



Clinical paper

Long-term survival in patients with acute myocardial infarction and out-of-hospital cardiac arrest: A prospective cohort study



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ABSTRACT

Aim: To compare short- and long-term survival in patients admitted to hospital after acute myocardial infarction (AMI) with and without out-of-hospital cardiac arrest (OHCA).

Methods: Prospective cohort study of all AMI patients admitted to Oslo University Hospital Ullevål from September 1, 2005 to December 31, 2011. All-cause mortality was obtained from the Norwegian Cause of Death Registry with censoring date December 31, 2013. Cumulative survival was assessed with the Kaplan-Meier and the Life-table method. Logistic- and Cox regression were used for risk comparisons.

Results: We identified 404 AMI patients with OHCA and 9425 AMI patients without. AMI patients without OHCA were categorized as ST-elevation myocardial infarction (STEMI, n = 4522) or non-STEMI (NSTEMI, n = 4903). Mean age was 63.6 ± standard deviation (SD) 12.5, 63.8 ± 13.1 and 69.7 ± 13.6 years in OHCA, STEMI and NSTEMI, respectively. Coronary angiography with subsequent percutaneous coronary intervention if indicated, was performed in 87% of OHCA, 97% of STEMI and 80% of NSTEMI patients. Thirty-day survival was 63%, 94% and 94%, and 8-year survival was 49%, 74%, and 57%, respectively. Among patients surviving the first 30 days, no significant difference in risk during long-term follow-up was found (adjusted Hazard Ratio (aHR)_{OHCAvsSTEMI} 1.15 [95% CI 0.82–1.60], aHR_{OHCAvsNSTEMI} 0.89 [95% CI 0.64–1.24]).

Conclusions: Long-term survival after OHCA due to AMI was good, with 49% of admitted patients being alive after eight years. Although short-term mortality remained high, OHCA patients alive after 30 days had similar long-term risk as AMI patients without OHCA.

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Introduction

Short-term prognosis of patients with out-of-hospital cardiac arrest (OHCA) has improved during the last 15 years due to extensive efforts to optimise both pre- and in-hospital treatment [1–3]. Still, the majority of patients die after OHCA, either pre-hospital due to lack of return of spontaneous circulation (ROSC) or in-hospital after ROSC due to cerebral or other complications.

Standardising post-resuscitation care improved 1-year survival with good neurological outcome among OHCA patients admitted to our hospital in 2003–2005 [4], and is currently recommended in international guidelines [5]. This post-resuscitation care strategy

includes targeted temperature management (TTM), early coronary angiography with subsequent percutaneous coronary intervention (PCI) if indicated, as well as lung-protective mechanical ventilation, control of blood glucose, haemodynamics and seizures, and a targeted prognostication plan [5].

Ischaemic heart disease and acute myocardial infarction (AMI) represent the most common causes of OHCA [6,7]. Some studies have suggested that short-term prognosis after OHCA due to AMI might be better than for other causes of OHCA [6,8–10]. On the other hand, we have previously shown that AMI among OHCA patients was associated with higher mortality [11]. With respect to long-term outcomes, 5-year survival of 44% [7] and 10-year survival of 12–38% [12] have been reported in patients with OHCA of presumed cardiac cause, depending on selection criteria. To our knowledge, long-term survival after OHCA due to AMI with or without ST-segment elevation has been specifically reported in only one study

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[8]. Hence, more knowledge about long-term prognosis in patients with OHCA due to AMI is needed.

The aim of this study was to compare short- and long-term survival in unselected AMI patients with and without OHCA admitted to a high-volume cardiac centre with a 24-h/7 days a week (24/7) coronary angiography/PCI service and standardised post-resuscitation care.

Methods

Study population

Oslo University Hospital (OUH) Ullevål is the primary medical centre for a population of 190,000 inhabitants, and serves as a secondary cardiac centre performing coronary angiography and PCI for a population of about 1 400 000 million people in South-Eastern Norway. The hospital has a 24/7 access to coronary angiography for primary PCI. Approximately 4400 coronary angiograms and 1600 PCIs are performed every year.

All AMI patients admitted to OUH Ullevål from September 1, 2005, to December 31, 2011, were prospectively registered into a local AMI registry upon admission. Registration closed on December 31, 2011 due to establishment of a national myocardial infarction registry with a new legislation for use of data. The registration procedure and variables have been described previously [13]. The AMI diagnosis was based on current international criteria [14,15] and troponin T was used as the cardiac biomarker. Patients with OHCA were included in the AMI registry if they were admitted to the hospital alive or with ongoing cardiopulmonary resuscitation (CPR) and an AMI diagnosis was confirmed.

Only the patient's first AMI admission during the study period was included (Fig. 1). AMI without OHCA were classified as ST-segment elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) according to the diagnostic electrocardiogram (ECG). As post-ROSC ECGs may have non-specific changes [16], AMI patients with OHCA were not further classified as STEMI or NSTEMI, but analyzed as one single group (OHCA).

All OHCA patients in the post-resuscitation care period were treated according to our local standardised treatment protocol described elsewhere [4,11]. This treatment protocol [4,11] was introduced at OUH Ullevål already in 2003, with only slight changes over the years. Routine coronary angiography with PCI if indicated was performed immediately after admission in patients with ST-segment elevation on the ECG and in other patients with presumed cardiac cause at the clinicians discretion. Comatose patients were treated with TTM at 33 °C for 24 h before gradual rewarming to normothermia. The majority of patients were treated in cardiac and medical intensive care units (ICUs).

Data quality and validation

Predefined variables were registered into a case report form by the responsible physician during admission. Trained study personnel checked the report form for completeness and errors, before entering the data into an electronic database developed by the Mid-Norway Regional Health Authority. A cross check against the hospital discharge register was performed monthly and missing patients were included if they met the diagnostic criteria for AMI [14]. Supplementary data for the OHCA patients were collected retrospectively from the hospital records according to the core elements suggested by the Utstein Resuscitation Registry OHCA Templates, where available [17].

Cardiogenic shock was defined as a systolic blood pressure (SBP) <90 mmHg with clinical signs of organ hypoperfusion, or need for inotropic drugs to keep SBP >90 mmHg in the absence of

hypovolemia. Ventricular arrhythmias were defined as ventricular fibrillation (VF) >15 s with a frequency >100 beats per minute or symptomatic ventricular tachycardia (VT).

In a random validation sample of 200 registered patients, we found >95% correspondence between data in the AMI registry and the patients' hospital records, except for the variables 'Previous hyperlipidemia' and 'Family history of coronary artery disease' with 8% discrepant values. The frequency of missing data was < 7% except for the variables 'smoker/ex-smoker' (13% missing), 'bystander CPR' (11% missing), time from cardiac arrest to bystander CPR (24% missing), time to advanced life support (27% missing) and time to ROSC (30% missing).

Follow-up and survival

Any deaths and death dates were obtained by linkage of the local AMI registry with the Norwegian Cause of Death Registry, containing vital status throughout 2013. Patients were censored if they were alive on December 31, 2013. Emigrated patients were censored at date of last hospital contact (n = 82). Follow-up time was calculated from admission until censoring or death before January 1, 2014, whichever came first, and varied between patients because of the dynamic cohort.

Ethics

The establishment of a local AMI registry was approved by the Privacy Protection Officer at OUH. The Norwegian Data Protection Authority provided concession for data linkage with the Norwegian Cause of Death Registry (January 5, 2012), with an exemption from the requirement of patient consent (The Ministry of Health and Care Services; November 16, 2011). All data for this study were anonymized before analysis.

Statistical analyses

Categorical variables were presented as percentages of non-missing values; denominators may vary. Continuous variables were presented as mean ± standard deviation (SD) or as median (25,75th percentile) in variables with many outliers. Between-group differences for categorical variables were assessed with Chi-square-test, and for continuous variables with the two-sample *t*-test or Mann-Whitney *U* test, as appropriate.

Cumulative survival was illustrated with the Kaplan-Meier plot and differences between OHCA versus STEMI and NSTEMI were assessed with the Log-rank test. The Life-table method was used to estimate the cumulative survival at 30 days and at eight years. In a landmark analysis, we estimated the long-term survival of patients still at risk at day 30, to allow for a dynamic prediction depending on survival in the first 30 days [18]. The proportional hazards assumption, evaluated using the log-log Kaplan-Meier plot, was unmet using Cox proportional hazards regression for risk of 30 day-mortality. We therefore used logistic regression to calculate the odds ratio (OR) for 30-day mortality in OHCA versus STEMI and NSTEMI patients, adjusting for age (Model 1) and for characteristics known at admission (age, gender, previous hypertension, diabetes mellitus, previous AMI, previous stroke, serum(s)-creatinine and pre-hospital thrombolysis [STEMI only]) (Model 2). Variables with >10% missing values (e.g. smoking habits) were not included in the regression analyses.

We used the Cox proportional hazards regression to calculate the hazard ratio (HR) for long-term mortality in OHCA versus STEMI and NSTEMI patients who survived the first 30 days. The Cox model was adjusted for age (Model 1), and for age, gender, previous hypertension, diabetes mellitus, previous AMI, previous stroke, s-creatinine at admission, pre-hospital thrombolysis [STEMI

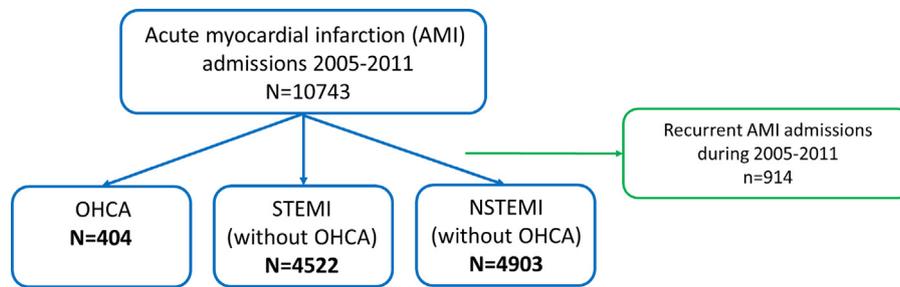


Fig. 1. Cohort creation flow chart.

AMI: Acute myocardial infarction. OHCA: Out-of-hospital cardiac arrest; STEMI: ST-elevation myocardial infarction; NSTEMI: Non-STEMI.

Table 1

Baseline characteristics, reperfusion therapy and invasive coronary procedures.

	AMI + OHCA, N = 404	AMI without OHCA		p-value ¹	p-value ²
		STEMI, N = 4522	NSTEMI, N = 4903		
Age, mean (SD)	63.6 (12.5)	63.8 (13.1)	69.7 (13.6)	0.80	<0.001
Female sex, n (%)	81 (20.0)	1123 (24.8)	1717 (35.0)	0.03	<0.001
Previous hypertension, n (%)	142 (35.1)	1553 (34.3)	2113 (43.1)	0.74	0.002
Diabetes mellitus, n (%)	49 (12.3)	578 (12.8)	930 (19.0)	0.71	<0.001
Previous myocardial infarction, n (%)	68 (17.0)	535 (11.8)	1204 (24.6)	0.003	<0.001
Previous cerebrovascular stroke, n (%)	16 (4.0)	261 (5.8)	550 (11.2)	0.13	<0.001
Smoker- or ex-smoker, n (%)	170 (65.1)	2804 (68.1)	2557 (61.2)	0.33	0.20
S-creatinine (μmol/l) at admission, median (25,75th percentile)	89 (72,110)	74 (63,88)	81 (68,98)	<0.001	<0.001
Reperfusion therapy and invasive coronary procedures					
Thrombolysis ^a , n (%)	43 (10.7)	488 (10.8)	2 (0)	0.93	–
Coronary angiography, n (%)	353 (87.4)	4366 (96.6)	3910 (79.7)	<0.001	<0.001
PCI, n (%)	273 (67.6)	3815 (84.4)	2011 (41.0)	<0.001	<0.001
Primary PCI, n (%)	261 (64.8)	3566 (78.9)	–	<0.001	–
Door-to-balloon, minutes, median (25,75th percentile)	40 (31,70)	36 (29,52)	–	<0.001	–
Symptom-to-balloon, minutes, median (25,75th percentile)	183 (125,291)	259 (160,485)	–	<0.001	–
CABG, n (%)	14 (3.5)	214 (4.7)	513 (10.5)	0.25	<0.001
Coronary artery disease in patients undergoing coronary angiography, n (%)	N = 353	N = 4366	N = 3910		
Normal vessels or atheromathosis	21 (5.9)	127 (2.9)	509 (13.0)	0.002	<0.001
One-vessel disease	146 (41.4)	2022 (46.3)	1460 (37.3)	0.07	0.14
Multi-vessel or left main disease	186 (52.7)	2208 (50.6)	1914 (49.0)	0.44	0.18

OHCA: Out-of-hospital cardiac arrest; STEMI: ST-elevation myocardial infarction; NSTEMI: Non-STEMI; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; SD: standard deviation.

p¹: OHCA vs STEMI, p²: OHCA vs NSTEMI.

^aThrombolysis pre hospital or at local hospital.

only], maximum troponin T, coronary angiography, PCI, cardiogenic shock, intraaortic balloon pump (IABP), heart failure (without cardiogenic shock) and atrial fibrillation/flutter (Model 2).

Analyses were performed with STATA 13 (Statacorp LP, Texas, USA). The study conforms with the STROBE (STrengthening the Reporting of OBServational studies in Epidemiology) checklist for reporting of observational studies [19].

Results

Study population

A total of 9829 AMI patients were included in the study (Fig. 1): 404 AMI patients with OHCA and 9425 without (4522 STEMI and 4903 NSTEMI). The baseline characteristics of the three patient groups are shown in Table 1 and 2. OHCA patients were 63.6 ± 12.5 years of age and they were more likely to be male (n = 323; 80.0%) compared to STEMI (75.2%) and NSTEMI (65.0%) patients. Their cardiovascular risk factor profile was similar to that of STEMI patients, except for a higher frequency of previous myocardial infarction and

higher levels of s-creatinine upon admission (Table 1). Bystander CPR was initiated in 72.0% of the OHCA patients, and VF was the first monitored rhythm in 82.0% (Table 2).

In-hospital management and mortality

A majority of OHCA patients underwent coronary angiography (n = 353; 87.4%) and PCI (n = 273; 67.6%), although fewer than in the STEMI cohort (Table 1). In the OHCA group, door-to-balloon times were significantly longer, but symptom-to-balloon times shorter compared to STEMI patients (Table 1). The frequency of multi-vessel or left main stem disease was similar in all three groups (Table 1). OHCA patients had a higher burden of in-hospital complications compared to AMI patients without OHCA, and assisted mechanical ventilation and IABP were more frequently used (Supplementary Table S1). Maximum troponin T levels (μg/L) were median 3.14 (1.32, 7.59) in OHCA patients, 3.79 (1.47, 7.63) in STEMI patients (p = 0.04) and 0.42 (0.13, 1.23) in NSTEMI patients (p < 0.001).

Table 2
Supplementary characteristics and pre-hospital treatment in AMI patients with OHCA.

	OHCA, N = 404
ST-elevation in first ECG, n (%)	305 (75.5)
Witnessed out-of-hospital cardiac arrest, n (%)	400 (99.0)
Layman witnessed arrest, n (%)	294 (72.8)
Medical personnel ^a witnessed arrest, n (%)	106 (26.2)
VF as first monitored rhythm, n (%)	332 (82.0)
Bystander CPR, n (%)	315 (72.0)
Defibrillation + CPR, n (%)	335 (83.0)
Defibrillation only, n (%)	53 (12.8)
CPR only, n (%)	15 (3.7)
Achieved ROSC, n (%)	381 (94.5)
Time from cardiac arrest to CPR, minutes*	0 (0,2)
Time from cardiac arrest to ROSC, minutes*	17 (6,31)
Time from ALS to ROSC, minutes*	10 (4,25)
Comatose at hospital admission, n (%)	264 (66.0)
Therapeutic hypothermia, n (%)	206 (53.0)
Systolic blood pressure at admission, mmHg *	115 (95,132)
Diastolic blood pressure at admission, mmHg *	70.5 (60,82)
Heart rate at admission, beats per minute*	80 (70,98)

ALS: Advanced life support; AMI: Acute myocardial infarction; CPR: Cardiopulmonary resuscitation; ECG: Electrocardiogram; OHCA: Out-of-hospital cardiac arrest; ROSC: Return of spontaneous circulation; VF: Ventricular fibrillation.

*Median (25,75th percentile).

^aAmbulance personnel or physician present at cardiac arrest.

Hospital survival was 275/404 (68.1%) in the total cohort of OHCA patients admitted to our hospital. None of the patients admitted with ongoing CPR (n = 22) achieved ROSC. Hospital survival in OHCA patients achieving ROSC was 72.0% (275/382). Among AMI patients without OHCA, hospital survival was 95.7% (STEMI) and 95.8% (NSTEMI) (Table 3).

30-day survival

30-day survival was 63.4%, 94.1% and 93.8% among admitted OHCA, STEMI and NSTEMI patients, respectively. A marked difference in survival was seen the first days after admission, illustrated by the Kaplan–Meier survival curve for the first 30 days (Fig. 2a). The crude and adjusted OR of 30-day mortality in OHCA versus STEMI and NSTEMI are shown in Table 4. In OHCA patients achieving ROSC, 30-day survival was 67.0% (95% CI: 62.1–71.5).

Long-term survival

Patients were followed for up to eight years (median follow-up time 1446 days [892,2125]). Among OHCA patients, a total of 195/404 patients died. Cumulative survival from admission to end of follow-up was 48.7% (95% CI: 43.7–54.1) in OHCA patients, and 77.6% (95% CI: 70.6–83.1) in OHCA patients surviving the first 30 days (Table 3).

Fig. 2b illustrates that OHCA patients surviving the first 30 days had estimated similar 8-year survival compared to STEMI patients. The crude HR revealed a higher risk of death for OHCA than for

Table 3
Cumulative survival in AMI patients with and without OHCA (Life table method).

	OHCA, N = 404	No OHCA	
		STEMI, N = 4522	NSTEMI, N = 4903
Hospital survival, n (%)	275 (68.1)	4328 (95.7)	4698 (95.8)
30-day survival, %	63.4 (58.5–67.9)	94.1 (93.3–94.7)	93.8 (93.0–94.4)
8-year survival (admission to end of study*), %	48.7 (43.1–54.1)	73.5 (71.2–75.6)	57.3 (55.0–59.4)
8-year survival (day 30 to end of study*), %	77.6 (70.6–83.1)	77.7 (75.2–80.0)	60.7 (58.3–63.1)

Results are given as percentage with 95% confidence interval.

*Median follow-up time: 1446 days (25,75th percentile: 892,2125).

AMI: Acute myocardial infarction; OHCA: Out-of-hospital cardiac arrest; STEMI: ST-segment elevation myocardial infarction; NSTEMI: Non-STEMI; CI: Confidence interval.

STEMI patients during follow-up, but after multivariate adjustment, there was no significant difference in risk (Table 4). OHCA patients surviving the first 30 days, had better estimated 8-year survival compared to NSTEMI patients (Fig. 2b), and the crude HR indicated a lower risk during follow-up. This was attenuated after adjustment for age and other confounders, showing a similar risk for OHCA and NSTEMI patients for up to eight years (Table 4). Thus, AMI patients with OHCA surviving the first 30 days, had similar chance of long-term survival during eight years of follow-up, compared with STEMI and NSTEMI patients without OHCA.

Discussion

In this large study of 9829 AMI patients, we found a lower 30-day survival in OHCA patients compared to STEMI and NSTEMI patients. However, after a maximum follow-up time of eight years, almost half of the admitted OHCA patients were still alive. Interestingly, in those patients surviving the first 30 days, no significant difference in long-term risk was found between AMI patients with and without OHCA, after adjustment for age and other confounders. Among OHCA patients surviving the first 30 days, the 8-year survival rate was as high as 77.6%.

The higher short-term mortality in OHCA patients was mainly due to early deaths occurring the first 4–5 days after admission, and this is in accordance with previous studies on STEMI patients with and without OHCA [6,10,20,21]. However, a 30-day survival rate of 63.4% in unselected AMI patients with OHCA is higher than in most previous reports of short-term survival in OHCA without obvious non-cardiac origin [6,7,12,22,23]. Our OHCA patient group was heterogeneous, with a high proportion of patients being awake upon hospital admission. On the other hand, 22 patients had ongoing CPR never achieving ROSC, and died shortly after admission. All patients were aggressively treated with high rates of coronary angiography and PCI, previously shown to be associated with improved outcome [7,23], as well as good quality post-ROSC care [16,24–26].

The 8-year survival rate of nearly 80% in OHCA patients who survived until 30 days after admission is similar to results from Sideris et al. reporting a 5-year survival rate from discharge of 82% [8]. Other reports of long-term survival in OHCA patients of presumed cardiac origin is varying, with 5-year survival after discharge of 41% [27], 64% [28] and 84% [7], and 10-year survival after discharge of 46% [29]. Another study reported 10-year survival from admission of 12–38% depending on whether coronary angiography and PCI were performed or not [12]. A comparison of survival between studies is not straightforward due to different aetiologies, inclusion criteria and treatment strategies for OHCA patients. However, the good long-term prognosis of OHCA patients who survived until 30 days in our study is promising. Our follow-up time was longer than in most other studies, increasing the accuracy of the results.

Previous studies have reported a similar prognosis after discharge for STEMI patients with and without OHCA; but in most of these studies patients were highly selected [10,20,21]. To our knowledge, we are the first to compare survival in unselected AMI

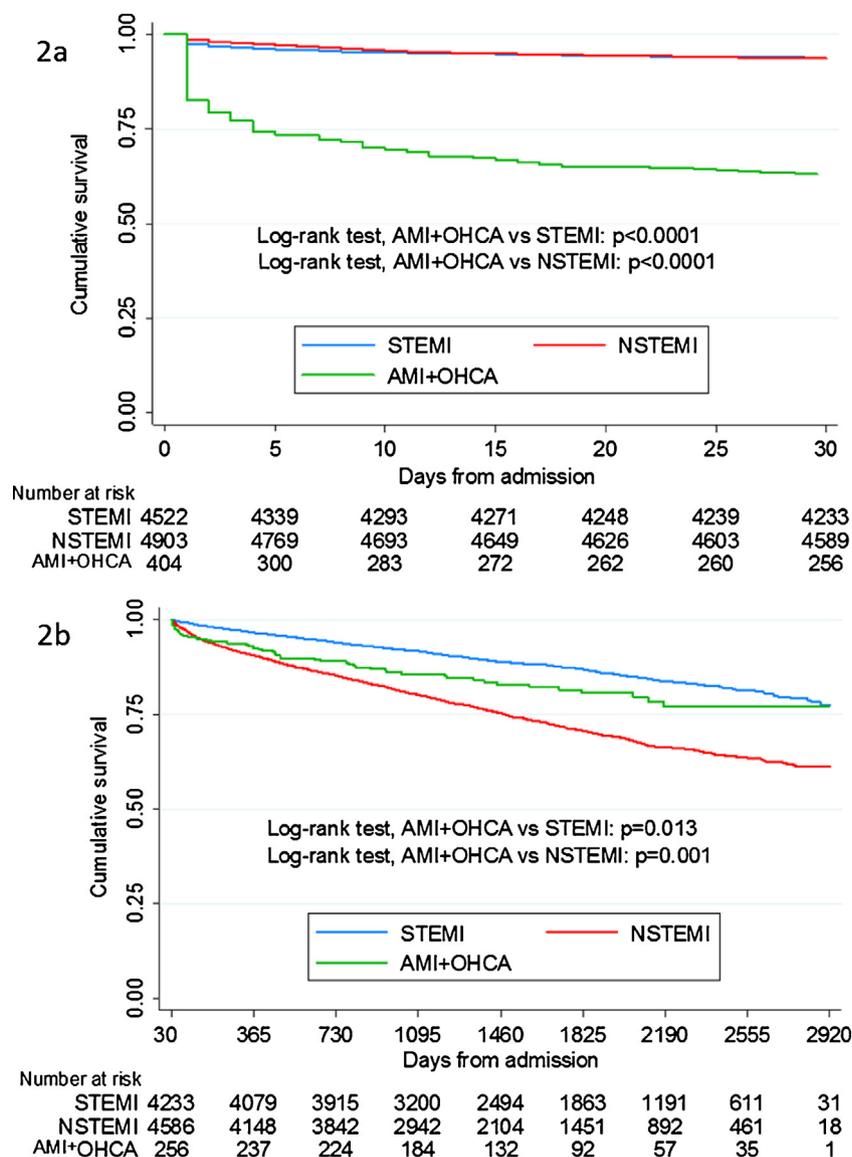


Fig. 2. Short- and long-term survival.

2a. Kaplan-Meier curve for 30-day survival.

2b. Kaplan-Meier curve with landmark analysis: Long-term survival among patients surviving the first 30 days.

AMI: Acute myocardial infarction; OHCA: out-of-hospital cardiac arrest; STEMI: ST-elevation myocardial infarction (no OHCA); NSTEMI: Non-STEMI (no OHCA). Median follow-up: 1446 days (25.75th percentile: 892,2125).

Table 4

Risk of 30-day mortality and long-term mortality after 30 days.

	OHCA vs STEMI	p-value	OHCA vs NSTEMI	p-value
30-day mortality:				
Crude OR (95% CI)	9.18 (7.24–11.6)	<0.001	8.60 (6.81–10.9)	<0.001
Model 1: Age-adjusted OR (95% CI)	12.4 (9.53–16.2)	<0.001	19.4 (14.6–25.8)	<0.001
Model 2: Multivariate ^a adjusted OR (95% CI)	10.6 (7.87–14.4)	<0.001	18.2 (13.1–25.1)	<0.001
Landmark analysis: Mortality from day 30 to end of study*:				
Crude HR (95% CI)	1.45 (1.08–1.95)	0.01	0.62 (0.47–0.83)	0.001
Model 1: Age-adjusted HR (95% CI)	1.78 (1.32–2.40)	<0.001	1.12 (0.83–1.50)	0.46
Model 2: Multivariate ^b adjusted HR (95% CI)	1.15 (0.82–1.60)	0.42	0.89 (0.64–1.24)	0.50

AMI: Acute myocardial infarction; OHCA: Out-of-hospital cardiac arrest; STEMI: ST-elevation myocardial infarction; NSTEMI: Non-STEMI; OR: Odds ratio; HR: Hazard ratio; CI: Confidence interval.

*Median follow-up: 1446 days (25.75th percentile: 892,2125).

^aAge, female gender, previous hypertension, diabetes mellitus, previous myocardial infarction, s-creatinine (mmol/l) at admission.

^bAll factors in ^a + Max troponin T ($\mu\text{g/l}$), coronary angiography, percutaneous coronary intervention, cardiogenic shock, heart failure, atrial fibrillation/flutter, intraaortic balloon pump.

patients with OHCA, with survival in NSTEMI and STEMI patients. In OHCA patients surviving the first 30 days, the unadjusted long-term risk of death was lower than for NSTEMI, but higher than for STEMI. After adjustment for age and other confounders, the long-term risk was not significantly different for OHCA compared to neither STEMI nor NSTEMI patients. NSTEMI patients were older and had more co-morbidities compared to OHCA patients, and the higher unadjusted risk of death after 30 days could partly be explained by these differences. Age and several comorbidities were similar for OHCA and STEMI patients, except for a higher frequency of previous myocardial infarction and higher levels of s-creatinine upon admission, probably contributing to the higher unadjusted risk in OHCA compared to STEMI patients. The lower rates of coronary angiography in NSTEMI compared to STEMI patients reflect the guideline-recommended management during the study period, taking into account risk stratification and comorbidities before selecting an invasive strategy in NSTEMI patients [30]. Also in OHCA patients, acute coronary angiography was not performed routinely in all patients, due to lack of consensus on the use of this procedure if absent ST-segment elevation in the post-ROSC ECG [16]. The between-group differences in use of coronary angiography and PCI were adjusted for in the regression analyses estimating long-term risk in patients alive after 30 days. Our results should encourage further optimisation of pre-hospital treatment and post-ROSC care of AMI patients with OHCA, not only due to the promising long-term results but also to try to improve short-term prognosis.

The strengths of the present study are a complete long-term follow-up of a high number of unselected AMI patients, with detailed description of risk factors and treatment, as well as estimates of long-term survival in AMI patients with and without OHCA. There were few missing values in the clinical variables, ensuring a detailed description of the study population and a lower probability of overestimating risk. The main limitation of the study was the observational nature so that effect of interventions and treatment could not be determined. We did not register clinical factors such as heart rate, blood pressure and medication at admission, nor left ventricular ejection fraction, which could be possible confounders in estimating risk. Furthermore, we did not have information about post-discharge treatment, such as medications, implantable cardioverter defibrillators or quality of life in the surviving patients. Variables with >10% missing values were not included in the regression analyses. Whether these or unmeasured variables contributed to confounding in the estimated HR for OHCA patients compared to STEMI and NSTEMI remains unknown. Reported median times from cardiac arrest to initiation of CPR, advanced life support and to achievement of ROSC, are somewhat uncertain due to many missing values. Finally, our study was conducted in a single centre with a 24/7 PCI service and an established post-resuscitation protocol, and the results are not necessarily generalizable to all AMI patients with OHCA. Although the majority of STEMI and resuscitated OHCA patients in the region are normally admitted to our hospital, we lack information about those AMI patients not being admitted. Future studies can reveal whether our results are reproducible for patients treated in other cardiac centres with 24/7 coronary angiography/PCI service and standardised post-resuscitation care.

Conclusion

Long-term survival in AMI patients with OHCA was good with 49% of patients being alive after eight years of follow-up. Although short-term mortality remained high in AMI patients with OHCA, patients surviving the first 30 days had similar chance of survival during eight years of follow-up as AMI patients without OHCA.

Conflict of interest

None

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.resuscitation.2017.11.047>.

References

- [1] Lund-Kordahl I, Olasveengen TM, Lorem T, Samdal M, Wik L, Sunde K. Improving outcome after out-of-hospital cardiac arrest by strengthening weak links of the local chain of survival: quality of advanced life support and post-resuscitation care. *Resuscitation* 2010;81:422–6.
- [2] Wong MK, Morrison LJ, Qiu F, Austin PC, Cheskes S, Dorian P, et al. Trends in short- and long-term survival among out-of-hospital cardiac arrest patients alive at hospital arrival. *Circulation* 2014;130:1883–90.
- [3] Wissenberg M, Folke F, Hansen CM, Lippert FK, Kragholm K, Risgaard B, et al. Survival after out-of-hospital cardiac arrest in relation to age and early identification of patients with minimal chance of long-term survival. *Circulation* 2015;131:1536–45.
- [4] Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2007;73:29–39.
- [5] Nolan JP, Soar J, Cariou A, Cronberg T, Moulart VR, Deakin CD, et al. European resuscitation council and European society of intensive care medicine guidelines for post-resuscitation care 2015: section 5 of the European resuscitation council guidelines for resuscitation 2015. *Resuscitation* 2015;95:202–22.
- [6] Larsen JM, Ravkilde J. Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—a systematic review and meta-analysis. *Resuscitation* 2012;83:1427–33.
- [7] Bergman R, Hiemstra B, Nieuwland W, Lipsic E, Absalom A, van der Naalt J, et al. Long-term outcome of patients after out-of-hospital cardiac arrest in relation to treatment: a single-centre study. *Eur Heart J Acute Cardiovasc Care* 2016;5:328–38.
- [8] Sideris G, Voicu S, Yannopoulos D, Dillinger JG, Adjedj J, Deye N, et al. Favourable 5-year postdischarge survival of comatose patients resuscitated from out-of-hospital cardiac arrest, managed with immediate coronary angiogram on admission. *Eur Heart J Acute Cardiovasc Care* 2014;3:183–91.
- [9] Fothergill RT, Watson LR, Viridi GK, Moore FP, Whitbread M. Survival of resuscitated cardiac arrest patients with ST-elevation myocardial infarction (STEMI) conveyed directly to a heart attack centre by ambulance clinicians. *Resuscitation* 2014;85:96–8.
- [10] Demirel F, Rasoul S, Elvan A, Ottervanger JP, Dambrink JH, Gosselink AT, et al. Impact of out-of-hospital cardiac arrest due to ventricular fibrillation in patients with ST-elevation myocardial infarction admitted for primary percutaneous coronary intervention: Impact of ventricular fibrillation in STEMI patients. *Eur Heart J Acute Cardiovasc Care* 2015;4:16–23.
- [11] Tomte O, Andersen GO, Jacobsen D, Draegni T, Auestad B, Sunde K. Strong weak aspects of an established post-resuscitation treatment protocol—a five-year observational study. *Resuscitation* 2011;82:1186–93.
- [12] Geri G, Dumas F, Bougouin W, Varenne O, Daviaud F, Pene F, et al. Immediate percutaneous coronary intervention is associated with improved short- and long-term survival after out-of-hospital cardiac arrest. *Circ Cardiovasc Interv* 2015;8:e002303, <http://dx.doi.org/10.1161/CIRCINTERVENTIONS.114.002303>.
- [13] Kvakkestad KM, Abdelnoor M, Claussen PA, Eritsland J, Fossum E, Halvorsen S. Long-term survival in octogenarians and older patients with ST-elevation myocardial infarction in the era of primary angioplasty: a prospective cohort study. *Eur Heart J Acute Cardiovasc Care* 2016;5:243–52.
- [14] Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *Eur Heart J* 2007;28:2525–38.
- [15] Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American Col-

- lege of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959–69.
- [16]. Staer-Jensen H, Nakstad ER, Fossum E, Mangschau A, Eritsland J, Draegni T, et al. Post-resuscitation ECG for selection of patients for immediate coronary angiography in out-of-hospital cardiac arrest. *Circ Cardiovasc Interv* 2015:e002784, <http://dx.doi.org/10.1161/CIRCINTERVENTIONS.115.002784>.
- [17]. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, 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 Council of Southern Africa). *Resuscitation* 2004;63:233–49.
- [18]. van Houwelingen HC. Dynamic prediction by landmarking in event history analysis. *Scand J Stat* 2006;34:70–85.
- [19]. STROBE statement—checklist of items that should be included in reports of observational studies (STROBE initiative). *Int J Public Health* 2008;53:3–4.
- [20]. Bendz B, Eritsland J, Nakstad AR, Brekke M, Klow NE, Steen PA, et al. Long-term prognosis after out-of-hospital cardiac arrest and primary percutaneous coronary intervention. *Resuscitation* 2004;63:49–53.
- [21]. Lettieri C, Savonitto S, De Servi S, Guagliumi G, Belli G, Repetto A, et al. Emergency percutaneous coronary intervention in patients with ST-elevation myocardial infarction complicated by out-of-hospital cardiac arrest: early and medium-term outcome. *Am Heart J* 2009;75:e1.
- [22]. Hollenbeck RD, McPherson JA, Mooney MR, Unger BT, Patel NC, McMullan Jr PW, et al. Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. *Resuscitation* 2014;85:88–95.
- [23]. Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, 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;3:200–7.
- [24]. Langhelle A, Tyvold SS, Lexow K, Hapnes SA, Sunde K, Steen PA. In-hospital factors associated with improved outcome after out-of-hospital cardiac arrest: a comparison between four regions in Norway. *Resuscitation* 2003;56:247–63.
- [25]. Herlitz J, Engdahl J, Svensson L, Angquist KA, Silfverstolpe J, Holmberg S. Major differences in 1-month survival between hospitals in Sweden among initial survivors of out-of-hospital cardiac arrest. *Resuscitation* 2006;70:404–9.
- [26]. Gaieski DF, Band RA, Abella BS, Neumar RW, Fuchs BD, Kolansky DM, et al. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Resuscitation* 2009;80:418–24.
- [27]. Naess AC, Steen PA. Long term survival and costs per life year gained after out-of-hospital cardiac arrest. *Resuscitation* 2004;60:57–64.
- [28]. Dumas F, White L, Stubbs BA, Cariou A, Rea TD. Long-term prognosis following resuscitation from out of hospital cardiac arrest: role of percutaneous coronary intervention and therapeutic hypothermia. *J Am Coll Cardiol* 2012;60:21–7.
- [29]. Holler NG, Manton T, Nielsen SL, Lippert F, Rasmussen LS. Long-term survival after out-of-hospital cardiac arrest. *Resuscitation* 2007;75:23–8.
- [30]. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliquet T, et al. Guidelines on myocardial revascularization. *Eur Heart J* 2010;31:2501–55.