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## Original article

## The impact of body mass index on post resuscitation survival after cardiac arrest: A meta-analysis

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## SUMMARY

**Background:** Observational studies examining the association between body mass index (BMI) and the outcome of cardiac arrest (CA) shows controversial results.**Methods:** We reviewed literature for studies assessing the impact of BMI on survival and neurological outcome following CA. Eligible studies were subsequently meta-analyzed and pooled odds ratios and their corresponding 95% confidence intervals for post CA survival and neurological status were derived.**Results:** A total of 7 studies with 24,651 patients were evaluable for this meta-analysis. The studies were also categorized by location of the CA and the use of therapeutic hypothermia. Our results suggested that BMI between 25 and 29.9 kg/m<sup>2</sup> had a favorable impact on survival after CA (OR = 1.172, 95% CI, 1.109–1.236) in comparison to normal weight subjects. Likewise, overweight patients presented increased odds for a favorable neurological outcome after CA (OR = 1.112, 95% CI, 1.020–1.213). On the contrary, underweight subjects presented decreased odds of surviving after CA as compared to normal BMI subjects (OR = 0.781, 95% CI, 0.652–0.935). Finally, BMI >30 kg/m<sup>2</sup> was not associated with improved survival or neurological outcome as compared to BMI 18.5–24.9 kg/m<sup>2</sup>.**Conclusions:** Overweight patients have a favorable prognosis after CA in terms of both survival and neurological outcome. This effect was amplified when the analysis is restricted in in-hospital cardiac arrest and in patients non-treated with therapeutic hypothermia.

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## Introduction

Numerous studies have implicated increased body weight or body mass index (BMI), a surrogate marker for obesity, as risk factors for various cardiovascular diseases [1–4]. The term obesity cardiomyopathy describes the complex cardiac alterations induced by obesity. Although obesity has been shown to increase the risk of out-of-hospital cardiac arrest (OHCA) [5,6] and BMI is considered a marker of poor prognosis in several pathological conditions [7–10], the influence of BMI on the outcome of CA is still debatable.

Until recently a number of studies have investigated the association of body weight or BMI with the survival and neurological outcome of patients after cardiac arrest. Nevertheless, the issue of prognostication linked with body weight or BMI in cardiac arrest remains unresolved. If patients at each stage of the BMI spectrum demonstrate different outcomes after CA, this may reflect to different requirements during the acute or post resuscitation care. We therefore reviewed the published studies and quantitatively evaluated the data regarding the association of BMI with the outcome in patients after cardiac arrest. The primary aim of this study was to assess the possible role of BMI as prognostic factor for post resuscitation survival after CA by carrying out a systematic review of the literature and a meta-analysis of the data. We aimed

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also at analyzing the influence of BMI on the neurological outcome of the resuscitated patients. Studies concerning the association between BMI with prognosis in terms of survival and neurological outcome after cardiac arrest were included. Emerging issues, gaps of knowledge and future researches requirement will be at least discussed throughout the sections.

## Methods

### Search strategy, data extraction and quality assessment

The present A search in MEDLINE and EMBASE databases was carried out using the search terms 'BMI' (MeSH term) OR 'body mass index' (MeSH term) OR 'obesity' (title/abstract) OR 'overweight' (title/abstract) AND 'cardiac arrest survival' (MeSH term), 'cardiac arrest outcome' (MeSH term) or 'cardiac arrest prognosis' (MeSH term). The references reported in the identified studies were also used to complete the search. An upper date limit of July 31, 2017 was applied. The search was limited to English language. The criteria for inclusion of a study in this meta-analysis were (I) record or measurement of BMI in patients resuscitated after cardiac arrest (II) available information on the primary outcome of survival and/or neurological outcome in the resuscitated patients after a short follow up time. The categorization of patients should use cut-off values of BMI applied in the World Health Organization classification as either: underweight ( $\leq 18.4 \text{ kg m}^{-2}$ ), normal ( $18.5\text{--}25 \text{ kg m}^{-2}$ ), overweight ( $25.1\text{--}29.9 \text{ kg m}^{-2}$ ) or obese ( $\geq 30 \text{ kg m}^{-2}$ ) [11]. Two reviewers (DK and GK) independently determined study eligibility and performed data extraction. Disagreements were resolved by consensus after discussion with another author (TS). For each eligible trial we extracted data on participants' baseline characteristics including classification in BMI categories, and outcomes regarding survival to discharge up to 6 months and neurological function at the same time frame. Based on these data we calculated the corresponding effect size (OddsRatio, OR) for each category of BMI in comparison to normal BMI category towards short term survival and/or good neurological outcome.

### Data synthesis and statistical analysis

To provide a more meaningful effect size, we compared patients classified in the normal BMI category (i.e.  $18.5\text{--}24.9 \text{ kg/m}^2$ ) versus all other alternative groups (i.e.  $<18.5$ ,  $25\text{--}29.9$ ,  $>30 \text{ kg/m}^2$ ). Neurological outcomes were grouped into two categories of good recovery and severe disability.

We performed the meta-analysis of studies investigating the impact of BMI classification in terms of cardiac arrest resuscitation to obtain the pooled estimate separately for: 1) short-term survival (until hospital discharge or 6 months after discharge) 2) neurological outcome in survivors of cardiac arrest and we attempted to follow the Preferred Reporting Items for Systematic Reviews and MetaAnalysis (PRISMA) guidelines. To test whether the true effect in all studies is the same (i.e. heterogeneity), we used the I-squared measure ( $I^2$ ) that permits quantification of discrepancy among studies ( $I^2 < 20\%$  low,  $20\% < I^2 < 60\%$  moderate,  $I^2 > 60\%$  high). Whenever significant heterogeneity was established among studies ( $p < 0.05$ ), a random-effects model was selected to calculate the pooled effect size using the DerSimonian & Laird method. Otherwise ( $P > 0.05$  for the test of heterogeneity across the meta-analyzed studies), fixed-effects models were implemented for deriving meta-analysis inference. The mean effect size and confidence intervals (CIs) of individual studies were illustrated with forest plots.

We conducted a between-study subgroup analysis to evaluate whether the estimates of the effect of BMI classification on study

main endpoints differ within certain populations (OHCA versus IHCA, increased  $>50\%$  versus decreased  $<50\%$  initial presentation of shockable rhythm after cardiac arrest, implementation of therapeutic hypothermia or not). BMI  $<18.5$  was not further explored in sub-group analyses due to limited number of observations. Differences in pooled effect sizes between subgroups were compared with a test of interaction (Cochran's Q test). Sensitivity analyses were also performed to assess consistency of results when excluding small size studies. To estimate the contribution of continuous study moderators (including variables such as age, the ratio of male to female patients, prevalence of CAD and DM and the ratio of patients with shockable versus non shockable cardiac rhythm immediately before resuscitation) to the overall heterogeneity, random-effects meta-regression was performed. Statistical analysis was performed with STATA package, version 11.1 (Stata-Corp, College Station, Texas USA). We deemed statistical significance at  $p < 0.05$ .

## Results

A detailed flow diagram of eligible articles is presented in Fig. 1. The electronic literature search based on our strategy initially returned 274 citations from MEDLINE, EMBASE and from Cochrane Library. Of them, 7 cohort studies met the inclusion criteria and were selected for further review [12–18]. Collectively, 4 prospective and 3 retrospective observational studies provided information about the association of BMI with the outcome after cardiac arrest. Overall, the meta-analysis included 7 studies and a total of 24,651 patients. Table 1 presents the characteristics of the included studies. Table 2 summarizes the outcome data provided by each study for every BMI category.

### Short-term survival after CA

All 7 studies reported the incidence of post CA survival in the index BMI category as well as in patients classified in

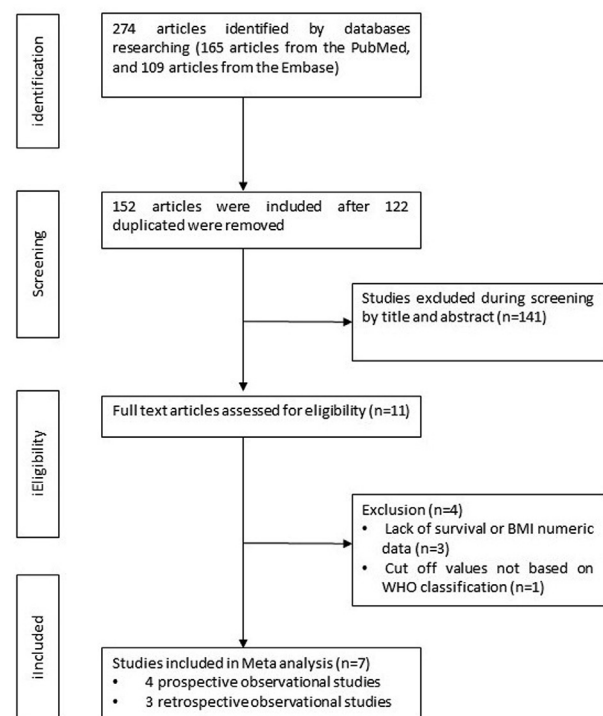


Fig. 1. A detailed flow diagram of the study selection process.

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