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Clinical Paper

Postresuscitation hemodynamics during therapeutic hypothermia after out-of-hospital cardiac arrest with ventricular fibrillation: A retrospective study

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ABSTRACT

Aims of the study: To evaluate the incidence of postresuscitation myocardial depression (PRMD) and hemodynamical parameters associated with PRMD in patients treated with therapeutic hypothermia (TH) after out-of-hospital cardiac arrest with ventricular fibrillation (OHCA-VF).
Methods: Analysis of hemodynamical data from computerized clinical databases of two academic ICUs during two year period. We analyzed hemodynamical data from a subgroup of patients with pulmonary artery catheter (PAC). We defined PRMD as a cardiac index (CI) less than 1.5 l/(min m^2) any time during the first 12 h and compared clinical variables and hemodynamical parameters in patients with or without PRMD.
Results: Of 120 included patients PAC monitoring was used in 47 (39%). Of 47, 31 (66%, 95% CI 52% to 80%) developed PRMD. There was no difference in urinary output, lactate, mean arterial or central venous pressures or mixed venous saturation between patients with or without PRMD. Low CI was reversed with dobutamine infusion. Presence or absence PRMD was not associated with 6-month neurological outcome.
Conclusion: Two-thirds of the OHCA-VF patients develops transient postresuscitation myocardial depression not easily detected without monitoring of CI during therapeutic hypothermia. Further controlled studies are warranted to evaluate the value of different hemodynamic targets and monitoring after cardiac arrest in terms of outcome.

1. Introduction

After successful resuscitation from cardiac arrest a complex pathophysiological process, recently named as post cardiac arrest disease (PCAD) involving several organ systems ensues.[1,2] This syndrome comprise pathophysiological mechanisms that resemble those in sepsis further contributing to multiple organ dysfunction.[1] An essential part of PCAD is myocardial dysfunction developing during the first hours after cardiac arrest. Myocardial dysfunction may manifest as low blood pressure, low cardiac output, and the need for vasoactive drugs.[3–6] The natural course of this phenomenon, its prevalence, and its association to outcome is poorly described and defined, especially during therapeutic hypothermia (TH).

Therapeutic hypothermia is used for treatment of hypoxic–ischemic injury after resuscitation from cardiac arrest.[6,7] Its beneficial effect on outcome is best documented for patients resuscitated from out-of-hospital cardiac arrest (OHCA) after ventricular fibrillation (VF).[8–10] Use of TH is recommended in current guidelines, although a recent RCT found no benefit compared with strict normothermia in a large population of OHCA patients.[11] TH may decrease brain oxygen consumption and also of heart and the body overall.[7,12] Bradycardia is physiologically related to TH and it may further decrease cardiac output. Whether a certain minimal threshold for brain perfusion and good neurological outcome exists is not known.

Several recommendations have been published for the intensive care treatment with PCAD.[2,6] Guidelines suggest monitoring of cardiac output, but do not recommend any specific target values.[2]

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A recent review found inadequate data on the topic[13] and, thus, optimal hemodynamic management has been designated as a clinical research priority.[14]

Accordingly, in this observational study we aimed to evaluate the prevalence of postresuscitation myocardial depression (PRMD) in OHCA-VF patients. In addition, we aimed to describe clinical factors associated with the development of PRMD.

2. Materials and methods

2.1. Patients and management protocol

The study population consists of patients treated with TH after OHCA in two ICUs of Helsinki University Central Hospital (HUCH). The study was accepted by the local ethics committee. All OHCA patients with VF in this area (population 1.5 million) are primarily referred to either of these ICUs. We analyzed the data of OHCA patients treated with TH between 2008 and 2009. Our policy was to use TH only after out-of-hospital VF and, thus, non-VF patients were excluded from this study.

Both participating ICUs followed the same institutional standard operating procedure (SOP) for postresuscitation treatment. Hypothermia was induced and maintained with invasive cooling device and inferior vena cava catheter (Coolgard 3000/ICY® catheter, Zoll Medical Corp., Chelmsford, MA, USA), with target of 33 °C for 24 h and slow rewarming (0.2–0.5 °C/h[6]). Sedation was maintained with propofol and opiates. Rocuronium boluses were used for paralysis. Normoventilation ($PaCO_2$ 4.5–5 kPa) and normoxia (SpO_2 94–96%) were targeted with controlled ventilation. Mean arterial pressure (MAP) of 75–85 mmHg was targeted and, if this was not reached with fluid loading, noradrenaline (norepinephrine) infusion was used. In the beginning of 2009, recommendation to monitor cardiac output for detection of PRMD was included. During hypothermia, cardiac index (CI) of 1.5 l/(min m^2) was considered sufficient and during rewarming a CI of 2.0 l/(min m^2). If these values were not reached with adequate fluid loading an inotrope (dobutamine) was used.

Immediate coronary angiography and percutaneous coronary intervention (PCI) were recommended, if prehospital or admission ECG showed ST-elevation myocardial infarction (STEMI). If PCI was not available without delay, pre- or in-hospital thrombolysis was used. For other patients, diagnostic coronary angiography was done after transfer to ward, unless unstable ischemia or shock occurred. Other diagnostic procedures were performed by discretion of cardiologist.

2.2. Data collection

Physiologic and treatment data were extracted from the ICU's clinical information system (CIS) database (PICIS, Draeger, Barcelona, Spain and Clinisoft, GE, Helsinki, Finland). The demographics and outcome data were extracted from the hospital's electronic patient records (Uranus, CGI, Helsinki, Finland).

Physiological data (MAP, heart rate [HR], central venous pressure [CVP], core temperature, mean pulmonary artery pressure, mixed venous oxygen saturation [SvO_2]) were recorded as 1 h medians for the first 48 h in ICU from the CIS database. Dosages of drugs were recorded as the highest infusion rate during every hour and mean doses were calculated for these data for different time intervals, including times without infusion, representing the total vasoactive load. Cardiac output (CO) was measured with pulmonary artery catheters (PAC) by thermodilution method and all measurements were recorded in the study database. Of biomarkers lactate, CK-Mb and Troponin T, admission and highest values during the 48 h were recorded.

Presumed etiology of the cardiac arrest was obtained from hospital records. Neurologic outcome was retrospectively estimated as Cerebral Performance Category (CPC) [15,16] class; CPC 1 and 2 represented good outcome.

2.3. Analysis of the data

The hemodynamics were analyzed from a subgroup with PAC inserted during 6 h after ICU admission. Of this subgroup, patients with lowest measured CI less than 1.5 l/(min m^2) during first 12 h in ICU were the early PRMD group. As there is no universal definition of PRMD[5] and no recommendations for target CI during TH,[17] this cut-off point was based on data showing cerebral metabolic rate lowering to 52–60% of normothermic level at 30 °C during cardiac surgery [18] and animal data suggesting CI lowering to around 60% of normothermic value at 33 °C.[19] The hemodynamic, demographic and laboratory parameters and outcome were compared between the subgroups (no PAC, PRMD and no-PRMD).

To demonstrate the acute phase myocardial depression, first, lowest and highest CI values measured during first 12 h in ICU were included. We defined the first two values of these to represent the manifestation of PRMD (prior to inotropic treatment) and the third value to represent the response to treatment with fluids and inotropes. At later phases, the medians of measurements in a 12-h timeframe were used. Stroke volumes were calculated from individual CO measurements divided with heart rate at the same time point.

Statistical analysis was performed using SPSS statistics 21.0 (IBM, Armonk, NY, USA). Categorical data are presented as numbers and percentages, and continuous data as medians and interquartile range. Chi-square test was used for categorical data and Mann–Whitney *U* or Kruskal–Wallis test for continuous data. Measurement series of different time points were analyzed with a repeated measures ANOVA analysis with values over time as within factors (5 time points) and various dichotomous variables as between factors. We tested for sphericity of variables and used Greenhouse Geisser *p*-values as indicated. For variables not normally distributed, logarithmic values were calculated for repeated measures ANOVA analysis. *p*-Values less than 0.05 were considered as significant.

3. Results

During the study period 124 OHCA VF patients were treated in ICUs with therapeutic hypothermia. Three patients died during the first 24 h, and hemodynamic data of one patient were missing. These four patients were excluded. Thus, the final study population comprised 120 patients (Fig. 1).

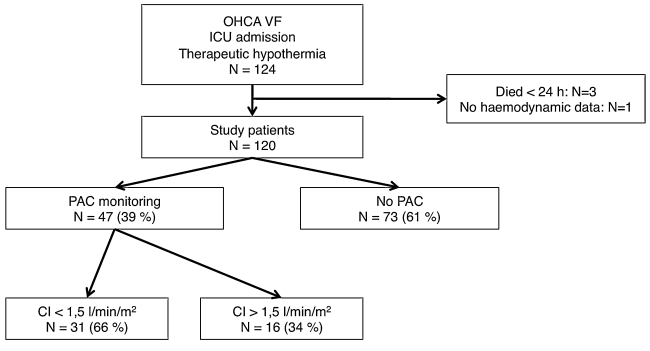

Fig. 1. Flow-chart of the study patients with out-of-hospital cardiac arrest after ventricular fibrillation (OHCA-VF) admitted to intensive care.