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Long-term outcome of patients after out-of-hospital cardiac arrest in relation to treatment: a single-centre study

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Abstract

Introduction: Outcome after out-of-hospital cardiac arrest (OHCA) remains poor. With the introduction of automated external defibrillators, percutaneous coronary intervention (PCI) and mild therapeutic hypothermia (MTH) the prognosis of patients after OHCA appears to be improving. The aim of this study was to evaluate short and long-term outcome among a non-selected population of patients who experienced OHCA and were admitted to a hospital working within a ST elevation myocardial infarction network.

Methods: All patients who achieved return of spontaneous circulation (ROSC) (n=456) admitted to one hospital after OHCA were included. Initial rhythm, reperfusion therapy with PCI, implementation of MTH and additional medical management were recorded. The primary outcome measure was survival (hospital and long term). Neurological status was measured as cerebral performance category. The inclusion period was January 2003 to August 2010. Follow-up was complete until April 2014.

Results: The mean patient age was 63±14 years and 327 (72%) were men. The initial rhythm was ventricular fibrillation, pulseless electrical activity, asystole and pulseless ventricular tachycardia in 322 (71%), 58 (13%), 55 (12%) and 21 (5%) of the 456 patients, respectively. Treatment included PCI in 191 (42%) and MTH in 188 (41%). Overall in-hospital and long-term (5-year) survival was 53% (n=240) and 44% (n=202), respectively. In the 170 patients treated with primary PCI, in-hospital survival was 112/170 (66%). After hospital discharge these patients had a 5-year survival rate of 99% and cerebral performance category was good in 92%.

Conclusions: In this integrated ST elevation myocardial infarction network survival and neurological outcome of selected patients with ROSC after OHCA and treated with PCI was good. There is insufficient evidence about the outcome of this approach, which has a significant impact on utilisation of resources. Good quality randomised controlled trials are needed. In selected patients successfully resuscitated after OHCA of presumed cardiac aetiology, we believe that a more liberal application of primary PCI may be considered in experienced acute cardiac referral centres.

Keywords

Out-of-hospital cardiac arrest, ST-elevation myocardial infarction, percutaneous coronary intervention, mild therapeutic hypothermia, management

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Introduction

Despite several advances in the field of resuscitation, the management of patients after out-of-hospital cardiac arrest (OHCA) can still be improved.[1–5] Factors influencing outcome after OHCA are the initial rhythm, whether the arrest was witnessed or not, early good quality cardiopulmonary resuscitation (CPR), early defibrillation and organisation of care. Efforts have been undertaken to improve outcome after OHCA. Organisational measures, such as teaching of CPR in courses and other initiatives to promote early bystander CPR,[6–8] optimisation of emergency medical systems responses[9] and systems to ensure very rapid access to automated external defibrillators,[10] have been shown to improve outcome.[11] Survival is most likely if the initial rhythm was ventricular fibrillation (VF),[12] which is most frequently caused by myocardial infarction due to coronary artery disease.[12,13] In our region an ST-elevation myocardial infarction (STEMI) network was created in conjunction with ambulance services, the emergency, cardiology and intensive care departments. It involves a defined treatment plan for patients with return of spontaneous circulation (ROSC), the goal of which is to allocate definitive care as expediently as possible guided on the clinical signs and electrocardiographic (ECG) or echocardiographic signs of acute myocardial ischaemia. In guidelines and recommendations the use of reperfusion therapy, either primary percutaneous coronary intervention (PCI) or thrombolysis, is recommended regardless of Glasgow coma score.[14–17] Studies on the effect of primary PCI as treatment of a ST-segment elevation myocardial infarction, in the setting of OHCA, are increasingly common.[18–23] Despite this, data on the effect of primary PCI after OHCA on the (long-term) outcome among all patients admitted to hospital are sparse. We aimed to evaluate short-term and long-term outcome among consecutive patients treated after OHCA within a regional STEMI network.

Methods

Setting

The University Medical Center Groningen is a tertiary referral hospital, which serves the north eastern part of the Netherlands. In this region it is the only hospital that performs PCI. With referral hospitals, this centre provides 24/7 emergency care in a region with 750,000 inhabitants.[24] In the case of an emergency, the closest ambulance is sent to the scene and when resuscitation is necessary a second ambulance is always sent as back-up. Patients are then transported to the centre, especially when there is suspicion of coronary occlusion (e.g. VF or STEMI). There resuscitation is continued or post-resuscitation care is given following advanced cardiovascular life support guidelines.[25] Ambulance services in the area have the discretion to discontinue CPR in the case of a non-shockable rhythm if it persists after 20 minutes in adult patients. As a consequence, these patients were not presented to the centre.

On arrival at the hospital, stable patients with STEMI were transferred directly to the catheterisation laboratory. Unresponsive patients were admitted to the emergency department and following stabilisation transferred directly to the catheterisation laboratory in the case of STEMI. In patients without STEMI the decision to go to the catheterisation laboratory was made by the attending cardiologist and based on haemodynamic stability and echocardiographic signs of ischaemia. At the catheterisation laboratory PCI was performed if a culprit was identified according to the current guidelines.[26,27]

Patients underwent delayed PCI based on the discretion of the attending physician. Reasons not to perform immediate coronary angiography (CAG) were haemodynamic instability and absence of ST-segment elevation on the electrocardiogram. If during the course after admission patients were more stable and when it was anticipated that myocardial ischaemia due to coronary artery stenosis was present delayed CAG and PCI was performed.

In all patients with a Glasgow coma scale (GCS) score of $\leqslant 8$ or patients with insufficient oxygenation and ventilation endotracheal intubation was performed. Mechanical ventilation was no contraindication for early coronary intervention, neither was time of day. If the GCS did not immediately improve to a score of >8 or if the patient was sedated and could not be scored and was already on mechanical ventilation, mild therapeutic hypothermia (MTH) was initiated, irrespective of early coronary intervention. Haemodynamic instability would preclude MTH. MTH aimed to cool patients to 32–34ºC for approximately 24 hours at the intensive care unit (ICU). Sedation was given according the local protocol. After 24 hours the patient's body temperature was allowed to return to normal spontaneously. At a temperature of 36ºC sedatives were stopped. Thereafter, the attending intensivist and the neurologist scored the patient neurologically. Somatosensory evoked potentials (SSEP) and electroencephalogram (EEG) were performed in comatose patients. After ICU treatment the patients were transferred to the cardiology ward. Outpatient follow-up was carried out at the cardiology, neurology or rehabilitation departments. Patients with a higher GCS (>8) and without respiratory problems were transferred either to the ICU or the coronary care unit.

Patients

We retrospectively studied all consecutive patients over 18 years of age admitted to our hospital after OHCA between January 2003 and August 2010. All patients were included in our analysis unless it was impossible to confirm OHCA or to define the initial rhythm (Figure 1). We collected baseline demographic and clinical characteristics that were anonymously entered in a dedicated database. Gathering

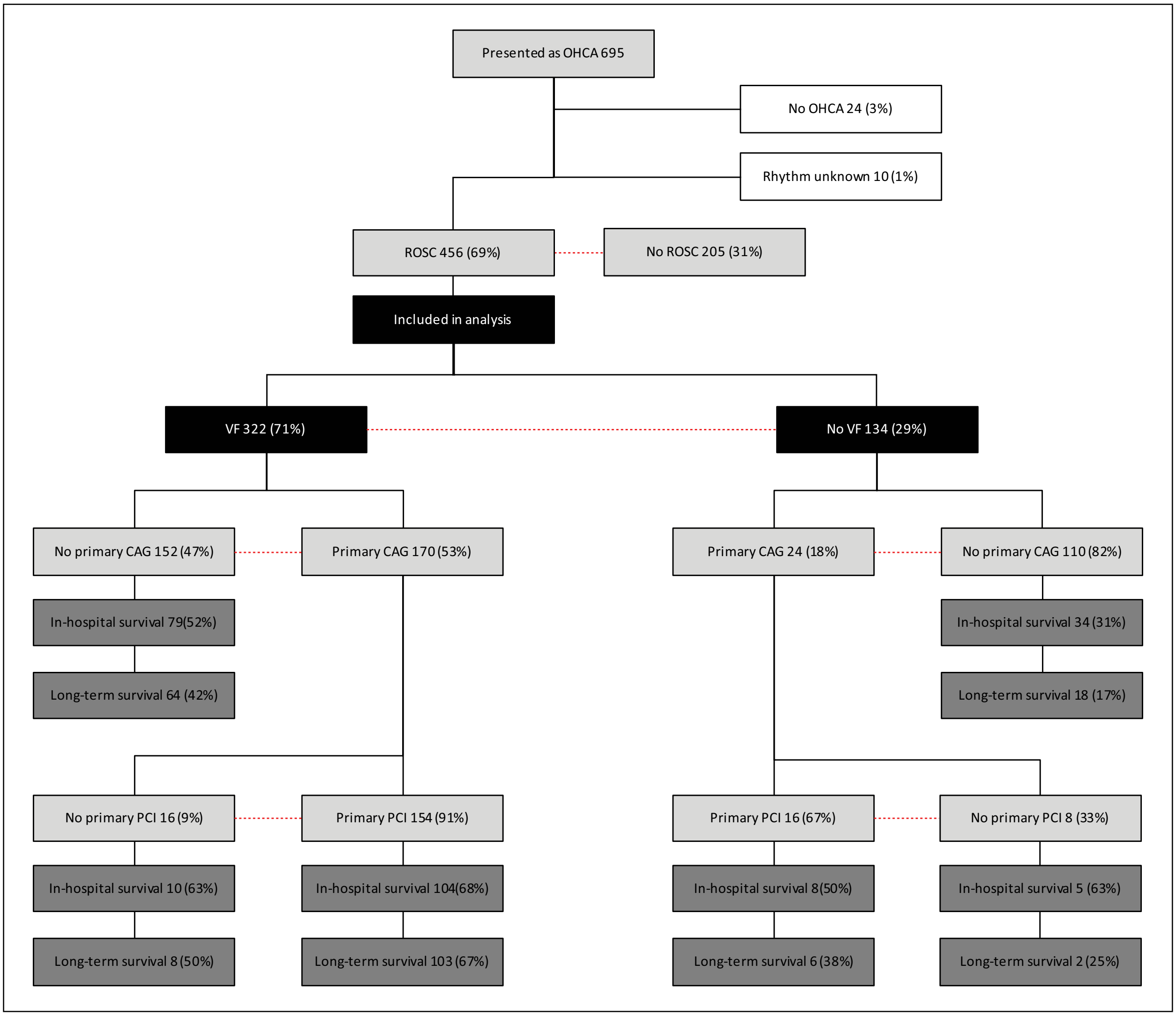


Figure 1. Flow chart of all patients presenting at the emergency room after out-of-hospital cardiac arrest. After each step the total percentage is set as 100%. VF: Ventricular fibrillation; PCI: percutaneous coronary intervention; ROSC: return of spontaneous circulation; OHCA: out-of-hospital cardiac arrest; CAG: coronary angiography.

information from the ambulance registry and the hospital information system comprising all medical records completed data collection.

Data from additional investigations such as ECG, echocardiography, SSEP, EEG and laboratory values were recorded and subsequently added to the cohort. Left ventricular function measured by echocardiography was scored as poor, moderate (<45%), reasonable and normal.

Outcome measures

Primary outcome measures were in-hospital and long-term survival at one and five years. The in-hospital cause of death was noted (based on the judgement of at least two physicians).

The neurological status after discharge was the secondary outcome measure. Neurological status was derived from information of the outpatient control visits of cardiologists, neurologists or rehabilitation specialists. Outcome was scored by the cerebral performance category (CPC) score comprising five categories: (a) conscious and alert with normal function or only slight disability; (b) conscious and alert with moderate disability; (c) conscious with severe disability; (d) comatose or persistent vegetative state; (e) brain dead or death from other causes.

Survival status and neurological outcome were determined until April 2014. This study complies with the Declaration of Helsinki; the local medical ethics committee approved the study (METC 2011.374) and waived the requirement for consent from patients or relatives to use their data.

Statistical analysis

Continuous data are presented as either means±standard deviation (SD) for normally distributed variables or medians and interquartile ranges (IQR) for skewed data or as group percentages for categorical variables. Statistical analysis was performed using the χ^2 test for categorical variables and the Mann–Whitney or independent sample *t*-test for skewed continuous and normal distributed variables, respectively. We determined outcome in subgroups, given initial rhythm (VF vs no VF), implemented treatment (PCI vs no PCI, MTH vs no MTH) and systolic left ventricular ejection fraction (LVEF) (LVEF <45% vs ⩾45%). A Kaplan–Meier survival analysis was used for our primary endpoint. We used hazard ratios (HRs) and associated 95% confidence intervals (CIs) by Cox regression analysis to compare the relative odds of survival after OHCA after hospital discharge imputing age and gender, and known factors associated with outcome: initial rhythm, in-hospital treatment (PCI and MTH) and left ventricular function. A univariate two-sided *P* value of <0.10 was required for inclusion in our multivariate model, which was constructed using a stepwise backward selection. Statistical significance was defined as a two-sided *P* value of <0.05. Propensity scoring was used to correct for age, sex, rhythm (VF vs no VF), performance of basic life support (BLS) and GCS score at admission. We conducted a successful match of the variables age, sex, rhythm (VF vs no VF) and performance of BLS; GCS score at admission could not be matched in our population. All statistical analyses were performed using Stata version 12.0 (StataCorp).

Results

Baseline demographic and clinical characteristics

During the study period 695 patients were admitted after suspected OHCA (Figure 1). Of these patients 34 (5%) were excluded because of a final diagnosis other than OHCA (n=24) or if their initial rhythm was undeterminable (n=10). Successful ROSC occurred in 322/425 (76%) of VF patients compared to 134/236 (57%) in the group without VF (*P*<0.001), thus excluding 205 (29%) patients who failed to achieve ROSC.

The 456 patients with ROSC were included in the analyses. The mean±SD age of these patients was 63±14 years and 72% were men (Table 1).

A total of 322 (71%) patients presented with VF as the initial rhythm. Of the non-VF patients (n=134), pulseless electrical activity was the initial rhythm in 58 patients (43%); 55 patients (41%) presented with asystole, and 21 patients (16%) with pulseless ventricular tachycardia.

Coronary angiography, reperfusion therapy and MTH

Coronary angiography after admission was performed in 257/456 (56%) patients, delayed in 63/456 (14%) patients (Table 1). The median time to CAG was 111 (IQR 62–180) minutes. Most patients undergoing immediate CAG were receiving mechanical ventilation: 62% versus 71% in VF versus non-VF, respectively. Primary CAG was performed in 170/322 (53%) patients with VF and in 24/134 (18%) patients without VF (*P*⩽0.001). Primary PCI was performed in 170/194 (88%) of these cases and three of 170 patients (2%) underwent emergency coronary bypass surgery after immediate CAG. In 21/257 (8%) patients delayed PCI was performed during hospitalisation. A total of 191 patients were eventually diagnosed with a significant coronary occlusion, of which 137/191 (72%) showed an ST-segment elevation on the initial ECG. The characteristics of patients who underwent emergent versus delayed PCI are summarised in Table 1.

MTH was instituted in 188/456 (41%) patients with ROSC. Of these, 80/188 (43%) patients also underwent PCI. Survival for these patients who underwent PCI was 42/80 (53%) versus 46/108 (43%). However, this difference did not reach statistical significance (*P*=0.12).

In-hospital survival after ROSC

Hospital survival was 240/456 (53%) in all patients. A total of 193/322 (60%) in the VF group and 47/134 (35%) in the non-VF group survived to hospital discharge (*P*<0.001). Patients undergoing primary PCI had a good hospital survival rate, with 112/170 (66%) of patients who underwent primary PCI surviving compared to 128/286 (45%) in the group that did not have primary PCI. A successfully matched population using propensity scoring was assessed for age, sex, rhythm (VF vs no VF) and performance of BLS. In this matched population of 286 patients, 62/143 (43%) survived in the group that did not have primary PCI, versus 99/143 (69%) in the primary PCI population (*P*⩽0.001). When examining subgroups (VF±primary PCI) and (no VF±primary PCI) we did not find statistically significant differences in outcome in these groups. In addition, there was no statistical difference in outcome between patients who had primary versus secondary PCI 18/21 (86%) in the group that received secondary PCI (*P*=0.251).

Unadjusted, MTH was associated with a worse outcome: survival was 88 (47%) with MTH versus 150 (56%) without MTH, *P*<0.03 overall. This was true for patients treated with MTH after VF in whom survival was 81/158 (51%) in patients treated with MTH versus 111/164 (68%) in patients not treated with MTH (*P*=0.002). However, when correcting for confounding factors (sex, age, performance of BLS and GCS score) through propensity analysis there was no significant difference in survival. Furthermore, MTH was not an independent predictor of mortality in our multivariate Cox regression model. In patients treated after non-VF, survival also did not differ significantly between groups (*P*=0.11). Outcome was also associated with systolic LVEF. Of the patients who regained ROSC, 225

Table 1. Baseline, angiographic and procedural data of three groups: VF versus no VF, primary CAG versus no CAG and in the primary CAG group: primary PCI versus no PCI.

	Total N=456	VF N=322	No VF N=134	*P* value	Primary CAG N=194	No primary CAG N=262	*P* value	Primary PCI[d] N=170	Secondary PCI[d] N=21	*P* value
Clinical characteristics										
Age[a]	63±14	63±13	66±17	0.042	61±12	65±15	<0.001	60±12	60±13	0.957
Male sex (%)	327 (72%)	241 (75%)	86 (64%)	0.023	148 (76%)	179 (68%)	0.062	131 (77%)	18 (86%)	0.366
History of CVD (%)	156 (34%)	118 (37%)	38 (28%)	0.084	48 (25%)	108 (41%)	<0.001	37 (22%)	11 (52%)	0.002
Location (%)				0.001			<0.001			0.033
• Home	218 (48%)	135 (42%)	83 (62%)		81 (42%)	137 (52%)		69 (41%)	6 (29%)	
• Public place	110 (24%)	92 (29%)	18 (13%)		46 (24%)	64 (24%)		41 (24%)	10 (48%)	
• Other	60 (13%)	43 (13%)	17 (13%)		28 (14%)	32 (12%)		23 (14%)	5 (24%)	
• Ambulance	34 (8%)	27 (8%)	7 (5%)		27 (14%)	7 (3%)		27 (16%)	0 (0%)	
• Unknown	34 (8%)	25 (8%)	9 (7%)		12 (6%)	22 (8%)		10 (6%)	0 (0%)	
Witnessed (%)	369 (81%)	269 (87%)	100 (76%)	0.026	166 (86%)	203 (78%)	0.013	143 (84%)	17 (81%)	0.385
BLS performed (%)	280 (61%)	211 (70%)	69 (54%)	0.002	136 (70%)	144 (55%)	0.001	122 (72%)	18 (86%)	0.309
Initial rhythm (%)				<0.001			<0.001			0.273
• VF	322 (71%)	322 (100%)	0 (0%)		170 (88%)	152 (58%)		154 (91%)	17 (81%)	
• PEA	58 (13%)	0 (0%)	58 (43%)		8 (4%)	50 (19%)		6 (4%)	2 (10%)	
• Asystole	55 (12%)	0 (0%)	55 (41%)		7 (4%)	48 (18%)		4 (2%)	0 (0%)	
Pulseless VT	21 (5%)	0 (0%)	21 (16%)		9 (5%)	12 (5%)		6 (4%)	2 (10%)	
ROSC before arrival ED (%)	389 (85%)	285 (89%)	104 (78%)	0.001	175 (90%)	214 (82%)	0.015	153 (90%)	21 (100%)	0.316
Unknown where (%)	36 (8%)	24 (8%)	12 (9%)		13 (7%)	23 (9%)		12 (7%)	0 (0%)	
ROSC (%)	456 (100%)	322 (100%)	134 (100%)		194 (100%)	262 (100%)		170 (100%)	21 (100%)	
Glasgow coma scale at admission[b]	5 (12)	5 (12)	3 (12)	<0.001	6 (3–15)	3 (3–7)	<0.001	8 (3–15)	5 (3–8)	0.116
CPC score (%) at discharge				<0.001			<0.001			0.344
• 1	212 (47%)	174 (54%)	38 (28%)		118 (61%)	94 (36%)		105 (62%)	16 (76%)	
• 2	30 (7%)	23 (7%)	7 (5%)		11 (6%)	19 (7%)		9 (5%)	2 (10%)	
• 3	6 (1%)	3 (1%)	3 (2%)		0 (0%)	6 (2%)		0 (0%)	0 (0%)	
• 4	1 (0%)	1 (0%)	0 (0%)		1 (1%)	0 (0%)		1 (1%)	0 (0%)	
• 5	206 (45%)	120 (37%)	86 (64%)		64 (33%)	142 (54%)		55 (32%)	3 (14%)	
STEMI (%)	159 (35%)	139 (43%)	20 (15%)	<0.001	141 (73%)	18 (7%)	<0.001	135 (79%)	2 (10%)	<0.001
MTH (%)	188 (41%)	158 (49%)	30 (22%)	<0.001	81 (42%)	107 (41%)	0.845	69 (41%)	11 (52%)	0.301
Mechanical ventilation (%)	333 (73%)	233 (72%)	100 (75%)	0.645	123 (63%)	210 (80%)	<0.001	104 (61%)	19 (91%)	0.008
Length of stay (days)[b]	6.6 (14.3)	7 (14)	8 (14)	<0.001	6.1 (2.7–14.9)	4.3 (1.7–20.2)	0.479	5.6 (2.5–13.7)	16.9 (8.8–36.8)	0.001
Hospital survival (%)	240 (53%)	193 (60%)	47 (35%)	<0.001	127 (66%)	113 (43%)	<0.001	112 (66%)	18 (86%)	0.066
Long-term survival (5 years) (%)	202 (44%)	175 (54%)	27 (20%)	<0.001	118 (61%)	78 (30%)	<0.001	108 (64%)	16 (76%)	0.251

(Continued)

Table 1. (Continued)

	Total N=456	VF N=322	No VF N=134	*P* value	Primary CAG N=194	No primary CAG N=262	*P* value	Primary PCI[d] N=170	Secondary PCI[d] N=21	*P* value
Laboratory data										
Glucose[a]	13.8±14.3	13.6±5.3	14.2±7.9	0.348	13.5±5.3	14.0±6.7	0.411	13.7±5.5	12.9±3.5	0.558
pH[a]	7.20±0.19	7.24±0.16	7.24±0.16	<0.001	7.25±0.16	7.17±0.20	<0.001	7.25±0.17	7.23±0.14	0.537
Lactate[a]	6.7±4.5	6.2±4.1	8.2±5.2	0.001	5.7±3.9	7.9±4.9	<0.001	5.5±4.0	5.7±4.0	0.888
Base excess[a]	−9.4±7.6	−8.6±6.9	−11.8±8.9	<0.001	−8.4±7.2	−10.6±8.0	0.014	−8.3±7.3	−6.8±4.8	0.466
Creatine kinase max[a]	4856 (8309)	5943 (9354)	2240 (3900)	0.001	7768 (9389)	2715 (6664)	<0.001	8289 (9626)	4006 (9925)	0.001
Creatine kinase-MB[a]	463 (679)	544(752)	266 (392)	<0.001	798 (868)	216 (320)	<0.001	871 (69)	211 (305)	<0.001
Troponin I[a]	164 (442)	218 (503)	68 (284)	0.046	352 (559)	104 (381)	<0.003	458 (608)	77 (184)	0.001
Troponin T[a]	3.93 (8.4)	4.78 (9.46)	1.47 (3.07)	0.003	6.8 (10.8)	0.87 (1.5)	<0.001	7.4 (11.3)	0.8 (1.03)	<0.001
CAG (%)	257 (56%)	227 (71%)	30 (22%)	<0.001	194 (100%)	63 (24%)	<0.001	170 (100%)	21 (100%)	
• Primary	194 (43%)	170 (53%)	24 (18%)	<0.001	194 (100%)	0 (0%)		170 (100%)	0 (0%)	
• Secondary	63 (14%)	57 (18%)	6 (5%)	<0.001	0 (0%)	63 (100%)		0 (0%)	21 (100%)	
Door to balloon time (min)[b]	111 (62–180)	97 (57–160)	135 (80–208)	<0.001	55 (33–89)	–		54 (34–86)	–	
Culprit lesion (%)[c]				0.889			<0.001			0.045
• RCA	59 (23%)	51 (23%)	8 (25%)		51 (26%)	8 (13%)		49 (29%)	3 (14%)	
• LAD	99 (39%)	89 (40%)	11 (35%)		87 (45%)	12 (19%)		85 (50%)	9 (43%)	
• Cx	39 (15%)	34 (15%)	5 (16%)		28 (14%)	11 (18%)		25 (15%)	9 (43%)	
• LM	13 (5%)	10 (4%)	3 (10%)		11 (6%)	2 (3%)		9 (5%)	0 (0%)	
• Graft	4 (2%)	4 (2%)	0 (0%)		1 (1%)	3 (5%)		0 (0%)	0 (0%)	
• Unknown (multiple)	24 (9%)	21 (9%)	1 (3%)		7 (4%)	15 (24%)		1 (1%)	0 (0%)	
• No culprit	19 (7%)	16 (7%)	3 (10%)		8 (4%)	11 (18%)		0 (0%)	0 (0%)	
PCI (%)	191 (42%)	171 (53%)	20 (15%)	<0.001	170 (88%)	21 (8%)	<0.001	170 (100%)	21 (100%)	
• Primary	170 (37%)	154 (48%)	16 (12%)	<0.001	170 (87%)	0 (0%)		170 (100%)	0 (0%)	
• Secondary	21 (5%)	17 (5%)	4 (3%)	0.092	0 (0%)	21 (8%)	<0.001	0 (0%)	21 (100%)	
CABG (%)	6 (1%)	6 (2%)	0 (0%)	0.187	3 (2%)	3 (1%)	0.710	3 (2%)	0 (0%)	0.539

Clinical characteristics of patients after ROSC.

[a]Mean±SD.

[b]Median (interquartile range).

[c]If CAG performed; total number 257.

[d]If PCI performed; total number 191.

VF: ventricular fibrillation; CVD: cardiovascular disease; BLS: basic life support; PEA: pulseless electrical activity; VT: ventricular tachycardia; ROSC: return of spontaneous circulation; STEMI: ST-segment elevation myocardial infarction; MTH: mild therapeutic hypothermia; LVEF: left ventricular ejection fraction; WMAs: wall motion abnormalities; MB: myocardial band; CAG: coronary angiography; RCA: right coronary artery; LAD: left anterior descending; Cx: circumflex; LM: left main; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

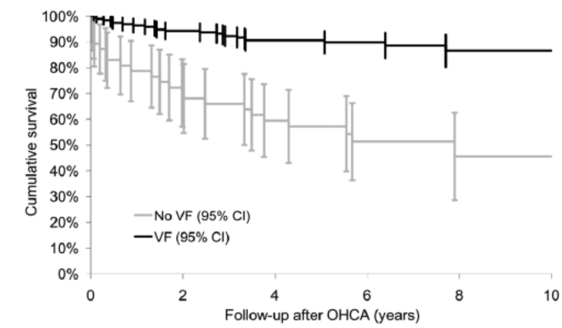
underwent transthoracic echocardiography. Neurological outcome, as reflected by the CPC score, differed markedly with a CPC score of 1–2 in the VF and no VF groups 46% versus 19%, respectively (P<0.001).

Factors associated with in-hospital mortality after ROSC were refractory cardiogenic shock (15%) and multiple organ failure (6%). In 144 patients (67%) the team of specialists (senior intensivists and neurologists) concluded that neurological injury was so severe that it was incompatible with survival. Decisions about withdrawal of treatment were based on clinical examination and additional assessment of SSEP or EEG at day 3 after CPR according to Dutch guidelines.[28,29]

In the case of absent brainstem reflexes (i.e. absent pupillary light response and corneal reflexes) and absent motor scores, treatment was stopped. In all other cases, additional SSEP was performed and in the case of absent bilateral N20 potentials treatment was withdrawn. An EEG was only performed when seizures or myoclonus were present. Seizures were treated with antiepileptic drugs; in the case of myoclonus status epilepticus treatment was withdrawn. This information obtained by repetitive clinical evaluation, and sometimes additional EEG and SSEP recordings (EEG in 22 (15%) cases, SSEP in seven (5%) cases or SSEP and EEG combined in eight (6%) cases). In these patients active therapies (mechanical ventilation, endotracheal intubation, inotrope administration) were discontinued, while general end-of-life measures to maintain dignity were continued.

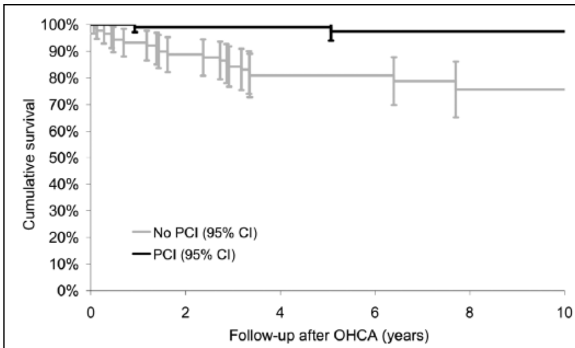
Survival after hospital discharge

The overall survival after hospital discharge was 93% and 84% at one and five years, respectively. Survival after hospital discharge was 96% at one-year and 91% at five-year follow-up for the 193 patients after VF. The long-term survival among the noc VF group of patients (n=47) was 79% at one year and 57% at five years after hospital discharge (Figure 2). The highest survival rate was observed in patients presenting with VF and treated with immediate PCI (one-year survival 99%, five-year survival 99%) (Figure 3).



Years	2	4	6	8	10
VF (n)	182	164	79	36	15
Non-VF (n)	33	27	15	8	2

Figure 2. Kaplan–Meier survival analysis after discharge of the out-of-hospital cardiac arrest (OHCA) survivors comparing ventricular fibrillation (VF) with no VF with associated 95% confidence interval (CI). Table below showing the number of patients in follow-up.



Years	2	4	6	8	10
PCI (n)	118	108	44	17	8
No PCI (n)	64	56	35	19	7

Figure 3. Kaplan–Meier survival analysis after discharge of patients after out-of-hospital cardiac arrest (OHCA) presenting with ventricular fibrillation (VF) comparing percutaneous coronary intervention (PCI) with no PCI with associated 95% confidence interval (CI). Table below showing the number of patients in follow-up.

Independent predictors of long-term survival

A multivariate Cox regression (including the factors age, sex, glucose and pH on admission, door to balloon time, witnessed arrest, location, performance of BLS, GCS, VF as initial rhythm, presence of STEMI, MTH, performance of primary PCI, induction of MTH, need for mechanical ventilation and length of hospital stay) was performed to predict long-term mortality. Age (one year step, HR 1.02, 95% CI 1.02–1.04, P<0.000), GCS (HR 0.89, 95% CI 0.85–0.93, P<0.001), myocardial infarct size (area under the curve of creatine kinase myocardial band, HR 1.24, 95% CI 1.08–1.42, P=0.002), pH on admission (HR 0.19, 95% CI 0.07–0.51, P=0.001), no initial rhythm of VF (HR 1.35, 95% CI 1.19–1.53, P<0.001), performance of emergency PCI (HR 0.56, 95% CI 0.35–0.77, P=0.006) and performance of BLS (HR 0.56, 95% CI 0.41–0.77, P<0.001) were independent predictors of long-term mortality after ROSC.

Discussion

In a large group of consecutive patients treated within a STEMI network, outcome after OHCA remained poor. However, in patients with an initial rhythm of VF, who showed ROSC and were treated by immediate PCI outcome was good. In-hospital survival reached 66% and, even more remarkably, survival after discharge was 99% after five years. Therefore, the outcome is comparable to figures reported for patients with STEMI without cardiac arrest treated with PCI.[30]

Patients with poor cardiac function and co-morbidities might not regain ROSC or survive to hospital discharge. For our patients we found that survival was higher in patients with higher LVEF, a better GCS, higher pH values and lower glucose and lactate levels, in accordance with observations by others.[31–33] Moreover, patients with an initial rhythm other than VF showed a lower rate of ROSC and decreased GCS scores at admission compared to patients with VF.

In spite of ROSC in both groups, primary CAG was performed in 53% of patients with VF and only in 18% of patients without VF ($P \leqslant 0.001$). STEMI on ECG, regional wall motion abnormalities (WMAs) were drivers for CAG. There was a lower incidence of STEMI in the no VF group, 43% (VF) versus 15% (no VF), $P \leqslant 0.001$. In addition, of the patients in whom an echocardiogram was recorded 60/162 (37%) with VF had regional WMAs. This is in contrast to patients with no VF, in whom only seven of 53 (13%) had regional WMAs.

Therefore, treatment within a STEMI network might especially benefit patients with VF as the first observed rhythm. Patients presenting with another initial rhythm might have an underlying mechanism other than myocardial ischaemia due to significant coronary occlusion. This is supported by the lower levels of cardiac markers such as troponin, creatine kinase and creatine kinase-MB in the no VF group. The lack of treatment options apart from defibrillation, MTH and supportive care may explain the poorer outcome of patients with another initial rhythm. Even after hospital discharge, survival is worse when compared to patients who presented with VF.

The same was apparently the case for patients who underwent PCI, as they had better in-hospital survival as shown in the propensity matched score. This improved survival continued after hospital discharge. It could be that patients who did not undergo PCI were not amenable to treatment, explaining their poorer survival.

In subgroup analysis, however, (VF±primary PCI, no VF±primary PCI) we could not demonstrate a survival benefit. This could be due to the low number of patients in the VF group who did not undergo primary PCI after primary catherisation, as angioplasty was performed in 91% of these patients. In this latter group in-hospital survival was even somewhat lower in the group that underwent primary PCI while in contrast long-term survival was more favourable. However, neither of these differences was statistically significant most likely due to the small number of patients in these groups.

Neurological function, our secondary outcome measure, was also more favourable in these PCI treated patients. Thus, the chance of surviving after an initial VF in good quality is realistic. Several reasons may explain the favourable neurological outcome. Recent evidence in comatose survivors of cardiac arrest showed that combining primary PCI and MTH might improve the probability of survival with good neurological outcome.[34–39] It might be that treatment with PCI preserves myocardial function and therefore provides sufficient cerebral perfusion. It might also prevent haemodynamic disturbances due to recurrent rhythm disturbances, especially during MTH. False negative ECG can occur during total coronary occlusion. The prevalence of coronary abnormalities is high in this group of patients. A recent prospective registry questioned the benefit of emergency CAG in comatose patients presenting without a STEMI pattern on ECG.[40] In our study only 79% of the patients who underwent primary PCI met traditional STEMI criteria on initial ECG, but all had coronary occlusion as judged by Thrombolysis In Myocardial Infarction trial criteria.[41] The fact that only 79% of patients with a coronary artery occlusion had STEMI signs on the ECG is interesting and supportive of the notion that even patients without STEMI on the ECG may benefit from CAG. This is in agreement with a recently published study that showed a very high prevalence of coronary artery disease in patients who underwent CAG after OHCA.[42] In patients who underwent catherisation after OHCA based on VF/ventricular tachycardia prevalence of significant coronary artery disease was 100%. In addition, acute coronary occlusion was discovered in 26.2% of patients who underwent early CAG compared to 29.3% of patients treated with secondary CAG. There was no significant difference in the rate of PCI between the early and late CAG groups (32.8% vs 39.0%, P=0.628). In our studies most PCIs were emergent but also 5% of successfully resuscitated patients underwent a PCI at a later date.

Furthermore, other diagnostic criteria such as a history reported by bystanders or laboratory results have only very limited clinical utility in this setting.[22] More research will be needed in this area, possibly performing CAG on all patients regardless of neurological status and/or regardless of ECG criteria.

Outcome in patients after OHCA has often been studied. Most results underline our observations although differences exist. Gorjup et al. showed that 36% of patients (n=135) with ROSC and undergoing PCI had a good outcome.[43] Cronier et al. studied 111 patients resuscitated successfully following OHCA with an initial shockable rhythm.[36] The incidence of coronary artery occlusion was 73%, which is comparable to our findings. Although the authors studied a selected group of patients, they showed that PCI was associated with increased survival.[36] Gräsner et al. studied 584 patients after OHCA.[35] In normothermic patients (n=405), PCI was independently associated with good neurological outcome.[35] However, that study primarily focused on outcome after 24 hours and lacked follow-up after this period. Zanuttini et al. could even observe that PCI was effective in unconscious patients (n=79) after OHCA, still only for in-hospital outcome.[44] Moreover, in an Australian study (n=35) the effects of an early invasive strategy on outcome were not confirmed.[45] Dumas and Rea studied patients (n=5958) who survived to hospital discharge after OHCA and investigated the relationship between treatment (MTH or PCI) and long-term outcome.[46] Their data showed a five-year survival of 78.7% after PCI. A more recent study by Sideris et al. also showed similar survival rates after hospital discharge.[47] Our overall survival after five years was 85% regardless of intervention or rhythm. Combined MTH and PCI has been associated with better in-hospital outcomes in cohort studies.[48] This benefit of PCI and MTH has, however, been questioned by some.[49,50] A recent study showed no difference in outcome between patients cooled to 33ºC versus 36ºC, leading to the question as to whether MTH itself is beneficial at all or the main beneficial effect might only be the prevention of fever. On first multivariate analysis MTH was an independent predictor of long-term mortality in our study. This is likely to be due to the fact that these patients had more severe neurological injury than patients not treated with MTH. When correcting for GCS at admission there was no significant difference in survival for patients treated with or without MTH. Regarding PCI, Weisner et al. recently showed in a prospective study of 492 STEMI patients that treatment with PCI was not related to neurological outcome after 30 days.[51] The prospective design allowed for multivariate analyses leading to this conclusion. Taken together, results from over the world vary on short and long-term outcome. It is likely that differences in inclusion account for these differences. However, most studies confirm the benefit of an early invasive strategy.

In our region we have optimised treatment for STEMI patients; as a result an infrastructure is present that allows expedient treatment of all patients who are suspected of having an acute coronary occlusion. Relatively short distances in our region and an extensive ambulance network help in this expedient treatment allocation. Wnent et al. have already showed that admission to a centre with PCI facilities is associated with favourable outcomes in patients after OHCA.[52] As a result of this STEMI network it is likely that other patients who have an indication to undergo CAG have a better chance of survival. Based on these observations we changed our practice and more liberally accept patients for CAG. Whether these patients benefit to the same degree from angiography and PCI still has to be elucidated.

Several limitations have to be mentioned. First, this concerns a retrospective study of patients admitted to our hospital. Therefore, detailed data are sometimes absent, such as the time to BLS, advanced life support and ROSC. Second, selection bias limits the external validity of the efficacy of PCI and MTH. As in other studies, among our patients the GCS score was the second most powerful predictor of outcome (after initial rhythm), and thus the beneficial outcomes of patients who underwent primary PCI might be attributable to better initial GCS scores than among those present in the non-PCI group. This creates an interesting avenue for research and possible improvement of treatment. Finally, these results only relate to patients presenting to the emergency unit of a single centre. More patients were resuscitated in our region in the same period, but patients with poor prognostic signs could have been presented to peripheral hospitals and pronounced dead there. As our centre is the only regional facility that offers PCI, patients suspected of coronary occlusion are primarily presented at our centre. In addition, in our region ambulance services have the discretion to stop CPR if there is a non-shockable rhythm present for more than 20 minutes. This might explain differences in patient populations in comparison with other studies, such as the Arrest study.[53,54] In essence we have a higher percentage of patients presenting with VF and after ROSC. Therefore, the outcome data we present do not pertain to the total population of patients with OHCA. However, our purpose was to investigate outcome among patients who presented to the emergency department, because they still have a chance of survival.

In conclusion, survival and neurological outcome in our patients resuscitated after VF and treated with PCI within a STEMI network was remarkably good. In our opinion these observations underscore the fact that the current chain of treatment allows optimal patient survival. However, there is insufficient good quality evidence about the outcome of immediate angiography and coronary intervention in patients with ROSC after OHCA of presumed cardiac aetiology. As the impact of this strategy on the utilisation of resources is significant, good quality randomised controlled trials are needed. In selected patients successfully resuscitated after OHCA of presumed cardiac aetiology, we believe that a more liberal application of angiography and coronary intervention may be considered in experienced acute cardiac referral centres.

Conflict of interest

The authors have no conflicts of interest to declare.

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