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Optimal blood pressure for favorable neurological outcome in adult patients following in-hospital cardiac arrest

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ABSTRACT

Background: Adequate cerebral blood flow maintained by optimal blood pressure is important in neurological recovery for patients sustaining transient brain ischemia. Few clinical studies have investigated the relationship between blood pressure and neurological outcomes of patients resuscitated following cardiac arrest.

Methods: This was a retrospective observational study, from a single medical center, of adult patients between 2006 and 2012 who had in-hospital cardiac arrest and achieved sustained return of spontaneous circulation (ROSC). Multivariable logistic regression analysis was used to identify factors associated with a favorable neurological outcome at hospital discharge. Maximal mean arterial pressure (MAP) during the initial 24 h after sustained ROSC was used for analysis.

Results: Of the 319 study patients, 56 (17.6%) achieved a favorable neurologic outcome. The mean MAP was 95 mm Hg. MAP above 85 mm Hg was found to correlate with a favorable neurological outcome (odds ratio [OR] 4.12, 95% confidence interval [CI] 1.47–14.39, $p = 0.01$). For patients without arterial hypertension, the optimal MAP was between 85 and 115 mm Hg (OR 8.80, 95% CI 3.13–28.55, $p < 0.001$); for patients with arterial hypertension, the threshold MAP for achieving a favorable neurological outcome was above 88 mm Hg (OR 4.04, 95% CI 1.41–13.03, $p = 0.01$).

Conclusions: The blood pressure over the first 24 h following resuscitation was correlated with neurological outcome. There may be a threshold blood pressure required to affect a favorable neurological outcome. The optimal blood pressure may be dependent on the presence or absence of arterial hypertension.

1. Introduction

Cardiac arrest is a common and potentially fatal emergency condition [1,2]. In patients who initially achieve return of spontaneous circulation (ROSC) after cardiac arrest, significant subsequent morbidity and mortality can be attributed largely to multi-system dysfunction following prolonged whole-body ischemia. This condition, termed the post-cardiac arrest syndrome (PCAS), comprises anoxic brain injury, post-cardiac arrest myocardial dysfunction, systemic ischemia/reperfusion response, and persistent precipitating pathology [3,4].

Therapeutic hypothermia has been recommended by the American Heart Association (AHA) for the management of PCAS following out-of-hospital cardiac arrest with ventricular fibrillation to protect the brain and other organs [3]. However, for other patients, such as patients sustaining in-hospital cardiac arrest, the benefit of therapeutic hypothermia has not yet been confirmed [3]. It is therefore mandatory to investigate other potentially modifiable factors to improve the dismal neurological prognosis of PCAS.

The systemic ischemia/reperfusion response involved in PCAS has many features in common with sepsis [4]. Like sepsis, similar goal-directed therapy has been applied in an effort to improve the PCAS outcome [5,6]. Based on limited evidence [3], the AHA suggests achieving systolic blood pressure above 90 mm Hg or mean arterial pressure (MAP) above 65 mm Hg to be the blood pressure goal following ROSC.

Nonetheless, a physiological study of arterial hypertension [7], a condition prevalent among patients of PCAS [8], has showed that such hypertension causes a rightward shift in cerebral pressure-flow autoregulation, which might justify targeting a higher MAP in PCAS to improve cerebral perfusion. Sundgreen et al. have also observed that within the first 24 h after resuscitation following cardiac arrest, auto-

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regulation of cerebral blood flow (CBF) is either absent or right-shifted, indicating that MAP might be kept at a higher level than is currently commonly accepted so as to secure cerebral perfusion [9].

Therefore, we conducted this retrospective cohort study of in-hospital cardiac arrest patients with the hypothesis that to improve neurological outcomes of PCAS, the target optimal MAP may be higher than that recommended by the AHA and this optimal MAP might be influenced by the presence or absence of arterial hypertension.

2. Materials and methods

2.1. Setting

National Taiwan University Hospital is a 2600-bed tertiary medical center with a total of 220 beds in the hospital's intensive care units (ICUs). Following an episode of cardiac arrest in the general wards, a code team is mobilized, consisting of a senior resident, several junior residents, a respiratory therapist, a head nurse, and several registered nurses from the ICUs. Each code team member is capable of providing basic and advanced life support according to current AHA guidelines and has been certified for providing advanced cardiac life support. Hospital policy does not mandate mobilization of a code team for ICU patients suffering from cardiac arrest since a sufficient number of experienced staff is always present in the ICUs. Resuscitation is performed by the staff of the particular ICU where the patient is located, and by staff from the neighboring ICUs. This study was approved by the Institutional Review Board of National Taiwan University Hospital. Prior to collection of the data, the Board provided a waiver for written informed consent.

2.2. Participants

We included patients who had had an in-hospital cardiac arrest at the National Taiwan University Hospital between 2006 and 2012. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) independent functional status prior to cardiac arrest; (3) documented absence of pulse and performance of chest compression for ≥2 min; and (4) sustained ROSC (ROSC ≥ 20 min without resumption of chest compression). If multiple cardiac arrest events occurred in a patient, only the first event would be recorded. We excluded patients with cardiac arrest related to trauma. We also excluded patients without blood pressure measurements.

2.3. Data collection

We abstracted the following variables: demographics, comorbidities, variables derived from the Utstein template [10], post-ROSC interventions (percutaneous coronary interventions, extracorporeal membrane oxygenation, and therapeutic hypothermia), vital signs during the first 24 h following sustained ROSC, and neurological status at hospital discharge (assessed using the Cerebral Performance Category [CPC] [11] score). The definitions of comorbidities were appended in the Supplemental Table 1.

The recordings of blood pressure included measurements through noninvasive automatic cuff-style or invasive intraarterial devices. The highest systolic blood pressure and its simultaneous corresponding diastolic blood pressure during the first 24 h after sustained ROSC were recorded. Maximal MAP was calculated as 1/3 of the highest systolic blood pressure plus 2/3 of the corresponding diastolic blood pressure [12]. The presence or absence of arterial hypertension was obtained from the admission medical records, depending on whether patients had been receiving antihypertensive treatment or had a past history of arterial hypertension [13].

2.4. Outcome measures

The primary outcome was favorable neurological status at hospital discharge, defined as a CPC score of 1 or 2. The CPC score is a validated 5-point scale of neurological disability (1, good cerebral performance; 2, moderate cerebral disability; 3, severe cerebral disability; 4, coma/vegetative state; 5, death) [11]. The CPC score was developed as a measure of central nervous system function after cardiac arrest and has become the most commonly used outcome assessment tool for this purpose. In this study, the CPC score was retrospectively determined by reviewing medical records for each patient. Patients with a CPC score of 1 or 2 had sufficient cerebral function to live independently.

2.5. Statistical analysis

Categorical data were expressed as counts/proportions and compared using the Fisher's exact test. Continuous data were expressed as mean values/standard deviations and examined using the Wilcoxon rank-sum test. A 2-tailed p-value of ≤ 0.05 was considered statistically significant. Odds ratios (ORs) were obtained using multivariable logistic regression analysis to determine whether independent variables were

Table 1
Baseline characteristics of the study patients.

Variables	All patients n = 319	Patients with favorable neurological outcome n = 56	Patients without favorable neurological outcome n = 263	*P* value
Age, y (SD[a])	63.5 (0.9)	62.8 (16.6)	63.6 (15.8)	0.73
Male, n (%)	200 (62.7)	45 (80.4)	155 (58.9)	0.002
Comorbidities, n (%)				
Arterial hypertension	127 (39.8)	20 (35.7)	107 (40.7)	0.55
Heart failure, this admission	65 (20.4)	14 (25.0)	51 (19.4)	0.36
Heart failure, past history	45 (14.1)	11 (19.6)	34 (12.9)	0.21
Myocardial infarction, this admission	35 (11.0)	17 (30.4)	18 (6.8)	<0.001
Myocardial infarction, past history	11 (3.4)	5 (8.9)	6 (2.3)	0.03
Arrhythmia	58 (18.2)	12 (21.4)	46 (17.5)	0.57
Hypotension	65 (20.4)	10 (17.9)	55 (20.9)	0.72
Respiratory insufficiency	193 (60.5)	24 (42.9)	169 (64.3)	0.004
Renal insufficiency	126 (39.5)	15 (26.8)	111 (42.2)	0.04
Hepatic insufficiency	63 (19.7)	7 (12.5)	56 (21.3)	0.14
Metabolic or electrolyte abnormality	59 (18.5)	5 (8.9)	54 (20.5)	0.06
Diabetes mellitus	101 (31.7)	17 (30.4)	84 (31.9)	0.88
Baseline evidence of motor, cognitive, or functional deficits	62 (19.4)	10 (17.9)	52 (19.8)	0.85
Acute stroke	16 (5.0)	0 (0)	16 (6.1)	0.08
Pneumonia	98 (30.7)	13 (23.2)	85 (32.3)	0.20
Bacteremia	20 (6.3)	3 (5.4)	17 (6.5)	1.00
Metastatic cancer or any blood borne malignancy	78 (24.5)	1 (1.8)	77 (29.3)	<0.001

[a] SD: standard deviation.