Journal of Critical Care 32 (2016) 56–62

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Can mortality due to circulatory failure in comatose out-of-hospital cardiac arrest patients be predicted on admission? A study in a retrospective derivation cohort validated in a prospective cohort☆

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ARTICLE INFO

Keywords:
Cardiac arrest
Circulatory failure
Prognostic factors
Mode of death
Circulatory assistance
Catecholamine treatment

ABSTRACT

Purpose: Circulatory failure (CF) influences management of out-of-hospital cardiac arrest (OHCA) patients and the decision of circulatory assistance. We performed a study to identify on hospital admission patients at risk for CF-related death.
Materials and methods: This is a single-center study including OHCA patients without obvious extracardiac cause and sustained return of spontaneous circulation, in a retrospective derivation (RC) and prospective validation cohort (PC). Univariate/multivariate logistic regression was used in the RC to determine a score predicting CF-related death (due to rearrest or persistent shock despite adequate fluid and catecholamine treatment). The score was validated in the PC.
Results: We included 207 patients in the RC and 96 in the PC. Circulatory failure occurred in 59% of RC and 63% of PC patients ($P = .70$); 35% in both cohorts died of CF. In multivariate regression, correlates of CF-related death making up the logistic score were arterial pH ($P < .0001$) and shock requiring catecholamines on admission ($P = .0045$). In the PC, for a logistic score cut-off of 0.5, sensitivity for CF-related death was 50%; specificity, 92%. Patients with shock and arterial pH less than or equal to 7.11 had a CF-related death probability greater than 0.5.
Conclusion: A logistic score based on arterial pH and shock requiring catecholamines on admission can predict CF-related death in OHCA patients.

1. Introduction

Despite continuous efforts to improve outcome [1,2], many patients resuscitated from out-of hospital cardiac arrest (OHCA) die due to prehospital or inhospital rearrest, due to the onset of shock during the first days of hospitalization, and later due to the complications of postanoxic brain injury [3]. Neurologic failure and circulatory failure (CF) are the most frequent modes of death of OHCA patients [3] after resuscitation, and efforts should be made to improve circulatory and neurologic status to improve survival.

Circulatory failure is frequently present during the postresuscitation phase due to a high incidence of acute myocardial infarction (AMI) [2,4] and myocardial dysfunction and/or vasodilation caused by the postresuscitation syndrome [5]. The presence of CF is associated with increased mortality [6,7], but little data exist regarding patients in whom CF is the direct cause of death after resuscitation from OHCA. This is an important issue because the optimization of catecholamine therapy and the use of circulatory assistance devices may improve circulatory function and prognosis. In some patients, circulatory assist devices may allow for cardiac function improvement in reversible conditions such as revascularized AMI [8] or myocarditis. Even when CF is not fatal in the first hours after resuscitation, it may lead to multiple

☆ Funding: None.
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http://dx.doi.org/10.1016/j.jcrc.2015.11.007
0883-9441/

organ failure by inducing and/or worsening vital organ ischemia [9-11]; therefore, CF may represent an important therapeutic target.

Several predictors including blood pressure, lactate concentration, and the type and rate of infusion of catecholamines were reported as criteria for assessing severity of the CF [6,7]. Moreover, several studies attempted to predict death in OHCA patients by identifying prognostic factors and creating prognostic scores on admission or in the first days after the OHCA [12,13]. However, these studies attempted to predict inhospital death irrespective of the system failure that induced it (neurologic, circulatory, or other) and the question remains as to which patients will die of CF despite appropriate catecholamine treatment. Reversal of CF is more effective if initiated early during the hospital stay to avoid multiple-organ failure (MOF) [10,11], and these patients should be identified as early as possible. We therefore performed a study to determine on admission to the hospital the predictors of death due to CF in patients resuscitated from an OHCA. The study used a retrospective derivation cohort to determine a logistic score predictive of death due to CF and a prospective cohort to validate the results.

2. Materials and methods

This single-center observational study was conducted according to the principles of the Declaration of Helsinki (2008 version) of the World Medical Association. The national French Ethics Committee approved the study (CE 11-330). According to the ethics committee recommendations, no signed informed consent was required from the patients or the next of kin. According to the French law, in the prospective cohort, information was provided to patients when conscious or the next of kin if patients remained unconscious. Patients were excluded if they or their next of kin refused participation in the study.

We screened all patients aged at least 18 years old admitted to our center for OHCA between January 2002 and October 2011. Patients were included irrespective of the initial rhythm of the OHCA. We excluded patients without sustained return of spontaneous circulation (ROSC), patients in whom the cardiac arrest occurred in the hospital or was obviously due to a noncardiac cause (including obvious hypoxemia, trauma, hemorrhagic or septic shock, drowning, hypothermia, and drug poisoning), and patients in whom the mode of death in the intensive care unit (ICU) could not be determined.

Inclusions were performed from 2002 to 2008 in the retrospective cohort and from 2009 to 2011 in the prospective cohort.

2.1. Management of the patients

The emergency medical system in Paris, France, has been previously described [14]. Resuscitation in the prehospital phase includes defibrillation, mechanical ventilation, venous access, and catecholamine treatment according to guidelines [15]. After effective resuscitation in the prehospital setting, the emergency team continues mechanical ventilation, sedation, and hemodynamic optimization using fluid repletion and/or catecholamine treatment. Blood pressure is measured noninvasively.

Presence of shock was defined in our study by the presence of systolic blood pressure less than 90 mm Hg despite at least 30 mL/kg fluid repletion [10]. Dobutamine, noradrenaline, or adrenaline is used in the prehospital phase according to the physician in charge to restore systolic blood pressure to greater than 90 mm Hg and mean blood pressure to greater than 65 mm Hg [15]. In the prehospital setting, adrenaline is the preferred drug especially in case of severe hypotension [10,15]. Out-of-hospital cardia arrest patients with ROSC without an obvious noncardiac cause of arrest are transported to the cardiac catheterization laboratory for routine coronary angiogram and angioplasty if indicated. Patients with CF may receive intraaortic balloon pump (IABP) in the catheterization laboratory especially if AMI is present or an Impella assistance device according to the physician in charge.

In the ICU, ventilation is performed using the volume-controlled mode with tidal volumes of 6 to 8 mL/kg to achieve plateau pressure less than 30 cm H_2O. Positive end-expiratory pressure is initially set to 5 cm H_2O and is subsequently modified together with the inspired oxygen fraction to achieve an arterial O_2 partial pressure of 70 to 120 mm Hg. Respiratory rate is adjusted to achieve an arterial CO_2 partial pressure of 36 to 42 mm Hg [16].

Circulatory function in the ICU is monitored using an intraarterial catheter for continuous blood pressure monitoring as well as PiCCO, Vigileo, or echocardiography according to the physician in charge. If hypotension less than 90 mm Hg persists despite fluid repletion, catecholamine treatment is initiated [17]. In the inhospital phase, dobutamine is preferred in case of low cardiac output or low left ventricular ejection fraction, and noradrenaline is preferred in case of decreased systemic vascular resistance. The target mean arterial pressure is greater than or equal to 65 mm Hg, and the target systolic blood pressure is greater than or equal to 90 mm Hg. In case of CF requiring increasingly high catecholamine infusion rates in the ICU, patients may be treated with venoarterial extracorporeal life support (ECLS) according to age, comorbidities, and physiological status. Venoarterial ECLS is inserted by surgical technique in the ICU [18].

Therapeutic hypothermia (TH) is performed for all OHCA patients with ventricular fibrillation as initial rhythm but also nonshockable rhythms according to recommendations [15]. Therapeutic hypothermia is usually initiated on admission to the hospital using 30 to 50 mL/kg cold saline and then maintained for 12 to 24 hours using external (ice and cooling blankets) or endovascular methods for target temperature of 32°C to 34°C [15]. During the rewarming phase, the core temperature is increased by maximum 0.5°C/h. Standard care is continued subsequently until discharge from the hospital or death.

2.2. Studied parameters and predictors of death due to CF

Clinical and biological characteristics of the patients and usual parameters of the OHCA were recorded. Blood gas, arterial pH, blood lactate, and serum creatinine concentrations are routinely measured on admission in our center.

No flow was defined as the time interval between the patient's collapse and the beginning of cardiopulmonary resuscitation; and low flow, as the time interval between the beginning of cardiopulmonary resuscitation and the ROSC. *Sustained ROSC* was defined as spontaneous circulation with palpable pulse for at least 20 consecutive minutes [19]. Data were recorded according to "Utstein style"–recommended guidelines for uniform reporting of data from OHCA [19].

The type and rate of catecholamine infusion on admission were recorded, and an inotropic score (IS) adjusted to body weight was calculated according to the catecholamine infusion rate as follows: IS ($\mu g \times kg^{-1} \times min^{-1}$) = dopamine + dobutamine + 15 × milrinone + 100 × adrenaline + 100 × noradrenaline + 100 × isoproterenol [6,20].

We considered survivors to hospital discharge patients who had a cerebral performance category (CPC) less than or equal to 3 [21].

2.3. Analysis of the mode of death in the ICU

Death from CF was considered death from a persistent shock state despite adequate fluid repletion and catecholamine treatment or due to recurring cardiac arrest [3].

Patients without a circulatory cause of death and in whom brain death or persistent deep coma due to postanoxic injury or persistent myoclonic status was documented were considered deceased due to neurologic causes [3].

Patients who died due to miscellaneous causes (sepsis, aortic dissection, acute hemorrhage, tension pneumothorax, etc) were considered deceased due to other causes.

Multiple-organ failure associated with CF was diagnosed if one of the following organ dysfunctions was present before death based on the