American Journal of Emergency Medicine 35 (2017) 268–273

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

The association of body mass index with outcomes and targeted temperature management practice in cardiac arrest survivors

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ARTICLE INFO

Article history:
Received 19 September 2016
Received in revised form 25 October 2016
Accepted 28 October 2016

Keywords:
Obesity
Heart arrest
Prognosis
Therapeutic hypothermia

ABSTRACT

Purpose: Obesity is a well-known risk factor in various health conditions. We analyzed the association between obesity and clinical outcomes, and its effect on targeted temperature management (TTM) practice for cardiac arrest survivors by calculating and classifying their body mass indexes (BMIs).
Methods: We conducted a retrospective data analysis of adult comatose cardiac arrest survivors treated with TTM from 2008 to 2015. BMI was calculated and the cohort was divided into four categories based on the cut-off values of 18.5, 23.0, and 27.5 kg m^{-2}. The primary outcome was six-month mortality and the secondary outcomes were neurologic outcome at hospital discharge, cooling rate, and rewarming rate.
Results: The study included 468 patients. Poor neurologic outcome at discharge and six-month mortality were reported in 311 (66.5%) and 271 (57.9%) patients, respectively. A multivariate logistic analysis showed that an overweight compared to normal BMI was associated with lower probability of six-month mortality (odds ratio [OR], 0.481; 95% confidence interval [CI], 0.274–0.846; $p = 0.011$) and poor neurologic outcome at discharge (OR, 0.482; 95% CI, 0.258–0.903; $p = 0.023$). BMI correlated with cooling rate (B, −0.073; 95% CI, −0.108 to −0.039; $p < 0.001$), but had no association with rewarming rate (B, 0.003; 95% CI, −0.001–0.008; $p = 0.058$).
Conclusion: Overweight BMI compared to normal BMI classification was found to be associated with lower six-month mortality and poor neurologic outcome at discharge in cardiac arrest survivors treated with TTM. Higher BMI correlated with a slower induction rate.

1. Introduction

Obesity is a major public health problem worldwide and a well-known risk factor for numerous health conditions, including cardiovascular diseases [1-3]. Previous studies have examined the association between obesity and clinical outcomes in cardiac arrest survivors [4-7]. A study including cardiac arrest survivors treated with therapeutic hypothermia reported that obese body mass index (BMI) was associated with mortality [4]. However, other studies demonstrated that moderately elevated or overweight BMI was associated with good neurologic outcomes or survival to discharge [5,6]. This finding corresponds to the "obesity paradox", which suggests that obesity is associated with better clinical outcome in heart failure patients [8,9]. However, the association between obesity and the clinical outcomes in cardiac arrest survivors has not yet been fully elucidated.

Targeted temperature management (TTM) is a standard care in comatose cardiac arrest survivors [10]. Although the optimal time for TTM initiation remains unknown, it is recommended to be initiated as soon as possible after return of spontaneous circulation (ROSC) in comatose cardiac arrest survivors. This is because several studies have reported that a lag between ROSC and the initiation of TTM is associated with poor neurologic outcomes or mortality [11,12]. In TTM, the induction and rewarming duration are defined as the temperature changing phases during which cooling and rewarming to target temperatures are achieved. High BMI can interfere with the time required for cooling and rewarming to achieve the target temperature. A previous study reported that a higher BMI was associated with prolonged induction time [7]. However, there is a lack of evidence on the association between BMI and cooling and rewarming rates.

We hypothesized that the obesity paradox would be acceptable for comatose cardiac arrest survivors and that BMI has an effect on induction and rewarming durations. The present study, therefore, analyzed the association between BMI and six-month mortality or neurological outcomes at discharge, and the effect of BMI on TTM practice, including cooling and rewarming rates, for cardiac arrest survivors.

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http://dx.doi.org/10.1016/j.ajem.2016.10.070
0735-6757/

2. Methods

2.1. Study Design and Population

We performed a retrospective observational cohort study including comatose cardiac arrest survivors treated with TTM (target temperature, 33 °C; maintenance of therapy duration, 24 h) at OO Hospital between January 2008 and December 2015. This study was approved by the Institutional Review Board of OO Hospital (OO-2016-104).

Adult cardiac arrest survivors over 18 years of age having completed TTM were included. Patients were excluded based on the following criteria: (i) transfer during TTM; (ii) receipt of a TTM protocol with a different target temperature of 32 °C or duration with 72 h; (iii) extracorporeal membrane oxygenation applied during post-cardiac arrest care; or (iv) incomplete BMI data.

2.2. TTM Protocol

TTM was applied to all comatose patients after non-traumatic cardiac arrest excluding the following cases: i) refusal of TTM by next-of-kin; ii) terminal illness or significant bleeding; iii) hemorrhagic stroke. TTM was applied according to a written TTM protocol. The induction phase of TTM is defined as the time interval from the initiation of cooling to attainment of target temperature. TTM was induced with ice packs, intravenous cold saline, and cooling devices as soon as possible after the decision to apply TTM. The maintenance phase is a 24-hour period during which a target temperature of 33 ± 1 °C is maintained. During TTM, the target temperature was maintained using either feedback-controlled endovascular catheters (COOLGARD3000® Thermal Regulation System, Alsius Corporation, Irvine, USA) or surface cooling devices (Blanketrol® II, Cincinnati Subzero Products, Cincinnati, USA or Artic Sun® Energy Transfer Pads™, Medivance Corp, Louisville, USA). The rewarming phase is defined as the time interval from completion of the maintenance phase to achieving a target temperature. Patients were rewarmed at a target rate of 0.25 °C h^{-1} or 0.5 °C h^{-1}.

2.3. Data Collection and Outcomes

The following data were obtained for each patient: age, sex, comorbidities, first monitored rhythm, etiology of cardiac arrest, location of cardiac arrest (out-of-hospital or in-hospital), presence of a witness on collapse, bystander cardiopulmonary resuscitation (CPR), downtime, Glasgow coma scale (GCS) after ROSC, BMI, initial temperature, induction duration, cooling rate, rewarming duration, target rewarming rate (0.25 °C h^{-1} or 0.5 °C h^{-1}), actual rewarming rate, cooling device (blanket, endovascular, or hydrogel pad), neurologic outcome at discharge, and vital status at six-month after collapse (alive or dead). BMI was categorized according to World Health Organization classification for Asian populations as follows: underweight (<18.5 kg m^{-2}), normal (18.5–22.9 kg m^{-2}), overweight (23.0–27.4 kg m^{-2}), or obese (≥27.5 kg m^{-2}) [13]. The sequential organ failure assessment (SOFA) score within the first 24 h after admission was used to assess the severity of multiple organ dysfunction [14]. Neurologic outcome was assessed using the Glasgow-Pittsburgh Cerebral Performance Categories (CPC) at discharge and recorded as CPC 1 (good performance), CPC 2 (moderate disability), CPC 3 (severe disability), CPC 4 (vegetative state), and CPC 5 (brain death or death) [15]. Neurologic outcomes were dichotomized as either good (CPC 1 and CPC 2) or poor (CPC 3 to 5). The primary outcome was six-month mortality. The secondary outcomes were neurologic outcome at discharge and TTM practice.

2.4. Data Analysis

Continuous variables were given as median values with interquartile ranges according to the results of a normality test. Mann-Whitney *U* tests and Kruskal-Wallis tests were conducted for comparisons of continuous variables as appropriate. Categorical variables were presented as frequencies and percentages. Comparisons of categorical variables were performed using χ^2 or Fisher exact tests, as indicated. Logistic regression analysis was used to examine the association between BMI and six-month mortality or neurologic outcome at discharge after adjusting for relevant covariates. Backward selection was used to obtain the final model. The goodness-of-fit of the final model was evaluated using the Hosmer-Lemeshow test. BMI and BMI classifications were modeled using different models to avoid confounding errors. Multivariate linear regression analysis was used to identify the association between BMI and TTM practice (cooling and rewarming rates). All variables where $p < 0.2$ in univariate analyses of BMI classifications were included in the multivariate linear regression analysis. Backward selection was used to obtain the final model. Data were analyzed using PASW/SPSS™ software, version 18 (IBM Inc., Chicago, IL, USA). A two-sided significance level of 0.05 was used for statistical significance.

3. Results

3.1. Patient Population

During the study period, 636 adult cardiac arrest survivors were treated with TTM. As summarized in Fig. 1, 46 were treated with extracorporeal membrane oxygenation, 69 were treated with a different TTM protocol, 7 were transferred, and 44 had incomplete BMI data. Finally, 468 patients were included in this study (Fig. 1).

The median age was 60.0 (47.0–70.0) years; 146 (31.2%) patients had shockable rhythm, 262 (56.0%) had cardiac etiology, 378 (80.8%) had out-of-hospital cardiac arrest, 358 (76.5%) were witnessed on collapse, 234 (50.0%) received bystander CPR, and the median downtime was 28.0 min (17.0–40.0 min) (Table 1). Poor neurologic outcome at discharge and six-month mortality were reported in 311 (66.5%) and 271 (57.9%) patients, respectively.

3.2. Association of BMI With Six-Month Mortality

Table 1 compares survivor and non-survivor data six months after cardiac arrest. The six-month survivor group was younger, male dominant, had significantly lower incidence of comorbidities (hypertension, diabetes, pulmonary disease, and renal disease), and was more likely to have a shockable rhythm, cardiac etiology, and witnessed collapse (Table 1). Survivors also had a shorter downtime, higher GCS after

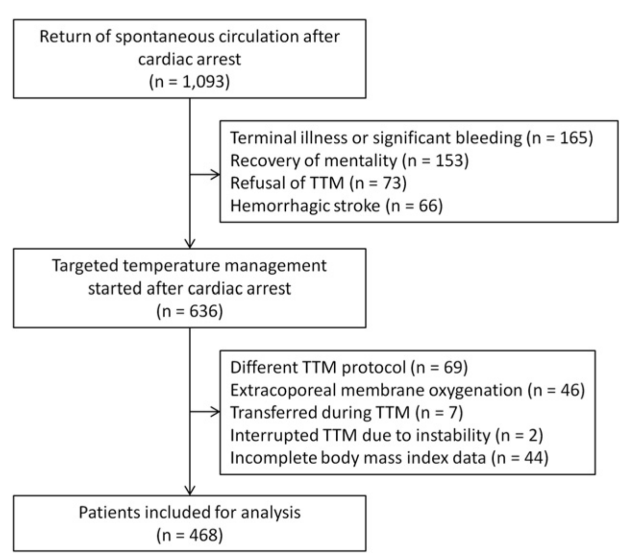

Fig. 1. A schematic diagram showing the selection process of patients for analysis.