Clinical Paper

Early coronary angiography and induced hypothermia are associated with survival and functional recovery after out-of-hospital cardiac arrest☆

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ABSTRACT

Background: The rate and effect of coronary interventions and induced hypothermia after out-of-hospital cardiac arrest (OHCA) are unknown. We measured the association of early ($\leq$24 h after arrival) coronary angiography, reperfusion, and induced hypothermia with favorable outcome after OHCA.

Methods: We performed a secondary analysis of a multicenter clinical trial (NCT00394706) conducted between 2007 and 2009 in 10 North American regions. Subjects were adults ($\geq$18 years) hospitalized after OHCA with pulses sustained $\geq$60 min. We measured the association of early coronary catheterization, percutaneous coronary intervention, fibrinolysis, and induced hypothermia with survival to hospital discharge with favorable functional status (modified Rankin Score $\leq$ 3).

Results: From 16,875 OHCA subjects, 3981 (23.6%) arrived at 151 hospitals with sustained pulses. 1317 (33.1%) survived to hospital discharge, with 1006 (25.3%) favorable outcomes. Rates of early coronary catheterization (19.2%), coronary reperfusion (17.7%) or induced hypothermia (39.3%) varied among hospitals, and were higher in hospitals treating more subjects per year. Odds of survival and favorable outcome increased with hospital volume (per 5 subjects/year OR 1.06; 95%CI: 1.04–1.08 and OR 1.06; 95%CI: 1.04, 1.08, respectively). Survival and favorable outcome were independently associated with early coronary angiography (OR 1.69; 95%CI 1.06–2.70 and OR 1.87; 95%CI 1.15–3.04), coronary reperfusion (OR 1.94; 95%CI 1.34–2.82 and OR 2.14; 95%CI 1.46–3.14), and induced hypothermia (OR 1.36; 95%CI 1.01–1.83 and OR 1.42; 95%CI 1.04–1.94).

Interpretation: : Early coronary intervention and induced hypothermia are associated with favorable outcome and are more frequent in hospitals that treat higher numbers of OHCA subjects per year.

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1. Introduction

Out-of-hospital cardiac arrest (OHCA) is the third leading cause of death in North America, afflicting an estimated 382,000 persons in the US per year,[1] with a case-mortality rate of 94.7%.[2] Reversal of cardiac arrest requires rapid restoration of cardiac activity using defibrillation, reperfusion, mechanical or pharmacological support.

Differences between communities and emergency medical services (EMS) response systems contribute to differences in survival after OHCA between regions.[2,3]

In-hospital interventions after OHCA[4–7] may prevent secondary injury and ameliorate ischemia-reperfusion injury to multiple organs, especially the heart and brain.[8] Induced hypothermia,[9,10] coronary artery reperfusion,[11–13] hemodynamic optimization,[7,14] ventilator management[15] and neurological prognostication[16] all can influence outcomes. However, the use of these interventions is variable. While there are a number of European studies about the prevalence of hypothermia implementation,[17–19] in North America neither the prevalence of these intervention nor the relationship of these interventions with patient outcomes have been measured.

This study was a planned secondary analysis of a randomized controlled trial to examine the relationship between in-hospital interventions and outcomes after OHCA in a large North American network. The parent trial tested the influence of two EMS interventions, which were found to have no effect on outcome.[20,21] The primary hypothesis of this study was that early coronary angiography or reperfusion and induced hypothermia are associated with survival and favorable functional status after OHCA.

2. Methods

2.1. Study design and setting

Between June 2007 and October 2009, 10 US and Canadian clinical sites in the Resuscitation Outcomes Consortium (ROC) enrolled consecutive OHCA patients treated by 150 EMS agencies in a multicenter, randomized controlled trial (ROC-PRIMED; clinicaltrials.gov NCT00394706). This trial tested the effect on functional recovery and on survival to hospital discharge of performing cardiopulmonary resuscitation (CPR) for a brief (~30 s) interval or for 3 min prior to rhythm analysis and defibrillation attempt for ventricular fibrillation (VF). The trial simultaneously compared the effect of using an impedance threshold device (ITD) with using a sham device. Neither the CPR strategies nor the ITD device affected survival or functional outcome.[20,21]

Institutional review boards or research ethics boards at all sites and hospitals granted an Exception from Informed Consent for enrollment. As soon as feasible, we notified surviving subjects or their legally authorized representatives about the study and provided opportunity to withdraw from continued data collection. We reviewed hospital medical records for all subjects until hospital discharge. Primary outcomes were available for all subjects in this secondary study.

2.2. Patient population

This secondary analysis studied all screened or randomized adult (age > 18 years) subjects with OHCA, defined as receiving chest compressions from a professional provider or a rescue shock from a defibrillator. We included only subjects who were delivered to any of 151 participating hospitals with a pulse or who regained a pulse in the emergency department, and who survived for >60 min after hospital arrival, because these subjects were potential recipients of in-hospital interventions. We excluded subjects for whom resuscitation efforts were discontinued prior to hospital arrival or for whom no pulse was established even after hospital arrival (Fig. 1). Patients with EMS-witnessed cardiac arrest and patients with tracheostomies were included although these subgroups were excluded from some out-of-hospital interventions in ROC-PRIMED. We excluded prisoners, pregnant women, patients with "do not resuscitate" directives made prior to EMS treatment, and patients
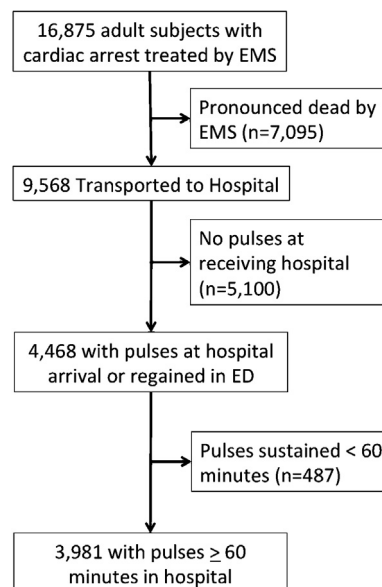

Fig. 1. Subjects included and excluded from analysis.

with blunt, penetrating or burn-related trauma or with cardiac arrest due to exsanguination.

2.3. Data collection

Research coordinators abstracted data into web-based case report forms from EMS and hospital records and from the electronic data captured by EMS monitor–defibrillators. The Data Coordinating Center trained data abstractors, provided on-line assistance with ambiguous cases, and performed site visits and audits to ensure data integrity. Automated within-form and between-form data checks followed by written resolution of conflicting data were performed to reduce errors.

2.4. Interventions and covariates

We recorded whether any coronary angiography was performed, whether the angiography was early (<24 h from admission) or >24 h after admission, and whether a percutaneous coronary intervention (PCI) was performed. More precise timing of PCI was not available in this dataset. We noted the acute administration of any fibrinolytic drugs. Because acute coronary artery reperfusion can be accomplished using fibrinolysis or PCI, we examined a composite intervention of early coronary reperfusion therapy (any fibrinolysis or PCI).

We defined induced hypothermia as any active attempt to lower core body temperature at the hospital. We recorded the time of the first attempt to initiate hypothermia, the time when rewarming began, and the lowest temperature achieved. In this cohort, documented efforts to lower body temperature by EMS were rare (n = 188 cases), and the time of initiation of hypothermia for those cases was defined as the time of hospital arrival.

We recorded the presence or absence of ST-elevation myocardial infarction (STEMI) on the first ECG obtained at the hospital, in-hospital events (stroke, seizures, bleeding requiring transfusion, pulmonary edema, recurrent cardiac arrest, organ failure, pneumonia or sepsis, myocardial infarction at any time), and hospital length of stay.

Prior studies using different data sets reported associations between the number of cardiac arrest subjects treated at each