ORIGINAL STUDIES

Outcome predictors of patients with out of hospital cardiac arrest and immediate coronary angiography

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Abstract
Background: Out of hospital cardiac arrest (OHCA) is common and associated with low survival rates. Guidelines propose a fast work-up after OHCA including coronary angiography (CA) but little is known about the actual outcome of those patients who undergo immediate CA after OHCA with suspected cardiac origin.

Aim: The aim of this retrospective single-center study was to evaluate the short-term outcomes and predictors of in-hospital mortality in patients who underwent immediate CA after OHCA with suspected cardiac origin.

Methods: We included all consecutive patients with OHCA who underwent immediate CA between January 2011 and December 2015. We defined immediate CA after OHCA as angiography within 2 hr after admission.

Results: Two hundred and nineteen consecutive patients with OHCA were included. Fifty six patients (26%) underwent CA without previous return of spontaneous circulation (ROSC) and with ongoing CPR using the LUCAS-device. One hundred and forty nine patients (67%) died in hospital. Of the 56 patients with CA with ongoing CPR, 55 died and only 1 patient survived to hospital discharge. In a multivariate analysis, older age (OR = 2.03, 95%CI 1.35–3.03; \( p = .001 \)), initial shockable rhythm (OR = 0.28, 95%CI 0.07–1.13; \( p = .076 \)), CA with ongoing CPR (OR = 11.63, 95%CI 1.20–122.55; \( p = .035 \)), and initial arterial pH (OR = 0.008, 95%CI 0.00–0.228; \( p < .005 \)) remained as independent predictors for in-hospital mortality.

Conclusions: In this study older age, metabolic derangement on admission, initial nonshockable rhythm and failure to achieve ROSC before admission predicted in-hospital mortality. While CA with ongoing CPR with the LUCAS-device was feasible, mortality in patients without previous ROSC was extremely high, questioning whether this approach is medically useful.

Abbreviations: AUC, area under the curve; CA, coronary angiography; CABG, coronary arteries bypass graft; CAD, coronary artery disease; Cathlab, catheterization laboratory; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; ICA, immediate coronary angiography; ICD, implantable cardiac defibrillator; ICU, intensive cardiac unit; LUCAS, Lund hospital cardiac arrest system; mCPR, mechanical cardiopulmonary resuscitation; NSTEMI, non-ST elevation myocardial infarction; OHCA, out of hospital cardiac arrest; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; STEMI, ST-elevation myocardial infarction.
KEYWORDS
CAD—coronary artery disease, CS—cardiogenic shock, AMI—acute myocardial infarction, OHCA—out of hospital cardiac arrest, ROSC—return of spontaneous circulation

1 | INTRODUCTION

Out of hospital cardiac arrest (OHCA) is the leading cause of mortality and disability in the western world. 166,000–310,000 people suffer from OHCA per year in USA and less than 10% of these survive. The most common cause of OHCA is cardiovascular disease. Mortality remains high at 60% even despite improved guidelines for acute treatment and the rapid and broad development of interventional cardiology in the last decade. The impact of immediate coronary angiography which is proposed in the current European Resuscitations guidelines is not well known. Current guidelines for ACS give a Class I recommendation for immediate angiography and primary PCI in STEMI, whereas this recommendation in patients without STEMI but with high suspicion of coronary artery disease is a weaker Class IIa recommendation. This is based on relatively small retrospectively studies. Furthermore, there is no clear recommendation for patients with suspected CAD arriving at catheterization laboratory (cathlab) with ongoing CPR. In our study we examined the clinical outcomes after OHCA in patients undergoing immediate coronary angiography including those presenting with OHCA but no ROSC.

2 | METHODS

This is a single center, retrospective, nonrandomized study. We included all consecutive patients who were resuscitated after OHCA and underwent emergency coronary angiography at the RWTH Aachen university hospital between January 2011 and December 2015. The study was approved by the local ethics committee of the University Aachen.

2.1 | Setting and prehospital management

The University Hospital Aachen is a tertiary care center treating ~48,000 in-house patients per year. It is part of a local myocardial infarction network including local ambulance services, local city and area hospitals, and the University hospital as the interventional center. Within the myocardial infarction network there is intensive communication between the local hospitals and local ambulances and the University hospital’s intensive care unit through dedicated emergency phones and mobile phone fax for optimized prehospital triage and early notification of the interventional teams which are available 24/7. These communication channels are also used in patients with OHCA for which the University Hospital Aachen functions as a cardiac arrest center. The treatment paths are as follows: After successful resuscitation a patient is immediately transferred to the catheterization laboratories to perform CA if there is ST-segment elevation in the ECG or any of the following are present: (a) initial shockable initial rhythm; (b) known coronary artery disease; (c) angina pectoris before OHCA; (d) Regional wall motion of left ventricle in transthoracic echocardiography on admission to the ICU or emergency department; (e) Non-ST elevation myocardial infarction in serologic testing after admission to the ICU. If the patient without ROSC and the OHCA is of suspected cardiac origin, the patient will be transferred to cathlab while under ongoing CPR with LUCAS Device. The decision to transport a patient with ongoing CPR is taken by the treating emergency physician in charge of the resuscitation.

2.2 | Coronary angiography setting

Coronary angiography was carried out by an interventional team consisting of an interventional cardiologist and two nurses with support of an ICU team consisting of one fellow and one ICU-nurse. If the patient was admitted without ROSC, the interventional cardiologist would decide based on the clinical presentation and initial blood-gas analysis whether coronary angiography should be attempted with ongoing CPR. In either case coronary angioplasty was attempted if an acute coronary occlusion or severe coronary stenosis was identified. If the angiography was done with ongoing CPR, the LUCAS chest compression system was used. This system developed at the Lund University Hospital consists of a silicon rubber suction cup and pneumatic cylinder mounted on two legs and connected to stiff plate. It provides continuous chest compression and decompression with frequencies between 100 and 120 and a compression depth of 5 cm. In these circumstances, specialized views are needed to perform successful intubation of the left and right coronary artery in short time. Thus, intubation of the LCA was achieved mostly under spider view instead posterior anterior view and intubation of the RCA was done in LAO/cranial.

2.3 | ICU setting

All patients were treated on the cardiologic ICU of the University Hospital Aachen. Treatment was tailored according to guidelines for treatment of cardiogenic shock and included intravenous temperature control using the CoolGard System (Zoll) with controlled normothermia at 36°C for at least 72 hr.

2.4 | Study endpoints and definitions

We examined overall in-hospital mortality in all patients admitted as the primary endpoint of this study. Furthermore, we analyzed the following subgroups of patients for in-hospital mortality: patients who underwent coronary angiography with ongoing CPR using the LUCAS
device, patients with STEMI in their ECG immediately after ROSC from OHCA and patients with NSTEMI. For these subgroups we used the following definitions: ST elevation as presence of an elevated amplitude of >0.2 mV in men or > 0.15 mV in women in leads V2–V3 and or >0.1 mV in other leads in two or more contiguous precordial leads or in two or more adjacent limb leads or presence of a new left bundle branch block.7 NSTEMI: according to the universal definition of myocardial infarction.8 For results of the angiography we defined significant coronary artery disease as coronary artery stenosis more than 50%, ruptured plaques or staining on coronary angiography.

2.5 Statistical analysis

Statistical analyses were performed using MedCalc for Windows, version 04.20.011 (MedCalc, Software, Mariakerke, Belgium). Categorical data are presented as frequencies and were compared using Chi-square test. Continuous data are presented as mean ± standard deviation and were compared using t-test. Uni- and multivariate logistic regression analysis with consecutive backward selection for variables with a p-value <.10 was used to calculate the odds ratio for individual parameters to predict the in-hospital mortality in patients with OHCA and immediate coronary angiography. We analyzed the following variables: age, shockable rhythm, lactate level, pH, glucose, duration of CPR and coronary angiography under ongoing CPR with LUCAS device.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and optimal cut off value were calculated from receiver operating characteristic (ROC) curve to predict in-hospital mortality in patient with OHCA. A p-value of <.05 was considered statistically significant.

3 RESULTS

Three hundred and twenty one patients with OHCA believed attributable to cardiac etiology were admitted in cardiology department at the RWTH Aachen university hospital between January 2011 and December 2015. Two hundred and nineteen patients underwent immediate coronary angiography. One hundred and two patients did not undergo coronary angiography.

| Variable | Nonsurvival 148 patients | Survival 71 patients | p value |
|----------|--------------------------|---------------------|---------|
| Male, n (%) | 104 (70%) | 56 (76%) | .180 |
| Age (years, mean ± SD) | 67 ± 11 | 57 ± 14 | .028 |
| Coronary artery disease, n (%) | 115 (78%) | 52 (73%) | .468 |
| Single vessel disease, n (%) | 31 (21%) | 19 (27%) | .338 |
| Multi-vessel disease, n (%) | 84 (57%) | 33 (46%) | .154 |
| STEMI, n (%) | 48 (32%) | 23 (32%) | .942 |

**Therapeutic strategies**

- Successful PCI, n (%) | 77 (52%) | 42 (59%) | .322 |
- Nonsuccessful PCI, n (%) | 13 (9%) | 2 (3%) | .102 |
- Coronary artery bypass graft, n (%) | 0 (0%) | 1 (1%) | .148 |
- Conservative Therapy, n (%) | 24 (16%) | 8 (11%) | .332 |

| Initial shockable rhythm, n (%) | 91 (61%) | 62 (87%) | .0002 |
| Coronary angiography with ongoing CPR, n (%) | 55 (37%) | 1 (1%) | <.001 |
| CPR-duration (minutes) | 45 ± 33 | 20 ± 17 | <.001 |
| Initial arterial pH | 7.10 ± 0.19 | 7.25 ± 0.14 | .002 |
| Initial arterial lactate (mmol/l) | 9.5 ± 5.9 | 4.8 ± 4.1 | .001 |
| Glucose (mg/dl) | 308 ± 126 | 214 ± 83 | <.001 |
| Uric acid (mg/dl) | 8.2 ± 2.5 | 7.5 ± 1.8 | .067 |

Abbreviations: CPR, cardiopulmonary resuscitation; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

3.1 Patients with OHCA and immediate coronary angiography

One hundred and forty eight patients (67%) died, 71 patients (32%) survived to discharge. 153 patients (70%) had an initial shockable rhythm at the time of first medical contact. One hundred and forty six patients (75%) had a return of spontaneous circulation (ROSC) before admission while 56 patients (25%) underwent coronary angiography without...
previous ROSC and ongoing CPR using the LUCAS-device (Figure 1). We found significant coronary artery disease in 166 patients (76%) among them one third (32%) presenting with STEMI in ECG. Table 1 depicts baseline demographic and clinical data by survival status.

Non-survivors compared to survivors were older (67 ± 11 vs. 57 ± 14; \( p = .028 \), respectively), presented without shockable rhythm more often (61 vs. 87%; \( p = .0002 \), respectively), had more often ongoing CPR (37 vs. 1%; \( p < .001 \), respectively), longer CPR-duration (45 ± 33 vs. 20 ± 17 min; \( p < .001 \), respectively), higher glucose levels (308 ± 126 vs. 214 ± 83; \( p < .001 \), respectively), lower pH (7.10 ± 0.19 vs. 7.25 ± 0.14; \( p = .002 \), respectively) and higher lactate levels (9.5 ± 5.9 vs. 4.8 ± 4.1; \( p = .001 \), respectively). In those 56 patients without ROSC in whom coronary angiography was performed under CPR, 55 patients died and only 1 patient survived to hospital discharge with irreversible light brain damage after recanalization of a left anterior descending artery (LAD)-occlusion (Figure 2, Panel a–d).

Twenty five out of 56 patients have developed ROSC during the attempted PCI (18 patients had successful PCI, 1 patient had unsuccessful PCI, and 6 did not need PCI); Thirty one patients remained without ROSC and died in the cardiac catheterization laboratories. Thirteen of the survivors (18%) underwent ICD-implantation before discharge. Univariate predictors for hospital mortality were older age, coronary angiography without previous ROSC, non-shockable rhythm, duration of CPR, arterial pH, glucose and lactate level on admission. Table 2 presents the univariate and multivariate predictors for death

| Table 2 | Univariate and multivariate predictors of in-hospital mortality after OHCA and immediate CA |
|---------|---------------------------------------------|
| **Variable** | **Odds ratio** | **CI 95%** | **p value** |
| **Univariate predictors** | | | |
| Age (per 10 years) | 1.781 | 1.397–2.271 | <.001 |
| Initial shockable rhythm | 0.245 | 0.108–0.553 | .001 |
| Coronary angiography with ongoing CPR | 41.398 | 5,592–306.464 | <.001 |
| CPR-duration (per 10 min) | 1.502 | 1.275–1.769 | <.001 |
| Initial arterial pH | 0.004 | 0.000–0.040 | <.001 |
| Initial arterial lactate (mmol/L) | 1.203 | 1.119–1.294 | <.001 |
| Initial Glucose (per 10 mg/dl) | 1.090 | 1.052–1.129 | <.001 |
| **Independent predictors** | | | |
| Age (per 10 years) | 2.031 | 1.358–3.039 | .001 |
| Initial shockable rhythm | 0.286 | 0.072–1.139 | .076 |
| Coronary angiography with ongoing CPR | 11.636 | 1.203–112.556 | .034 |
| Initial arterial pH | 0.008 | 0.00–0.228 | .005 |

**FIGURE 2** Panel (a): Left coronary angiography in right anterior oblique cranial view during mCPR shows occlusion of proximal left anterior descending with TIMI flow 0. Panel (b): Successful recanalisation of LAD with coronary wire (pilot 50) during mCPR. Panel (c): Stent implantation in the LAD during mCPR. Panel (d): Finally good angiographic result after successful implantation of DES in LAD during mCPR.
in hospital. In the multivariate analysis, older age (OR = 2.03, 95% CI 1.35–3.03; \(p = .001\)), initial shockable rhythm (OR = 0.28, 95% CI 0.07–1.13; \(p = .076\)), Coronary angiography with ongoing CPR (OR = 11.63, 95% CI 1.20–122.55; \(p = .035\)), and initial arterial pH (OR = 0.008, 95% CI 0.00–0.228; \(p < .005\)) remained as independent predictors for hospital mortality.

### 3.2 Patients with OHCA who did not undergo immediate coronary angiography

One hundred and two patients (66 ± 18 years, 92 men) were admitted after OHCA between January 2011 and December 2015, who did not require CA. Sixty two patients (61%) arrived at our department under ongoing CPR without ROSC. From all patients who did not undergo immediate CA 90 patients (88%) died in hospital and 12 patients (12%) survived to discharge. Sixteen patients (16%) suffered from pulmonary embolism, four patients (4%) had aortic dissection, four patients (4%) had severe aortic valve stenosis, five patients (5%) had respiratory failure, two patients (2%) had ventricular rupture and pericardial tamponade after subacute myocardial infarction, two patients (2%) with terminal dilated cardiomyopathy, one patient (1%) had primary left ventricular sarcoma, one patient (1%) had long QT syndrome, one patient (1%) had hypertrophic cardiomyopathy, the remaining patients had unknown etiology of CPR.

Coronary angiography was not performed because of the following reasons:

1. Long duration of CPR without ROSC
2. Severe metabolic derangement on admission
3. The first work-up showed noncoronary artery reasons for CPR as: pulmonary embolism or aortic dissection.

### 3.3 Diagnostic efficiency of blood values at admission to predict in-hospital mortality in OHCA patients who did undergo immediate CA

In order to evaluate the diagnostic efficiency of blood values at admission to predict in-hospital mortality in patients with OHCA, ROC analysis was performed (Figure 3).

**FIGURE 3** Panel (a): Receiver operating characteristic curve analysis of lactate level of 219 patients with out-of-hospital cardiac arrest (OHCA) as predictor for death in hospital showing the cut-off value of >7 mg/100 ml as the most appropriate for maximizing both sensitivity (59.5%) and specificity (82.1%). Panel (b): Receiver operating characteristic curve analysis of pH level of 219 patients with OHCA as predictor for death in hospital showing the cut-off value of <7.16 as the most appropriate for maximizing both sensitivity (53.4%) and specificity (85.3%). Panel (c): Receiver operating characteristic curve analysis of glucose level by 219 patients with OHCA as predictor for death in hospital showing the cut-off value of >260 mg/dL as the most appropriate for maximizing both sensitivity (64.4%) and specificity (80.6%).
**TABLE 3** baseline demographic and clinical data by ROSC status

|                     | CA without ROSC | CA with ROSC | p value |
|---------------------|-----------------|--------------|---------|
| Male, n (%)         | 37 (66%)        | 123 (75%)    | .172    |
| Age (years, mean ± SD) | 64 ± 13         | 63 ± 13      | .994    |
| Coronary artery disease, n (%) | 47 (81%) | 119 (73%) | .100 |
| Single vessel disease, n (%) | 15 (27%) | 35 (21%) | .414 |
| Multi-vessel disease, n (%) | 32 (57%) | 84 (51%) | .469 |
| STEMI, n (%)        | 21 (37%)        | 50 (31%)     | .347    |
| CPR-duration (minutes) | 75 ± 32         | 24 ± 18      | <.001   |
| Initial arterial pH | 6.99 ± 0.2      | 7.2 ± 0.16   | <.001   |
| Initial arterial lactate (mmol/L) | 13 ± 5 | 6.4 ± 5.0 | <.001 |
| Glucose (mg/dl)     | 376 ± 133       | 249 ± 104    | <.001   |
| Uric acid (mg/dl)   | 8.5 ± 2.0       | 7.8 ± 2.3    | .105    |

Abbreviations: CA, coronary angiography; CPR, cardiopulmonary resuscitation; OHCA, out of hospital cardiac arrest; PCI, percutaneous coronary intervention.

**3.4 Subgroup of patients without ROSC before angiography**

Of the 56 patients without ROSC with coronary angiography under CPR using LUCAS device 34 patients had an initial shockable rhythm. Thirty patients were successfully treated with PCI under ongoing resuscitation, whereas in five patients the attempted PCI was unsuccessful. These 56 patients had longer CPR durations compared to patients with ROSC (75 ± 32 vs. 24 ± 18 min, p < .001), higher glucose levels, lower initial pH values and higher levels of lactate on admission. Despite the high rate of successful PCI under these extreme circumstances, only one patient, a 56-year-old male survived to hospital discharge after initial 100 min of CPR and successfully recanalization of LAD. Table 3 presents the summary on these patients and the interventions received.

**4 DISCUSSION**

Data regarding the impact of immediate coronary angiography after OHCA with and without ROSC on clinical outcome are scarce. Major findings of this retrospective single academic center study are as follows: (a) one third of patients survived to discharge after OHCA and immediate coronary angiography. (b) Mortality in patients without previous ROSC was extremely high. (c) Immediate coronary angiography with ongoing CPR using LUCAS device was technically feasible with a high rate of successful PCI but a high mortality. (d) Older age, metabolic derangement on admission, initial nonshockable rhythm, and failure to achieve ROSC before admission predict hospital mortality.

There are no randomized studies investigating the impact of immediate coronary angiography in patients after OHCA on clinical outcome. Larsen and his college9 reported in meta-analysis of ten comparative studies (3,103 patients) that acute coronary angiography was associated with improved survival. Callaway and his college10 demonstrated in a multicenter study between 2007 and 2009 with 3,981 patients that early coronary angiography was an independent predictor for survival and favorable outcome. More recently Khan et al.11 showed in a meta-analysis of eight studies (seven observational studies and one randomized study) that the use of coronary angiography was associated with decreased short-term (OR 0.46; 95% CI 0.36–0.56, p < .001) and long-term (OR 0.59; 95% CI 0.44–0.74, p < .001) mortality. Predictors of in-hospital mortality in our study were older age, metabolic derangement on admission, initial nonshockable rhythm and failure to achieve ROSC before admission.

These results are in line with several other studies. Martenelli et al.12 performed a post hoc analysis of 933 patients with OHCA of presumed cardiac cause. She identified ten independent predictors of poor clinical outcome: older age, cardiac arrest occurring at home, initial rhythm other than ventricular fibrillation/tachycardia, longer duration of no flow, longer duration of low flow, administration of adrenaline, bilateral absence of corneal and pupillary reflexes, Glasgow Coma Scale motor response 1, lower pH and a partial pressure of carbon dioxide in arterial blood value lower than 4.5 kPa at hospital admission. Momiyama et al.13 showed that patients with favorable outcome after OHCA had lower lactate and higher pH levels. Daviaud et al.14 observed a relationship between high blood glucose level and unfavorable clinical outcome after OHCA. Our study extends current knowledge by the above-mentioned studies.

To the best of our knowledge, there are no studies presently available assessing the potential benefit of an immediate coronary...
angiography in patients presenting with OHCA without ROSC with ongoing mechanical CPR using the LUCAS device. We found in this study an extremely high hospital mortality for patients with OHCA, who arrived at our catheterization laboratories under CPR and underwent CA with attempted PCI during CPR. Wagner et al.\textsuperscript{15} reported a large series of 43 patients, who developed cardiac arrest while in cathlab, in which then PCI was attempted in 36 of them with CPR using the LUCAS device. Eleven patients from those patients were discharged in a good neurologic condition. It is important to consider that all patients by Wagner had only developed cardiac arrest while already in the cathlab, while all our patients suffered from OHCA. We found that coronary angiography with ongoing CPR using the LUCAS device was technically feasible and attempted PCI was successfully performed without significant difference compared to the patients with successful CPR. In these patients, in which angiography was preformed while CPR was performed, ROSC could be achieved in a large proportion due to successful PCI. However, overall clinical outcome remained extremely poor with only one patient out of 56 surviving to discharge. This is highly suggestive of PCI in these circumstances being a futile treatment for a patient centric outcome.

Other studies have evaluated the use of mechanical chest compression system by patients with OHCA in wide spectrum not only in the context of coronary angiography. Hallstrom and college\textsuperscript{16} reported in a multicenter, randomized trial of patients with OHCA (1,071 patients) that the use of an automated LDB-CPR device was associated with poor neurological outcomes and a trend toward worse survival than manual CPR. More recently Gates et al.\textsuperscript{17} failed to demonstrate a difference regarding clinical outcomes at 30 days between mechanical CPR using LUCAS-2 device compared to manually compression in multicenter, randomized trials. These observations correspond to our results, that the LUCAS device showed no improvement in hospital survival by patients with OHCA.

Overall, we think our findings support a strategy of performing immediate coronary angiography in patients with OHCA with high likelihood of cardiac origin if ROSC can be achieved prior to admission to the hospital. Whenever this is not the case, angiography with ongoing CPR is possible, but due to the expected detrimental outcomes, patients eligible for such a treatment must undergo a careful selection to avoid futile treatments in many patients who will clearly not benefit from such an approach.

5 | LIMITATIONS

This was a retrospective, monocenter study including only patients with OHCA and immediate coronary angiography. Furthermore, there was no long-term follow-up and no parameters of neurological outcome for survivors were recorded. In some patients only clinical, laboratory, or ECG parameters were offered, while extended diagnostic imaging to detect the reasons of death, especially by patients without ROSC were not available.

6 | CONCLUSIONS

In patients with OHCA with suspected cardiac origin who underwent immediate CA older age, metabolic derangement on admission, initial nonshockable rhythm, and failure to achieve ROSC before admission were predictors of hospital mortality. While ANGIO under ongoing CPR with the LUCAS-device was feasible, mortality in patients without previous ROSC was extremely high, questioning whether this approach is medically useful.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DISCLOSURE

All authors have participated in the work and have reviewed and agree with the content of the article.

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