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Clinical Paper

Prognostic implication of out-of-hospital cardiac arrest in patients with cardiogenic shock and acute myocardial infarction☆

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ABSTRACT

Objectives: To compare outcome in patients with acute myocardial infarction (MI) and cardiogenic shock (CS) presenting with and without out-of-hospital cardiac arrest (OHCA).
Background: Despite general improvement in outcome after acute MI, CS remains a leading cause of death in acute MI patients with a high 30-day mortality rate. OHCA on top of cardiogenic shock may further increase mortality in these patients resulting in premature withdrawal of supportive therapy, but this is not known.
Methods and results: In a retrospective study from 2008 to 2013, 248 consecutive patients admitted alive to a tertiary centre with the diagnosis of CS and acute MI were enrolled, 118 (48%) presented with OHCA and 130 (52%) without (non-OHCA patients). Mean lactate level at admission was significantly higher in OHCA patients compared with non-OCHA patients (9 mmol/l (SD 6) vs. 6 mmol/l (SD 4) $p < 0.0001$). Co-morbidities were more prevalent in the non-OHCA group. By univariate analysis age (Hazard ratio (HR) = 1.02 [CI 1.00–1.03], $p = 0.01$) and lactate at admission (HR = 1.06 [CI 1.03–1.09], $p < 0.001$), but not OHCA (HR = 1.1 [CI 0.8–1.4], p = NS) was associated with mortality. In multivariate analysis, only age (HR = 1.02 [CI 1.01–1.04], $p = 0.003$) and lactate level at admission (HR = 1.06 [1.03–1.09], $p < 0.001$) were independent predictors of mortality. One-week mortality was 63% in the OHCA group and 56% in the non-OHCA group, p = NS.
Conclusion: OHCA is not an independent predictor of mortality in patients with acute MI complicated by cardiogenic shock. This should encourage active intensive treatment of CS patients regardless of OHCA.

1. Introduction

1.1. Background

Acute myocardial infarction (MI) complicated by cardiogenic shock (CS) is one of the most serious acute medical conditions with mortality rates of at least 40–50% in randomized clinical trials (RCT).[1–5] The SHOCK trial assessing the effect of early aggressive revascularization showed 30-day mortality rates of 46% in patients treated with primary percutaneous coronary intervention (pPCI) or coronary artery bypass graft (CABG) and 6-month mortality of 50%.[1] The recent IABP-SHOCK II study, assessing the effect of intra aortic balloon pump (IABP) counter pulsation, found 30-day and one-year mortality rates of 40% and 50%.[3,4] Mortality rates remain high today and presumably even higher in the real life clinical setting in CS patients not included in RCTs. Approximately 5% of patients with acute MI develop cardiogenic shock (CS).[6–9] Out-of-hospital cardiac arrest (OHCA) is estimated to occur in one in fifty MI patients, and is associated with increased early mortality in patients with ST-elevation myocardial infarction.[10] Furthermore, many OHCA patients also develop CS.[11] However, whether MI patients presenting with both OHCA and CS have increased mortality is not known. We therefore aimed to compare outcome

Abbreviations: IABP, intra aortic balloon pump; CABG, coronary arterial bypass graft; CPR, cardio pulmonary resuscitation; ROSC, return of spontaneous circulation; acute MI, acute myocardial infarction; CS, cardiogenic shock; OHCA, out of hospital cardiac arrest; ICCU, intensive cardiac care unit.

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in patients with acute MI and CS presenting with or without OHCA to evaluate if OHCA further increases the mortality rate in CS.

2. Methods

2.1. Inclusions

Consecutive patients presenting with CS complicating acute MI admitted to a tertiary Danish high volume PCI centre in the period from January 1st 2008 to February 1st 2013 were included. Initial registration with the diagnosis of CS was found in 517 patients. Two hundred and forty-eight patients with acute MI complicated by CS were included. The 269 excluded patients were in CS due to non-ischaemic causes (pulmonary embolism, septicaemia, hypovolemia etc.). CS was defined according to the SHOCK trial as a systolic blood pressure less than 90 mmHg and/or the need for vasopressor/inotropic agents to maintain a systolic blood pressure above 90 mmHg, and signs of organ hypoperfusion with cold extremities, and reduced urine output or an arterial lactate level above 2 mmol/l. Acute MI was defined according to current guidelines.[12,13] OHCA was defined as patients having received pre-hospital cardiopulmonary resuscitation. Only patients with return of spontaneous circulation (ROSC) were enrolled. Prehospital data and OHCA were registered in specific national prehospital ambulance records. Sex, age and co-morbidities in terms of hypertension, diabetes, nephropathy, pulmonary disease, alcohol/substance abuse and cancer were registered by reviewing charts for all patients. Patients with other causes of shock and patients without ROSC were excluded.

2.2. Physiologic characteristics and in-hospital management

Baseline haemodynamics, in-hospital haemodynamics, treatment variables, and mortality data were collected from hospital records.

In-hospital management and blood gas levels were collected from the intensive cardiac care unit (ICCU) database. Left ventricular ejection fraction (LVEF), evaluated by echocardiography at admission was recorded if available.

The use of pharmacological circulatory support with adrenaline (epinephrine), noradrenaline (norepinephrine) and/or dopamine, additional circulatory support and time of initiation of mechanical circulatory support using Intra Aortic Balloon Pump (IABP) and/or Impella pump, mechanical respiratory support and haemodialysis were registered according to the ICCU database and charts.

2.3. Outcomes

Time of death or time of ICU discharge was registered in the ICCU. Long-term mortality was obtained from The Civil Registration System, which holds information on all Danish citizens, by a unique civil personnel registration number.

2.4. Statistics

Data are presented as mean ± standard deviation (SD) for continuous, normal distributed data or median and interquartile range for non-normal data, as appropriate. Categorical data are presented as number and percentage. Comparison between groups was performed using Students *t*-test or rank-test, and χ^2-test when appropriate.

Survival rates are presented as Kaplan–Meier plots, and differences between groups tested by log-rank test. Proportional hazard models (Cox) were applied to calculate hazard ratio (HR and 95% confidence intervals (95% CI)). Multivariable modelling was used to adjust for potential confounders. The underlying assumption of linearity, proportionality and lack of interactions was tested. An α-level of 5% was used. All statistical computation was performed using the SAS statistical software version 9.13, Cary, NC, USA.

3. Results

3.1. Demographics

In total 248 patients were admitted with CS complicating acute MI (Fig. 1 and Table 1). In 118 patients (48%) initial presentation was OHCA with ROSC after 25 min (SD 18). Initial rhythm was ventricular fibrillation or pulseless ventricular tachycardia in 76 patients (64%), and cardiac arrest was witnessed in 84 cases (71%), with bystander cardiopulmonary resuscitation initiated in 69 (58%) of OHCA cases. Patients in the OHCA group were younger (64 years (SD 13) vs. 68 years (SD 12), $p = 0.03$) than non-OHCA patients. Patients in the non-OHCA group more often had a history of hypertension, diabetes mellitus, pulmonary disease and renal dysfunction (Table 1 and Fig. 2).

3.2. Characteristics at hospital admission

Haemodynamic parameters in terms of blood pressure and LVEF% were not significantly different in the CS patients with and without OHCA, however heart rate was lower in the OHCA group, Table 2. Both metabolic and respiratory acidosis was more profound in OHCA patients with higher lactate concentration (9 mmol/l (SD 6) vs. 6 mmol/l (SD 4) $p < 0.0001$), lower base excess (−11.8 (SD 6.2) vs. −6.7 (SD 9.8) $p < 0.0004$). Blood glucose was higher in OHCA than non-OHCA (Table 2).

3.3. In-hospital management

In the ICCU 92% of all patients were mechanically ventilated. However, significantly more patients in the OHCA group 97% than the non-OHCA group 88%, $p = 0.004$. The non-OHCA group also had a higher frequency of haemodialysis and use of temporary pacemakers. Circulatory support with IABP was used in 28% of all patients with majority in the non-OHCA group whereas an Impella pump was used in 16% of all patients almost equally distributed in both groups. Both groups where treated equally with adrenaline, noradrenaline and dopamine infusion. Four percent were treated with bail out acute surgical assistance in terms of coronary artery bypass grafting and/or valve replacement. Seventy eight percent of all patients received coronary angiography (CAG). Successful pPCI was performed in 84% in the non-OHCA group and 89% in the OHCA group. Total pPCI success rate was 87% overall (Table 3).

3.4. Univariate and multivariate risks of mortality

One-week mortality was 63% in the OHCA group and 56% in the non-OHCA group, p = NS. Median follow up time was 5 days with a maximum of 2149 days (5,8 years). Long-term mortality was 76% among OHCA patients and (77%) in the non-OHCA patients. OHCA was not a significant and independent predictor of excess long-term mortality neither in the univariate analysis (HR = 1.08 [CI 0.82–1.44], p = NS), nor in the multivariate analysis (HR = 1.05 [CI 0.79–1.40], p = NS). When excluding patients dying within the first 7 days, OHCA was still not significantly associated with mortality (Table 4).

Regarding other risk factors of mortality we performed univariate and multivariate analyses. In the univariate models two significant predictors of mortality were found: age (HR = 1.02 [CI 1.00–1.03], $p = 0.01$) and lactate levels at admission (HR = 1.06 [CI 1.03–1.09], $p < 0.001$). Similarly, in the multivariate model,