivors of out-of-hospital cardiac arrest (OHCA) from cardiac causes has evolved in recent years with more efficient prehospital management and implementation of therapeutic hypothermia which has been associated with improved outcome in terms of both survival and cerebral outcome.^{1–4} Coronary artery disease, defined as stenosis of more than 50% in major coronary arteries, is present in 58–70% of patients, depending on the initial ECG.^{5,6} Emergency coronary

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angiography (CAG), and thus an opportunity for emergency percutaneous coronary intervention (PCI), is established and widely implemented as first-line treatment in patients with ST-segment elevation myocardial infarction (STEMI) complicated with OHCA. It is less clear whether OHCA patients presenting with other ECG patterns benefit from emergency CAG and subsequent revascularization.⁷ The 2010 guidelines for resuscitation have emphasized the use of early invasive strategy after OHCA when coronary pathology is suspected. But selection of patients with high likelihood of coronary artery disease may be challenging as the initial obtained ECG and history of chest pain seem to be poor predictors of occlusive coronary disease, and the ECG may in some cases only be slightly abnormal despite extensive coronary disease.⁸ The proportion of patients without an indication for emergency revascularization or lesions suitable for emergency PCI is increased in non ST-elevation ECG patterns compared to STEMI.⁶ Guidelines recommend immediate CAG when life-threatening ventricular arrhythmias or haemodynamic instability are present.⁹ Furthermore non-specific ECG changes are often seen early after OHCA. Finally, intracranial haemorrhage is an example of a clinical scenario associated with various non-specific ECG changes, where emergency CAG and antithrombotic treatment could even be fatal.¹⁰ Therefore the benefits and potential complications of emergency CAG and emergency PCI in consecutive patients should be balanced against a less invasive strategy.

This study reports a large centre experience on the association between revascularization strategy and survival in consecutive comatose survivors of OHCA admitted to a tertiary cardiac centre for advanced post-resuscitation care including hypothermia treatment.

Materials and methods

Patient population

The Copenhagen University Hospital, Rigshospitalet is a tertiary cardiac centre and offers 24-hour cardiology service including invasive coronary and surgical interventions. Copenhagen, the capital of Denmark covers 97 km² and has approximately 525,000 inhabitants, increasing during daytime by 20%. Patients suffering cardiac arrest in central Copenhagen and in the greater area of Copenhagen (population 820,000) are treated by the mobile emergency care unit (MECU) and referred to the nearest available hospital after return of spontaneous circulation (ROSC). Patients presenting with ST-elevation in ECG were referred directly to Rigshospitalet for emergency CAG/PCI and post-resuscitative care. The MECU system runs a 24/7 service and has been described in detail elsewhere.¹¹ In addition patients resuscitated after OHCA in need for specialized treatments are transferred from hospitals in the region of

Zealand (approximately 820,000 inhabitants) from up to 150 km away if urgent CAG is indicated.

This study prospectively included consecutive patients, 18 years or older, who were admitted to the Copenhagen University Hospital Rigshospitalet with sustained ROSC after OHCA in the period from 1 June 2004 to 31 December 2010. All patients presenting with ST-segment elevation were received in the catheterization laboratory for emergency CAG. An ST-segment elevation was defined as an elevation of ≥ 2 mm in precordial leads in men and ≥ 1.5 mm in precordial leads in women or ST-segment elevation ≥ 1 mm in two contiguous leads in standard leads.¹² New-onset left bundle branch block was considered an equivalent to STEMI. The No-STEMI group was defined as all other ECG patterns without significant ST-segment elevation. Decision on timing of CAG in the No-STEMI group was made by the attending physician. Emergency CAG was defined as CAG within 12 hours of the cardiac arrest. Late CAG (≥ 12 hours and ≤ 30 days) was performed in survivors with good cerebral outcome after post-resuscitative care.

Patients were excluded from the analysis for Glasgow Coma Scale (GCS) ≥ 9 upon admission or presence of cardiogenic shock defined as hypotension with sustained systolic blood pressure (SBP) < 80 mmHg for more than 30 min or administration of inotropes to maintain SBP > 80 mmHg and signs of organ hypoperfusion. Patients with cardiogenic shock were excluded because of a well-known serious prognosis and because the SHOCK trial suggested benefit of emergency CAG and early revascularization.¹³

Data regarding cardiac arrest, including initial arrhythmia, witnessed arrest, whether bystander cardiopulmonary resuscitation (CPR) was administered, comorbidities if any, and initial ECG changes, were systematically collected upon admission according to the Utstein guidelines.¹⁴

ICU treatment protocol

All comatose survivors were admitted to the cardiac intensive care unit (ICU) for intensive care to optimize haemodynamic and metabolic parameters. General treatment goals were mean arterial pressure (MAP) 65–100 mmHg, heart rate of 40–90 bpm, central venous pressure of 6–12 mmHg, and diuresis > 1.5 ml/kg/h.

Therapeutic hypothermia was administered according to guidelines as soon as possible upon arrival at the emergency department.¹⁵ Hypothermia was induced by infusion of 30 ml/kg of 4°C Ringer's solution and surface cooling continued in the ICU using an external cooling system (Allon Thermowrap; MTRE, Israel and Emcools Flex.Pad; Austria). Target core temperature was 32.5–33.5°C and was maintained for 24 h with subsequent active rewarming by 0.5°C per hour until normothermia (37°C) was achieved.

Coronary angiography

CAG was performed via femoral access in all patients. All coronary lesions resulting in a $\geq 50\%$ reduction in luminal diameter by visual estimation or presence of acute thrombus were described. The general revascularization strategy in patients with STEMI and 1-vessel disease was PCI of culprit lesion, PCI in STEMI with multivessel disease was performed in the culprit vessel when it could safely be identified while other significant lesions were revascularized in elective phase.

In No-STEMI patients PCI was performed in all stenosis suitable for PCI, but long and complex PCI procedures in chronic total occlusions were avoided in the acute phase.

Coronary intervention was defined as successful if it resulted in residual stenosis of $< 50\%$ and a thrombolysis in myocardial infarction (TIMI) grade III flow.

Outcome

Vital status of patients included in the present study was obtained by linkage to the Danish Central Personal Registry using the unique personal identification number of the patients in September 2011. Data on censoring (emigration) was also available from the registry. Patients with foreign nationality were censored upon discharge from hospital. Short-term survival was assessed after 30 days and at discharge from hospital. Long-term survival was assessed after 1 year in all patients.

Neurological outcome was assessed using the 5-item scale Cerebral Performance Category (CPC) according to the Utstein guidelines.¹⁶ CPC was assessed at discharge from hospital and we defined CPC of 1 or 2 as good cerebral outcome after cardiac arrest. CPC was assessed by investigators blinded to previous assessment and patient final outcome. Inter-observer agreement has previously been assessed to be 85–100%.⁴

Statistics

Data are presented as mean $\pm$ standard deviation (SD) or n (%), and differences were assessed by Student's t -test or χ^2 test, as appropriate. For variables with a non-normal distribution data are presented as median and interquartile ranges and differences were assessed by Wilcoxon signed rank test. Survival analysis was performed by Kaplan–Meier plots and groups were compared with the log-rank test. Survival free from cerebral death was analysed censoring patients experiencing cardiovascular death at time of death. For multivariable modelling, Cox proportional hazards models were applied after checking for underlying assumptions of linearity, proportionality and lack of interactions. Trends in proportions of CPC scores at hospital discharge were evaluated with Cochran–Armitage test for trend in survivors and logistic regression analysis was used in the

analysis of CPC scores in all patients (dichotomized into good and unfavourable outcome as previously defined).

All statistical analyses were performed using the SAS statistical software, version 9.1 (SAS Institute, Cary, NC, USA).

Results

Patient population

In the 6-year period, 2004–10, a total of 592 consecutive patients treated by MECU were admitted to Copenhagen University Hospital, Rigshospitalet after OHCA. A total of 113 (19%) patients were considered to be non-cardiac related, while 479 (81%) patients had a suspected cardiac cause of whom 50 (10%) died before admission to the ICU (Figure 1). ST-elevations were present in 150 patients (35%, STEMI group), including 19 (13%) patients having a GCS ≥ 9 and 15 (10%) patients met the criteria for cardiogenic shock and they were therefore excluded from further analysis. The No-STEMI group consisted of 279 patients (65%) with 25 (9%) patients having a GCS ≥ 9 and 10 (4%) patients were in cardiogenic shock; both groups were excluded from further analysis.

A total of 360 comatose OHCA patients were eligible for final analysis: 116 patients in the STEMI group and 244 patients in the No-STEMI group. Baseline demographic data showed that ventricular fibrillation and the use of therapeutic hypothermia were more frequent in the STEMI group, whereas a history of ischaemic heart disease and heart failure was more common in the No-STEMI group (Table 1).

In the No-STEMI group, 82 (34%) patients underwent an emergency CAG. No differences in sex, age, witnessed arrest, bystander CPR, or time to ROSC were found between patients with emergency CAG and no emergency CAG within the No-STEMI group. Ventricular fibrillation (90 vs. 68%, $p < 0.0001$) and therapeutic hypothermia (98 vs. 83%, $p = 0.0009$) were more frequent in the group who underwent an emergency CAG whereas median lactate levels at admission were lower (7 vs. 10 mmol/l, $p = 0.006$) and a history of chronic obstructive lung disease (5 vs. 15%, $p = 0.02$) were less prevalent in the group with emergency CAG.

Angiographic data

In the STEMI group all 116 patients underwent an emergency CAG and significant coronary lesions were found in 108 (93%) compared to 43 (52%) patients in the No-STEMI group ($p < 0.0001$). One-vessel disease was more frequent in the STEMI group (49 vs. 22%) compared to the No-STEMI group, while non-significant coronary artery disease or a normal angiography was found in 4% compared to 45%, respectively ($p < 0.0001$). In the No-STEMI group, late

Figure 1. Flow chart of patients admitted to Rigshospitalet after OHCA in the period 2004–10.

CAG, coronary angiography; CS, cardiogenic shock; GCS, Glasgow Coma Scale; ICU, intensive care unit; No-STEMI, other ECG patterns; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction in ECG.

CAG was performed in 57 (72%) patients who survived to ICU discharge and regained good cerebral function within 30 days after OHCA. The distribution of coronary vessel disease and results of revascularization is summarized in Table 2.

There were no differences in the extent of coronary lesions between emergency CAG and late CAG in the No-STEMI group. The location of identified culprit lesions did not differ between the STEMI and No-STEMI groups or within the No-STEMI group (emergency CAG vs. late CAG, $p=0.21$).

An initial rhythm of ventricular fibrillation ($OR_{\text{adjusted}}=3.2$, 95% CI 1.4–7.4, $p=0.008$) was the only independent predictor of emergency CAG being performed in the No-STEMI group.

PCI was more often attempted in the STEMI group [98 (91%) vs. 24 (56%), $p<0.0001$] and PCI was successful in 86 (88%) vs. 15 (63%, $p<0.0001$) where PCI was attempted, compared to the No-STEMI patients in whom emergency CAG was performed, respectively. There were no

differences in attempted PCI and successful PCI within the No-STEMI group (emergency CAG vs. late CAG, $p=0.50$). Significant lower time delays from OHCA to needle (126 vs. 159 min, $p=0.002$) and time to balloon (135 vs. 200 min, $p=0.004$) were found in the STEMI group compared to No-STEMI group. In the STEMI group, the median door to balloon time was 46 min (IQR: 25–77), $n=76$.

In the STEMI group, a complete revascularization status (<50% stenosis in vessels >2 mm) assessed at time for emergency CAG/PCI was achieved in 60 (64%) patients, compared to nine (43%) patients in the No-STEMI group ($p=0.10$). In the No-STEMI group, 10 (48%) patients could not be fully revascularized with PCI in the acute phase.

Survival

Overall 30-day survival was 65% in the STEMI group compared to 58% in the No-STEMI group ($p_{\text{log-rank}}=0.30$). After stratification, 30-day survival according to emergency CAG vs. no emergency CAG was 65% in the STEMI

Table 1. Baseline characteristics and concurrent diseases of consecutive patients with out-of-hospital cardiac arrest admitted to the ICU.

	Total (n=360)	Total population			No-STEMI population		
		STEMI (n=116)	No-STEMI (n=244)	p-value	Emergency CAG (n=82)	No emergency CAG (n=162)	p-value
Age, years (mean±SD)	61±14	60±12	61±14	0.54	59±14	62±15	0.14
Male	291 (81)	97 (84)	194 (80)	0.35	67 (82)	127 (78)	0.54
Comorbidities							
Hypertension	85 (24)	29 (26)	56 (24)	0.66	24 (30)	32 (21)	0.12
Diabetes mellitus	44 (13)	9 (8)	35 (15)	0.08	12 (15)	23 (15)	0.99
Known IHD	79 (23)	16 (14)	63 (27)	0.01	21 (26)	42 (27)	0.85
Heart failure	46 (13)	3 (3)	43 (18)	<0.0001	15 (19)	28 (18)	0.91
COPD	33 (10)	6 (5)	27 (11)	0.07	4 (5)	23 (15)	0.02
Renal failure	7 (2)	1 (1)	6 (3)	0.31	1 (1)	5 (3)	0.36
Previously cerebral stroke	27 (8)	6 (5)	21 (9)	0.25	6 (7)	15 (10)	0.57
Known malignancy	10 (3)	2 (2)	8 (3)	0.41	1 (2)	7 (5)	0.19
Alcohol abuse	48 (14)	11 (10)	37 (16)	0.14	10 (13)	27 (17)	0.34
Initial rhythm							
VF/VT	287 (80)	103 (89)	184 (75)	0.003	74 (90)	110 (68)	<0.0001
PEA/asystole	73 (20)	13 (11)	60 (25)		8 (10)	52 (32)	
Witnessed arrest	303 (86)	103 (90)	200 (85)	0.22	70 (88)	130 (83)	0.40
Bystander CPR	214 (59)	76 (66)	138 (57)	0.11	47 (57)	91 (56)	0.86
Time to MECU arrival (mins)	5 (4–7)	5 (3–7)	5 (4–7)	0.87	6 (4–8)	5 (4–7)	0.02
Time to ROSC (mins)	15 (10–24)	16 (11–26)	15 (10–24)	0.28	15 (10–24)	15 (10–24)	0.77
Lactate at admission (mmol/l)	9 (7–13)	9 (7–14)	9 (6–13)	0.54	7 (5–10)	10 (7–13)	0.006
Left ventricle ejection fraction (%)	40 (25–50)	40 (30–45)	40 (25–50)	0.66	40 (25–50)	40 (20–53)	0.77
Therapeutic hypothermia	324 (90)	110 (95)	214 (88)	0.04	80 (98)	134 (83)	0.0009
Final diagnosis of AMI	184 (51)	114 (98)	70 (29)	<0.0001	23 (28)	47 (29)	0.88

Values are mean±SD, n (%) or median and interquartile range. A significance level of $p<0.05$ was chosen.

AMI, acute myocardial infarction; CAG, coronary angiography; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; IHD, ischaemic heart disease; MECU, mobile emergency care unit; No-STEMI, other ECG patterns; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; STEMI, ST-elevation myocardial infarction in ECG; VF/VT, ventricular fibrillation/ventricular tachycardia.

group and 66% and 54% in the No-STEMI group, respectively ($p_{\log\text{-rank}}=0.11$, Figure 2A).

Long-term survival stratified according to emergency CAG vs. no emergency CAG was 63% in the STEMI group and 65 % and 49% in the No-STEMI group, respectively ($p_{\log\text{-rank}}=0.02$, Figure 2A insert). A survival analysis in the No-STEMI group stratified according to emergency CAG, assessing survival free of cerebral death, showed survival rates at 30 days of 74 vs. 63%, respectively ($p_{\log\text{-rank}}=0.07$, Figure 2B).

A multivariate logistic analysis in the STEMI and No-STEMI groups showed a tendency of successful PCI to be an independent predictor for hospital survival ($OR_{\text{adjusted}}=2.1$, 95% CI 1.1–4.1, $p=0.04$), whereas STEMI and emergency CAG were not significant predictors of hospital survival.

In the STEMI group a multivariable analysis showed that age (HR=1.2, 95% CI 1.0–1.4 per 5 year increase, $p=0.04$), time to ROSC (HR=1.2, 95% CI 1.1–1.2 per 5 min, $p=0.0004$), and absence of any comorbidities (HR=0.40, 95% CI 0.2–0.8, $p=0.01$) were independent

predictors of 30-day mortality in patients admitted to the ICU (Table 3). Adding time period as a covariate in the model did not show any significant effect. Predictors of long-term mortality in a similar model were not different (data not shown).

Multivariable analysis in the No-STEMI group showed that age (HR=1.2, 95% CI 1.1–1.3 per 5 year increase, $p<0.0001$), witnessed arrest (HR=0.4, 95% CI 0.3–0.7, $p=0.0006$), bystander CPR (HR=0.6, 95% CI 0.4–0.9, $p=0.009$), ventricular fibrillation (HR=0.5, 95% CI 0.3–0.7, $p=0.0004$), and time to ROSC (HR=1.1, 95% CI 1.0–1.2 per 5 min, $p=0.04$) were all independent predictors of 30-day mortality. The use of emergency CAG in the No-STEMI group was not significantly associated with reduced mortality ($HR_{\text{adjusted}}=0.69$, 95% CI 0.4–1.2, $p=0.18$). Predictors of long-term mortality were similar as predictors of 30-day mortality (data not shown).

Applying a survival analysis in the No-STEMI group according to models in the PROCAT study assessing the effect of successful PCI,⁶ the following long-term hazard ratios were

Table 2. Findings from CAG and PCI in patients resuscitated from OHCA and admitted in a comatose state at the ICU.

	STEMI	p-value ^a	No-STEMI	p-value ^b	No-STEMI
	Emergency CAG (n=116)		Emergency CAG (n=82)		late CAG (n=57)
Distribution of coronary vessel disease					
1-vessel disease	57 (49)		18 (22)		15 (26)
2-vessel disease	24 (21)		13 (16)		11 (19)
3-vessel disease	27 (23)	<0.0001	9 (11)	0.37	11 (19)
Unprotected left main disease	4 (3)		5 (6)		3 (6)
Ateromatosis without significant stenosis	3 (3)		17 (21)		5 (9)
No coronary pathology	1 (1)		20 (24)		12 (21)
Significant coronary artery disease	108 (93)	<0.0001	43 (52)	0.09	38 (67)
Identified culprit lesion					
Right coronary lesion	31 (29)		10 (23)		14 (35)
Left descending coronary lesion	42 (39)	0.54	17 (40)	0.21	17 (43)
Left circumflex coronary lesion	31 (29)		12 (28)		9 (23)
Left main stem lesion	4 (4)		4 (9)		0 (0)
PCI attempted in significant lesions	98 (91)	<0.0001	24 (56)	0.50	24 (63)
TIMI $\leq$ grade II before PCI attempt	87 (89)	0.007	16 (67)	0.01	7 (30)
TIMI grade III after PCI attempt	88 (90)	0.004	16 (67)	0.10	20 (87)
PCI successful	86 (88)	0.003	15 (63)	0.20	19 (79)
Revascularization status					
Complete	60 (64)		9 (43)		15 (63)
Incomplete, final	23 (25)	0.10	10 (48)	0.23	9 (38)
Incomplete, follow up	11 (11)		2 (9)		0 (0)
CABG performed after CAG/PCI	4 (4)	0.61	4 (5)	0.007	11 (19)
Time to needle from OHCA	126 (102–168)	0.002	159 (123–225)		NA
Time to balloon from OHCA	135 (109–177)	0.004	200 (135–275)		NA

Values are mean $\pm$ SD, n (%) or median and interquartile range. Differences were assessed by χ^2 -test or Wilcoxon, as appropriate. ^ap-value for emergency CAG between STEMI and No-STEMI. ^bp-value for No-STEMI between emergency CAG and late CAG. A significance level of $p < 0.05$ was chosen.

CABG, coronary artery bypass grafting; CAG, coronary angiography; NA, not applicable; No-STEMI, other ECG patterns; PCI, percutaneous coronary intervention; OHCA, out-of-hospital cardiac arrest; STEMI, ST-elevation myocardial infarction in ECG; TIMI, thrombolysis in myocardial infarction.

found: emergency CAG (HR=0.6, 95% CI 0.4–1.0, $p=0.04$), PCI successful (HR=0.4, 95% CI 0.2–0.8, $p=0.009$), and no or failed PCI (HR=2.4, 95% CI 1.0–5.4, $p=0.04$).

Neurological outcomes

Among survivors at hospital discharge good cerebral outcome (CPC 1+2) was found in 73 (96%) patients in the STEMI group compared to 134 (94%) patients in the No-STEMI group ($p=0.82$ (Table 4). Distribution of CPC scores within the No-STEMI group stratified according to emergency CAG was not significantly different, but nine (10%) patients in the no emergency CAG group had an unfavourable cerebral outcome while none experienced an unfavourable cerebral outcome in the emergency CAG group ($p=0.14$). A multiple logistic regression analysis in the No-STEMI group showed that emergency CAG was not significantly associated with good cerebral outcome (OR=1.5, 95% CI 0.8–2.9, $p=0.25$).

Discussion

The present study shows that comatose survivors after OHCA presenting with ST-segment elevation in the ECG have a high prevalence of coronary disease evaluated by emergency CAG and a major proportion have culprit lesions suitable for emergency PCI. In comatose patients presenting without STEMI pattern, an emergency CAG was performed in selected patients (34%) with coronary disease found in 52% and a low likelihood of complete revascularization. By univariate analysis, the use of emergency CAG tended to be associated with improved survival in the No-STEMI group, but emergency CAG may be a cumulative marker of 'total patient prognosis' as emergency CAG was not significantly associated with improved survival in a multivariable analysis. The benefit of an aggressive early invasive strategy can thereby be questioned even in selected comatose patients presenting without STEMI pattern in

Figure 2. Kaplan–Meier survival plots after admission to ICU after out-of-hospital cardiac arrest: (A) 30-day and long-term (inserted) plots of 360 comatose patients stratified by STEMI and No-STEMI (emergency CAG vs. no emergency CAG); (B) 244 comatose patients with No-STEMI stratified by emergency CAG (≤ 12 hours), patients with cardiovascular deaths were censored at time of death.

CAG, coronary angiography; No-STEMI, other ECG patterns; STEMI, ST-elevation myocardial infarction in ECG.

ECG. However, selection bias cannot be ruled out as emergency CAG could have been performed more frequently in patients with a presumed higher chance of survival. A tendency towards reduced cerebral death after emergency CAG (Figure 2B) indicates that selection bias does play a role.

Comatose survivors after OHCA represent a large proportion of OHCA patients (64–86%).^{6,17,18} In contrast to previous studies,^{18–22} this study included only comatose survivors of OHCA regardless of initial rhythm and

witnessed arrest to describe the outcome in real-life patients admitted to a tertiary cardiac centre.

STEMI

In agreement with other studies which have reported survival rates of 51–65%, we found a 30-day survival rate of 65% in the STEMI group. However, in contrast to those studies, we only included comatose patients, and the outcome of our population was considerably more favourable

Table 3. Univariate and multivariate proportional hazard models predicting 30-day mortality in comatose patients resuscitated from out-of-hospital cardiac arrest and admitted to the ICU at Copenhagen University Hospital, Rigshospitalet, 2004–10.

	STEMI (n=116)				No-STEMI (n=244)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value	HR (95 % CI)	p-value
Emergency CAG		NA			0.7 (0.4–1.0)	0.08		
Emergency PCI attempted	0.7 (0.3–1.6)	0.44			0.8 (0.4–1.7)	0.63		
Emergency PCI successful	0.6 (0.3–1.2)	0.14			0.7 (0.3–1.7)	0.44		
Sex, male	0.7 (0.3–1.4)	0.28			0.5 (0.3–0.8)	0.003		
Age, per 5 years	1.2 (1.0–1.4)	0.02	1.2 (1.0–1.4)	0.04	1.1 (1.1–1.2)	0.0004	1.2 (1.1–1.3)	<0.0001
Witnessed arrest	0.5 (0.2–1.2)	0.11			0.4 (0.2–0.6)	<0.0001	0.4 (0.3–0.7)	0.0006
Bystander CPR	0.7 (0.4–1.3)	0.30			0.4 (0.3–0.6)	<0.0001	0.6 (0.4–0.9)	0.009
Initial rhythm, VF/VT	0.4 (0.2–0.9)	0.03			0.4 (0.2–0.5)	<0.0001	0.5 (0.3–0.7)	0.0004
Time to ROSC, per 5 min	1.2 (1.1–1.3)	0.0002	1.2 (1.1–1.2)	0.0004	1.1 (1.0–1.2)	0.05	1.1 (1.0–1.2)	0.04
Mild therapeutic hypothermia	0.6 (0.2–2.1)	0.47			0.5 (0.3–0.7)	0.001		
No comorbidities	0.3 (0.1–0.6)	0.0005	0.4 (0.2–0.8)	0.01	0.8 (0.6–1.2)	0.34		

CAG, coronary angiography; CPR, cardio-pulmonary resuscitation; NA, not applicable; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; VF/VT, ventricular fibrillation/ventricular tachycardia.

Table 4. Neurological outcomes among survivors at hospital discharge.

CPC score at hospital discharge	Total (n=219)	Total population			No-STEMI population		
		STEMI (n=76)	No-STEMI (n=143)	p-value	Emergency CAG (n=54)	No emergency CAG (n=89)	p-value
CPC 1	163 (74)	55 (72)	108 (76)	0.82	42 (78)	66 (74)	0.14
CPC 2	44 (20)	18 (24)	26 (18)		12 (22)	14 (16)	
CPC 3	8 (4)	1 (1)	7 (5)		0 (0)	7 (8)	
CPC 4	4 (2)	2 (3)	2 (1)		0 (0)	2 (2)	

Differences in proportions were evaluated by trend test. A significance level of $p < 0.05$ was chosen.

CAG, coronary angiography; CPC, Cerebral Performance Category; No-STEMI, other ECG patterns; STEMI, ST-elevation myocardial infarction in ECG.

than what Gjorup et al.¹⁷ reported in comatose patients with OHCA and STEMI where the survival rate at 6 months was only 26%. Furthermore, treating patients within a well-functioning emergency care system focusing on all links in the chain of survival may also have beneficial implications for outcome.³ Prehospital use of telemedicine in diagnosing STEMI have decreased time delays significantly from OHCA to CAG/PCI compared to No-STEMI patients where telemedicine was not used as frequent. Moreover, No-STEMI patients might experience a delay in the emergency department due to exclusion of differential diagnoses.

Coronary lesions found in the STEMI and No-STEMI group differed in regard of number of diseased vessels and severity of lesions. The STEMI group had an expected high prevalence of significant coronary artery stenosis of 93%, where PCI was attempted in 91%. Similar findings have previously been reported in OHCA patients with STEMI, who all underwent consecutive emergency CAG.^{6,8,20} Coronary pathology seems to differ according to initial

ECG-pattern as 1-vessel disease suitable for PCI attempt and secondary successful PCI was highly frequent in the STEMI group compared to the No-STEMI group.^{6,20} Therefore the outcome and potential benefits of emergency CAG and PCI are hardly comparable in patients presenting with and without STEMI pattern in ECG. The present analysis supports the current guidelines and the use of emergency CAG and PCI in OHCA patients with STEMI since a large proportion of patients have significant lesion well suited for PCI and the overall prognosis is acceptable and the prevalence of important differential diagnoses seem low.

No-STEMI

Overall survival rate was 58% in the No-STEMI group which is in accordance of most studies ranging from 28–64%, although previous studies included all survivors of OHCA disregarding initial rhythm, ECG patterns, and level of consciousness at admission.^{21,23,24}

Significant coronary lesions were found in 43 (52%) patients in the No-STEMI group selected for emergency CAG, in whom PCI was attempted in 24 (56%) patients. If PCI was attempted it was successful in only 15 patients (63%) compared to 88% in STEMI patients. No-STEMI patients may have more irregular lesions without an acute thrombus and thus be more difficult to achieve a successful result with less stenosis and better TIMI flow. In a Parisian study, 435 consecutive survivors after OHCA had emergency CAG, and a similar rate of lesions suitable for PCI and similar rates of successful PCI were found. In patients with non-significant ST-segment elevation they reported significant lesions in 58% and successful PCI in 44%, but the majority (74%) of patients in the Parisian study had lesions unsuitable for PCI or had failed PCI attempts.⁶ Consequently only one in five patients with emergency CAG and non-significant ST-segment elevation were revascularized in the acute phase.

Our results suggesting no overall survival benefit of emergency CAG is somewhat contradictory to previous reports of series of OHCA patients which have suggested an association of an early invasive strategy with emergency PCI and a favourable outcome.^{6,19} Also a long-term survival benefit has been reported in a large OHCA registry in patients selected for PCI and/or hypothermia treatment during hospitalization and remained alive at hospital discharge.²⁵ Furthermore we found that the absolute relative risks between patients undergoing emergency CAG or no emergency CAG were virtually unaffected when censoring patients with cardiovascular deaths. This emphasize that the results must be interpreted with caution due to selection bias.

Recently the PROCAT study found a considerably more favourable outcome with successful PCI; however, 12% of procedures were reported as failures, 50% of which were potentially hazardous complications.⁶ These patients were included in the non-PCI group, which will likely lead to an overestimation of the effect of PCI if analysed in an intention-to-treat analysis. The present study found a similar effect of emergency PCI as reported in the PROCAT study, but the association of improved survival and an emergency invasive strategy was weaker and non-significant in an intention-to-treat analysis, even in patients selected for emergency CAG by a high clinical suspicion of coronary lesions.

In the No-STEMI group, emergency CAG was performed in patients at the discretion of the attending cardiologist. However, variables differed significant in prevalence of ventricular fibrillation as initial rhythm and applied therapeutic hypothermia being more frequent in those who underwent emergency CAG. Furthermore chronic obstructive lung disease was more frequent in the group where emergency CAG was not performed. In a previous study only the presence of STEMI or new left bundle branch block was associated with the use of emergency

CAG.²⁰ In comatose patients the cerebral prognosis is uncertain and since ventricular fibrillation and therapeutic hypothermia were more prevalent in the emergency CAG groups and has been associated with improved cerebral outcome a confounding effect of emergency CAG cannot be ruled out. The present study included consecutive patients and found no association with witnessed arrest, bystander CPR or time to ROSC and the probability for emergency CAG being performed in the No-STEMI group, whereas a previous report have excluded comatose patients from emergency CAG when significant brain damage was suspected.¹⁸

In the present study on consecutive patients, we found good cerebral outcome in 94 % among survivors at hospital discharge, which is comparable with previous studies.^{1-3,26} A limitation of the present study is that data on long term neurological outcome, i.e. >6 month post arrest, was not available.

Identifying patients who will benefit from emergency CAG and PCI in the acute setting at admission after OHCA is challenging as electrocardiography and biochemical markers are not sufficiently sensitive to detect acute myocardial ischaemia in all patients.^{8,27} Although significant coronary artery disease is frequently found in routinely performed CAG, their clinical importance is unclear and is only evident to be part of an acute coronary syndrome in minority of patients, when STEMI patients are excluded.²⁴

Current guidelines emphasize early revascularization when cause of OHCA is suspected to be underlying coronary artery disease, but the evidence supporting emergency CAG in all OHCA patients is weak and it is important that complications associated with emergency CAG and PCI are balanced against the potential benefits that are likely to be marginal in many cases. Thus it remains unclear whether an early invasive strategy is beneficial in the comatose survivors of OHCA.²⁸

There are no data from randomized trials in comatose survivors of OHCA. In an acute coronary syndrome/non-STEMI trial comparing an immediate vs. delayed intervention strategy, a 1–3% all-cause mortality was found. However a meta-analysis concluded that early catheterization followed by coronary intervention on the first day of hospitalization was safe, but immediate CAG/PCI was not associated with reduced infarct size.^{29,30} A similar 30-day all-cause mortality was found in the TIMACS study comparing early vs. delayed (≥ 36 hours) intervention in ACS patients/non-STEMI in general, but high-risk patients may still benefit from the early intervention.³¹ The relative low mortality rate in these studies concerning acute coronary syndrome must be weighed against an approximately 35% mortality rate in comatose survivors of OHCA where an estimation might be that approximately 70% of deaths are due to severe, irreversible anoxic brain injury.³² Cerebral protection with therapeutic hypothermia has a higher grade of evidence than emergency CAG and may therefore be

given a higher priority; however, in our experience initial cooling induction need not be delayed by emergency CAG/PCI. Moreover risk of bleeding complications after emergency CAG/PCI may be augmented by hypothermia and contrast infusion might potential cause renal damage if the circulation is compromised due to a sepsis-like-syndrome, which is common in the post-resuscitative phase.³³

A randomized study could be considered to overcome these factors, but as the effects of emergency revascularization in the No-STEMI population is likely to be relatively small in comparison to the hazards of brain injury related deaths in these patients, a randomized study will likely require a very large sample size.

Clinical implications

Studies reporting on prognosis in comatose OHCA patients should stratify patients in STEMI and No-STEMI patient as the prognosis, extent of coronary artery, and potential benefit of emergency PCI is likely to be different in these groups. The data presented here do not provide evidence that an emergency CAG and PCI which should be considered in all patients suspected of having coronary artery disease by current guidelines is of clinical benefit in comatose No-STEMI OHCA survivors. The net clinical benefit of emergency CAG in comatose OHCA survivors without STEMI can only be assessed in prospective randomized studies.

Conclusions

Comatose survivors of OHCA presenting with STEMI have a high prevalence of coronary artery disease and culprit lesions suitable for emergency PCI. In patients without STEMI pattern in ECG, significant coronary stenosis are less frequent with fewer lesions suitable for PCI and therefore clinical benefits of emergency CAG/PCI in No-STEMI patients could not be identified. These findings support an emergency invasive strategy in STEMI patients, whereas the optimal strategy in OHCA patients presenting without specific STEMI pattern ECG is less clear.

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Conflict of interest

None of the authors have potential financial conflicts of interest to disclose.

References

1. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; 346: 557–563.
2. Hypothermia After Cardiac Arrest Study G. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002; 346: 549–556.
3. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2007; 73: 29–39.
4. Bro-Jeppesen J, Kjaergaard J, Horsted TI, et al. The impact of therapeutic hypothermia on neurological function and quality of life after cardiac arrest. *Resuscitation* 2009; 80: 171–176.
5. Pell JP, Sirel JM, Marsden AK, et al. Presentation, management, and outcome of out of hospital cardiopulmonary arrest: comparison by underlying aetiology. *Heart* 2003; 89: 839–842.
6. Dumas F, Cariou A, Manzo-Silberman S, et al. 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.
7. Deakin CD, Nolan JP, Soar J, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 4. Adult advanced life support. *Resuscitation* 2010; 81: 1305–1352.
8. Spaulding CM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med* 1997; 336: 1629–1633.
9. Hamm CW, Bassand JP, Agewall S, et al. 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.
10. Mitsuma W, Ito M, Kodama M, et al. Clinical and cardiac features of patients with subarachnoid haemorrhage presenting with out-of-hospital cardiac arrest. *Resuscitation* 2011; 82: 1294–1297.
11. Horsted TI, Rasmussen LS, Meyhoff CS, et al. Long-term prognosis after out-of-hospital cardiac arrest. *Resuscitation* 2007; 72: 214–218.
12. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. *Circulation* 2007; 116: 2634–2653.
13. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. *N Engl J Med* 1999; 341: 625–634.
14. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare 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.

15. Nolan JP, Morley PT, Hoek TL, et al. Therapeutic hypothermia after cardiac arrest. An advisory statement by the Advancement Life support Task Force of the International Liaison committee on Resuscitation. *Resuscitation* 2003; 57: 231–235.
16. Cummins RO, Chamberlain DA, Abramson NS, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style. Task Force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. *Ann Emerg Med* 1991; 20: 861–874.
17. Gorjup V, Radsel P, Kocjancic ST, et al. Acute ST-elevation myocardial infarction after successful cardiopulmonary resuscitation. *Resuscitation* 2007; 72: 379–385.
18. Radsel P, Knafelj R, Kocjancic S, et al. Angiographic characteristics of coronary disease and postresuscitation electrocardiograms in patients with aborted cardiac arrest outside a hospital. *Am J Cardiol* 2011; 108: 634–638.
19. Garot P, Lefevre T, Eltchaninoff H, et al. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. *Circulation* 2007; 115: 1354–1362.
20. Reynolds JC, Callaway CW, El Khoudary SR, et al. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. *J Intensive Care Med* 2009; 24: 179–186.
21. Zimmermann S, Flachskampf FA, Alff A, et al. Out-of-hospital cardiac arrest and percutaneous coronary intervention for ST-elevation myocardial infarction: long-term survival and neurological outcome. *Int J Cardiol* 2011 (Epub ahead of print).
22. Stub D, Hengel C, Chan W, et al. Usefulness of cooling and coronary catheterization to improve survival in out-of-hospital cardiac arrest. *Am J Cardiol* 2011; 107: 522–527.
23. Pleskot M, Hazukova R, Stritecka H, et al. Long-term prognosis after out-of-hospital cardiac arrest with/without ST elevation myocardial infarction. *Resuscitation* 2009; 80: 795–804.
24. Anyfantakis ZA, Baron G, Aubry P, et al. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. *Am Heart J* 2009; 157: 312–318.
25. Dumas F, White L, Stubbs BA, et al. Long-term prognosis following resuscitation from out of hospital cardiac arrest: role of percutaneous coronary intervention and therapeutic hypothermia. *J Am Coll Cardiol* 2012; 60: 21–27.
26. Oddo M, Schaller MD, Feihl F, et al. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. *Resuscitation* 2006; 34: 1865–1873.
27. Dumas F, Manzo-Silberman S, Fichet J, et al. Can early cardiac troponin I measurement help to predict recent coronary occlusion in out-of-hospital cardiac arrest survivors? *Crit Care Med* 2012; 40: 1777–1784.
28. Bangalore S and Hochman JS. A routine invasive strategy for out-of-hospital cardiac arrest survivors: are we there yet? *Circ Cardiovasc Interv* 2010; 3: 197–199.
29. Montalescot G, Cayla G, Collet JP, et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. *JAMA* 2009; 302: 947–954.
30. Katritsis DG, Siontis GC, Kastrati A, et al. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. *Eur Heart J* 2011; 32: 32–40.
31. Mehta SR, Granger CB, Boden WE, et al. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med* 2009; 360: 2165–2175.
32. Laver S, Farrow C, Turner D, et al. Mode of death after admission to an intensive care unit following cardiac arrest. *Intensive Care Med* 2004; 30: 2126–2168.
33. Nielsen N, Hovdenes J, Nilsson F, et al. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. *Acta Anaesthesiol Scand* 2009; 53: 926–934.