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Clinical paper

Timing of coronary angiography in survivors of out-of-hospital cardiac arrest without obvious extracardiac causes

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ABSTRACT

Background: Indications and timing of coronary angiography in patients surviving out-of-hospital cardiac arrest (OHCA) remain controversial. The aim of the present study was to assess the impact of an early invasive strategy in patients presenting with an OHCA and no obvious extracardiac cause.
Methods: Between January 1st 2009 and December 31st 2014 a total 612 survivors of OHCA were admitted to our institution. Patients with no obvious extracardiac cause (n = 507) were stratified into two groups: patients that underwent cardiac catheterization ≤3 h (early invasive; n = 291) and patients not undergoing cardiac catheterization within 3 h (non-early invasive; n = 216). Primary endpoint was all-cause mortality at 30 days.
Results: All-cause 30-day mortality was 28.9% in the early invasive group vs. 36.6% in the non-early invasive group (log-rank p = 0.071). After propensity analyses, an early invasive strategy, as compared to a non-early strategy, was not associated with 30-day mortality (adjusted Hazard ratio [HR] 0.69; 95% CI 0.35–1.37; p = 0.029). Cox multivariable regression analyses demonstrated age (HR 1.04/year; 95% CI 1.02–1.07) and presentation with cardiogenic shock (HR 5.1; 95% CI 1.8–14.0) to be the sole independent predictors of 30-day mortality.
Conclusions: In this retrospective study, early coronary angiography (<3 h), as compared to a non-early invasive strategy, was not associated with reduced 30-day mortality in patients hospitalized after OHCA, irrespective of the presence of ST segment elevation or cardiogenic shock at presentation.

Introduction

Out-of-hospital cardiac arrest (OHCA) remains a challenging clinical problem frequently characterized by an unclear etiology and an overall poor survival [1]. Acute coronary thrombotic occlusion has been identified as the leading cause of OHCA and recent studies suggest that an early invasive strategy including immediate percutaneous coronary intervention (PCI) might improve outcome in selected patients [2–5]. In practice though, identification of those likely to benefit from an early invasive strategy is difficult and there is currently no dedicated prospective study confirming a benefit of an immediate invasive strategy in comatose survivors of OHCA, irrespective of the presence of ST-segment elevation [3]. Most previous studies focused on patients already selected for an immediate invasive strategy precluding any statements on when and if a patient should be referred coronary angiography [2,6].

The aim of the present study was to assess differences in 30-day mortality rates of an early invasive strategy as compared to a non-early invasive strategy in a large cohort of all-comer survivors of OHCA without obvious extracardiac causes presenting at a tertiary referral center.

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass surgery; CAD, coronary artery disease; CAG, coronary angiography; Cathlab, catheterization laboratory; CK, creatine kinase; CKMB, creatine kinase myocardial band; HR, hazard ratio; hsTnT, high sensitivity troponin T; MAP, mean arterial pressure; No-STE, No ST-segment elevation; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; SaO2, oxygen saturation; SD, standard deviation; STE, ST-segment elevation; ULN, upper limit of normal.

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Methods

Patients and treatment

This retrospective observational cohort study included 612 patients presenting with an OHCA at Erasmus Medical Centre Rotterdam (NL) between January 1st 2009 and December 31st 2014. Medical records review was performed by scrutinizing emergency room and intensive care admission reports, cathlab procedure reports, ECG data and laboratory results to acquire full patient data and to assess the presence of clear extracardiac causes (being mainly pulmonary embolism, stroke). All patient files were digitally available in our hospital throughout the entire study period. All other causes (ST-elevation, ST-depression, ventricular fibrillation and a history of coronary artery disease, new bundle branch block, AV block with suspicion of inferior myocardial infarction) were classified as possible ACS cases. Analyses were performed on those presenting with no obvious extracardiac cause of OHCA. Therapeutic hypothermia (33 °C) on hospital admission was systematically implemented in all patients during the first 24 h unless contraindicated. A high-resolution CT scan at admission was made in all patients with a suspicion of (head) trauma, stroke or pulmonary embolism. The final decision to refer a patient for an early invasive strategy was left at the discretion of the involved team (cardiologist, anesthesiologist and interventional cardiologist on-call) with an overall low threshold for an early invasive strategy in case an acute coronary problem was deemed likely.

This study was not subject to the Dutch Medical Research Involving Human Subjects Act. Consequently, approval from the local research ethics committee to conduct this retrospective observational cohort study was not required at the time of enrolment. Moreover, this study was conducted according to the Helsinki Declaration.

Study endpoints

The primary endpoint was all-cause mortality at 30 days. Secondary endpoint was all-cause mortality at one-year. Survival status was ascertained using hospital medical records or municipal civil registry. One-year follow-up was complete for 100% of the patients.

Socio-demographic characteristics comprised age and gender. Clinical characteristics comprised cardiac history (previous myocardial infarction, previous stroke, previous coronary artery bypass surgery (CABG) or PCI), and cardiovascular risk factors (hypercholesterolemia, smoking, diabetes mellitus, hypertension, family history of coronary artery disease, and body mass index (BMI)). Clinical parameters at admission included blood pressure, heart rate, hemoglobin (mmol/L), SaO2 (Oxygen Saturation, %), pH, temperature (degrees Celsius), CK (U/L), CKMB (μg/L), hsTnT (ng/L), lactate (mmol/L), time to ROSC, Cardiogenic shock). Cardiogenic shock was defined as a systolic blood pressure of <90 mmHg longer than 30 min or use of inotropic medication.

Statistical data analysis

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables are expressed as percentages. Continuous variables were compared using Student's *t*-test or one-way ANOVA. Pearson's Chi-Square test was used for categorical variables. Patients were stratified into 2 groups; patients that underwent cardiac catheterization ≤3 h, and patients not undergoing cardiac catheterization within 3 h.

The incidence of mortality over time was studied with the use of the Kaplan-Meier method, whereas the log-rank test was applied to evaluate differences between the treatment groups. Cox proportional-hazards regression analyses were applied to adjust for potential confounders. Variables with $p < 0.10$ in the univariate analyses were entered in the multivariable Cox proportional hazards models. Control of potential confounders was attempted by constructing a propensity score using logistic regression. The propensity score was the probability that a patient would undergo an early invasive strategy, and was computed using an extensive, non-parsimonious, logistic regression model including the following variables: age, sex, body-mass index (BMI), smoking, previous myocardial infarction, previous CABG, time of OHCA, time until return of spontaneous circulation (ROSC), ST- segment elevation on the electrocardiogram, hemoglobin level at admission, saturation, mean arterial pressure at admission, temperature, lactate level at admission and pH at admission. The selection of the variables was made so as to get the best discriminating model as assessed by the C-statistics. Final results are presented as adjusted hazard ratios with 95% confidence interval. Statistical analyses were performed using SPSS (version 21.0). All statistical tests are 2-tailed.

Sensitivity analyses were performed in order to test the heterogeneity of the treatment effect in patients presenting with STE, No-STE and shock as well as a definition of early invasive being 2 h and 6 h.

Results

This retrospective cohort consists of 612 patients presenting with an OHCA. Analyses were performed on those presenting with no obvious extracardiac cause of OHCA (n = 507) (Fig. 1). Of the 507 patients, 291 underwent cardiac catheterization ≤3 h (early invasive group) and 216 patients did not undergo cardiac catheterization ≤3 h (non-early invasive group. In the non-early invasive group, 100 patients underwent in-hospital cardiac catheterization later than 3 h after hospital admission at an average of 4120 ± 7116 min (corresponding to 69 ± 119 h). A total of 116 patients did not undergo coronary angiography.

Timing of angiography

Table 1 presents the differences between patients that underwent early invasive or non-early invasive treatment. In brief, patients in the early invasive group were younger and presented more often with ST-segment elevation and/or cardiogenic shock, had a lower MAP and temperature and higher cardiac enzymes at admission however, they also had a higher mean Hb and SaO2 at admission. Coronary artery disease was present in 84% of the patients in the early invasive group vs. 79% in the patients that underwent in-hospital angiography >3 h (n = 100) in the non-early invasive group. PCI was performed in 72% of the patients in the early invasive group versus 23% of the non-early group. All-cause 30-day mortality was 28.9% in the early invasive group and 36.6% in the non-early group (log-rank p-value 0.071) (Fig. 2). All-cause 1-year mortality was 32.3% in the early invasive group and 40.7% in the non-early group (p = 0.055). Propensity adjusted cox multivariable regression analyses demonstrated age (HR 1.04/year; 95% CI 1.02 −1.07) and presentation with cardiogenic shock (HR 5.1; 95% CI 1.8–14.0) to be the sole independent predictors of 30-day mortality while catheterization within 3 h was not associated with 30-day mortality (HR 0.69; 95% CI 0.35–1.37) (Table 2).

Sensitivity analyses

ST-segment elevation (STE) at presentation was present in 220 patients (43%) while ST-segment elevation was absent (No-STE) in the remaining 287 patients (57%). Cumulative 30-day all-cause mortality was 32.8% in patients presenting with No-STE vs. 31.4%

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