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Clinical paper

Impact of mean arterial pressure on clinical outcomes in comatose survivors of out-of-hospital cardiac arrest: Insights from the University of Ottawa Heart Institute Regional Cardiac Arrest Registry (CAPITAL-CARe)☆

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ABSTRACT

Aim of the study: We sought to assess the relationship between mean arterial pressure (MAP) and clinical outcomes in comatose survivors of out-of-hospital cardiac arrest (OHCA).
Methods: We identified consecutive comatose survivors of OHCA with an initial shockable rhythm treated with targeted temperature management. We examined clinical outcomes in relation to mean MAP (measured hourly) during the first 96 h of hospitalization. Co-primary outcomes were the rates of death and severe neurological dysfunction at discharge.
Results: In 122 patients meeting inclusion criteria, death occurred in 29 (24%) and severe neurological dysfunction in 39 (32%). Higher mean MAPs were associated with lower odds of death (OR 0.55 per 5 mmHg increase; 95%CI 0.38–0.79; p = 0.002) and severe neurological dysfunction (OR 0.66 per 5 mmHg increase; 95%CI 0.48–0.90; p = 0.01). After adjustment for differences in patient, index event, and treatment characteristics, higher mean MAPs remained associated with lower odds of death (OR 0.60 per 5 mmHg increase; 95%CI 0.40–0.89; p = 0.01) but not severe neurological dysfunction (OR 0.73 per 5 mmHg increase; 95%CI 0.51–1.03; p = 0.07). The relationship between mean MAP and the odds of death (p-interaction = 0.03) and severe neurological dysfunction (p-interaction = 0.03) was attenuated by increased patient age.
Conclusion: In comatose survivors of OHCA treated with target temperature management, a higher mean MAP during the first 96 h of admission is associated with increased survival. The association between mean MAP and clinical outcomes appears to be attenuated by increased age.

Introduction

Comatose survivors of out-of-hospital cardiac arrest (OHCA) are subject to significant morbidity and mortality, with neurological injury being the leading cause of death in patients surviving to hospital admission.[1–3] The extent of brain injury following OHCA is largely dependent on the duration of cerebral hypoperfusion during the index event, but also on further cerebral injury during the inflammatory milieu that characterises the reperfusion phase.[4,5] Adequate cerebral oxygen delivery during this phase may help mitigate cerebral damage, but is often compromised in OHCA patients.[4–6]

The early course of OHCA can be complicated by hypotension, myocardial dysfunction, and impaired cerebrovascular autoregulation—elements comprising the post-cardiac arrest syndrome.[4,7] In the presence of impaired cerebrovascular autoregulation, adequate cerebral oxygen delivery may become increasingly dependent on mean arterial pressure (MAP).[8] As a result, it is plausible that patients with a MAP outside newly shifted autoregulation zones following OHCA may be subject to ongoing cerebral ischaemia and worsened neurological outcomes. In addition, shifts

of cerebrovascular autoregulation zones may be dependent on specific baseline patient characteristics—such as age or a history of hypertension. Presently, the optimal MAP target during the early post-arrest period, and its relationship to baseline patient characteristics, has not been well established.[5,9]

In the current retrospective study, we sought to assess the effect of mean MAP during the first 96 h of hospital admission on survival and neurological outcomes in comatose survivors of OHCA undergoing targeted temperature management. In addition, we examined whether age or a history of hypertension had a modulating effect on this relationship.

Methods

The University of Ottawa Heart Institute (UOHI) is a large-volume tertiary care center and the single regional cardiac referral center for Eastern Ontario, servicing a catchment area of >1.3 million patients. In 2011, the UOHI established a CODE ROSC (Return of Spontaneous Circulation) program to provide timely, multidisciplinary care to OHCA patients in the region. Comatose survivors of OHCA referred to the UOHI are treated with targeted temperature management and routine early coronary angiography. In addition, demographic data, therapies, and clinical outcomes of all CODE ROSC patients are prospectively indexed in the University of Ottawa Heart Institute Regional Cardiac Arrest Registry (CAPITAL-CARe).

We identified consecutive patients treated with targeted temperature management between August 2010 and July 2013 following an OHCA with an initial shockable rhythm (ventricular fibrillation or pulseless ventricular tachycardia) and with a Glasgow Coma Scale (GCS) score <8. We retrospectively collected vital signs recorded on an hourly basis for the first 96 h following admission to the cardiac intensive care unit (CICU); these included MAP, systolic and diastolic blood pressures, and heart rate. When a direct arterial line measurement was not available, MAP was estimated using systolic and diastolic blood pressure recordings (i.e. 1/3 pulse pressure plus diastolic blood pressure). The data obtained was then used to calculate the mean MAP for each patient over the first 96 h of admission to the CICU.

In the current analysis, we examined clinical outcomes in comatose survivors of OHCA in relation to the mean MAP during the first 96 h following CICU admission. Co-primary outcomes were the rates of death and severe neurological dysfunction at discharge (defined as a cerebral performance category (CPC) ≥3).[10] Mean MAP was examined as both a continuous variable (primary analysis) and a categorical variable (secondary analysis) using three pre-specified strata: <70 mmHg, 70 to <80 mmHg, and ≥80 mmHg. The strata were chosen based on approximations of the 25th and 75th percentiles of mean MAP in the cohort.

We used logistic regression analyses to examine the relationship between mean MAP and co-primary outcomes following OHCA before and after adjustment for differences in key patient and index event characteristics. In the multivariable (adjusted) logistic regression models, the relationship between mean MAP and the incidence of co-primary outcomes was adjusted for differences in age, bystander cardiopulmonary resuscitation (CPR), and prolonged high-dose vasoactive agent use. We defined the latter as the use of a vasoactive agent at a high dose (e.g. norepinephrine ≥0.1 mcg/kg/min or epinephrine ≥0.1 mcg/kg/min) for >24 h during the first 96 h of CICU admission.

In ancillary multivariable logistic regression analyses, we examined the potential modulating effect of age, history of hypertension, and prolonged high-dose vasoactive agent use on the relationship between mean MAP and co-primary outcomes. Three separate models were used to assess the interaction between age, history of hypertension, and prolonged high-dose vasoactive agent use with
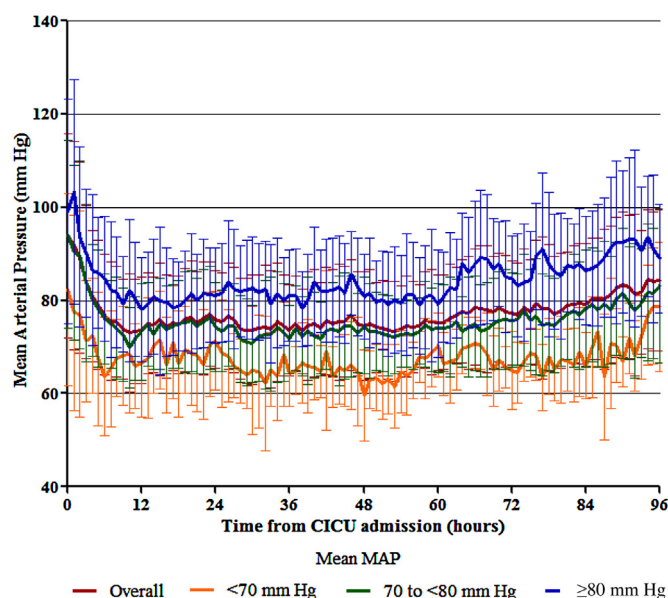

Fig. 1. Hourly mean MAP during first 96 h of CICU admission. MAP = mean arterial pressure; CICU = cardiac intensive care unit.

the effect of mean MAP on clinical outcomes. For this purpose, the models included interaction terms of age, history of hypertension, and prolonged high-dose vasoactive agent use by mean MAP.

Categorical variables are presented using percentages or frequencies, and continuous variables using means (±SD) or medians (25th, 75th percentiles), when appropriate. We compared categorical variables using the chi-square test (or Fisher's exact test when appropriate), and continuous variables using one-way analysis of variance or Kruskal–Wallis test for normally and non-normally distributed variables, respectively. Statistical analyses were conducted using SAS, version 9.13 (SAS Institute, Cary, North Carolina). Two-sided p values <0.05 were considered statistically significant.

Results

We identified 122 patients meeting inclusion criteria for this analysis (a mean age of 59 ± 13 years, 24% of patients being women, and 51% presenting with STEMI). Mean arterial pressure was <70 mmHg in 20 patients (16%), 70 to <80 mmHg in 67 patients (55%), and ≥80 mmHg in 35 patients (29%). Fig. 1 shows hourly mean MAP during the first 96 h of CICU admission for the overall patient population and after stratification based on mean MAP.

Baseline patient and index event characteristics are summarised in Tables 1 and 2, respectively. Patients with lower mean MAP were older and more likely to be female; baseline patient characteristics were otherwise well balanced between MAP strata. Characteristics of the index event, including estimated time from cardiac arrest to ROSC, initial vital signs, and GCS score on presentation, were comparable between mean MAP strata. Prolonged vasoactive agent use was more common in patients with a lower mean MAP.

Table 3 shows clinical outcomes stratified by mean MAP during the first 96 h of CICU admission. There was an association between mean MAP strata and the incidence of death (p = 0.001) and severe neurological dysfunction (p = 0.02). Higher mean MAPs were associated with lower rates of the co-primary outcomes.

In the primary logistic regression analyses, higher mean MAPs during the first 96 h following admission for OHCA were found to be associated with lower odds of death (OR 0.55 for every 5 mmHg increase in mean MAP; 95% CI 0.38 0.79; p = 0.002) and severe neurological dysfunction (OR 0.66 for every 5 mmHg increase in mean MAP; 95% CI 0.48–0.90; p = 0.01).