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Obesity is associated with better survival and functional outcome after acute intracerebral hemorrhage

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ABSTRACT

Objective: To evaluate the association of obesity measured by body mass index (BMI) with mortality and functional outcome in patients with acute intracerebral hemorrhage (ICH).
Methods: Data were from 1571 patients with ICH enrolled in a national, multi-centre, prospective, hospital-based register: the ChinaQUEST (Quality Evaluation of Stroke Care and Treatment) study. The outcomes included all-cause mortality at 12 months, and death or high dependency at 3 and 12 months. High dependency was defined as a modified Rankin Scale score of 3–5.
Results: Of 1571 patients with ICH, 109 were underweight (BMI < 18.5 kg/m^2), 657 were normal-weight (BMI 18.5–23 kg/m^2), 341 were overweight (BMI 23–25 kg/m^2) and 464 were obese (BMI ≥ 25 kg/m^2). Compared with normal-weight patients, obese patients had significantly decreased risks of death at 12 months (HR: 0.71, 95% CI: 0.56–0.91) and death or high dependency at 3 and 12 months (OR: 0.71, 95% CI: 0.53–0.95; OR: 0.69, 95% CI: 0.51–0.94) after adjusting for baseline characteristics. Neither underweight nor overweight was associated with these three outcomes significantly.
Conclusions: In patients with acute ICH, being obese is associated with a decreased mortality and better functional recovery. Further interventional studies are needed to guide the weight management strategy for patients with ICH.

1. Introduction

Obesity is one of the major risk factors of cardiovascular diseases and stroke [1,2]. In general population, obesity is associated with an increased morbidity and mortality [3,4]. Whereas some studies have reported a paradoxical decrease in mortality with increasing body mass index (BMI) in a range of disease conditions, such as heart failure, coronary artery disease, and chronic kidney disease [5–7]. In patients who have had these diseases, obesity seems to carry a survival advantage, which is called as the obesity paradox [5–7]. More recently, this phenomenon has been noted in patients suffering from intracerebral hemorrhage (ICH). A study has found a nearly 40% reduction of long-term mortality after ICH in obese patients compared with normal-weight patients [8]. However, few studies to date have investigated the relationship between obesity and functional outcome in ICH patients.

The aim of the present study was to evaluate the association between obesity measured by BMI and stroke outcomes, including mortality and functional disability, in patients with established acute ICH.

2. Methods

2.1. Patients and study protocol

This study was on data from the ChinaQUEST (Quality Evaluation of Stroke Care and Treatment), a multicentre, prospective, registry study in a 62-hospital network located in 37 cities across China, as described elsewhere [9]. In brief, consecutive patients (aged ≥ 15 years) admitted to hospital with a recent (<1 month) acute stroke were enrolled from 1 July to 5 December 2006 [9]. Patients with ischemic stroke, intracerebral hemorrhage or undetermined subtype were included. Those with subarachnoid hemorrhage were excluded.

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Baseline information on socio-demographics (age, sex, living alone, low level of education [primary education only or illiterate], annual household income), medical history (hypertension, diabetes, hyperlipidemia, atrial fibrillation, prior stroke/transient ischemic attack, coronary artery disease [any history of heart attack/myocardial infarction, angina, or coronary heart disease] either self-reported or diagnosed in-hospital poststroke, prior dependency, current cigarette smoking, and regular alcohol consumption within the 3 months before stroke onset) and clinical features of the index stroke (time of presentation at the hospital, and Glasgow Coma Scale [GCS] score on admission), was obtained predominantly by face-to-face interviews with patients or proxies. Prior dependency was assessed using a single question: "Does the patient require help from another person for everyday activities?". In-hospital details on diagnostic/treatment strategies were obtained through medical records and interviews with patients or proxies. Functional outcome as measured by the modified Rankin Scale (mRS) was collected mainly by telephone interview (>80%) at 3 and 12 months. Death during follow-up was ascertained by family (64.7%), a health professional (18.4%), records (e.g. medical, police [11.8%]), death certificate (3.5%) or other sources (1.5%). The face-to-face interviews and the telephone interviews were performed by physicians [9].

Written informed consent was obtained from all patients or an appropriate family member (if the patient was unable to give it) to participate. The study was approved by the ethics committees of Peking University First Hospital (Beijing), Ruijin Hospital (Shanghai), Prince of Wales Hospital (Hong Kong), and The University of Sydney.

2.2. Variable of interest and outcomes

BMI was calculated as weight (in kilograms) divided by the square of height (in meters squared). Height and weight were measured by nurses or obtained from the patient or the accompanying relatives on admission. The patient population was classified as underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 to <23 kg/m^2), overweight (BMI 23 to <25 kg/m^2) and obese (BMI ≥ 25 kg/m^2) using the World Health Organization (WHO) Western Pacific Regional Office definition [8,10].

The outcomes included all-cause mortality at 12 months, and a composite of death or high dependency at 3 and 12 months after ICH. High dependency was defined as a mRS score of 3–5.

2.3. Statistical analysis

Differences in baseline characteristics between BMI subgroups were determined using the one-way analysis of variance (ANOVA) and Chi-square test where appropriate. For those variables with a significant difference in the distribution, one-way analysis of variance with a contrast to linear trend or Chi-square test for trends in proportion was further tested. Cox proportional hazard models were performed to assess the relationship between obesity status and all-cause mortality at 12 months. Similarly, logistic regression models were performed to evaluate the relationship between obesity status and the composite outcome of death or high dependency at 3 and 12 months post-ICH. All multivariable analyses were adjusted for age, sex, living alone, low level of education, annual household income, medical history (hypertension, diabetes, hyperlipidemia, atrial fibrillation, prior stroke/transient ischemic attack, coronary artery disease), prior dependency, current cigarette smoking, regular alcohol consumption, time of presentation at the hospital, and GCS score on admission. Additionally, we performed several sensitivity analyses to evaluate the robustness of our findings. First, we utilized another obesity definition which had been used for Chinese in previous studies [11,12]. Individuals were categorized as underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 to <24 kg/m^2), overweight (BMI 24 to <28 kg/m^2) and obese (BMI ≥ 28 kg/m^2). Second, we restricted the study population to those who survived beyond 1 week after onset of ICH. Third, we excluded those patients who had received neurosurgical intervention. Fourth, we excluded those patients who had prior dependency. Statistical significance was considered at $P < 0.05$. All analyses were performed with SPSS version 13.0 (SPSS, Chicago, IL, USA).

3. Results

Of 13,038 patients screened for eligibility of the ChinaQUEST study, 6530 patients (50.1%) were excluded because the final diagnosis was not stroke or stroke of recent onset (30.9%), patients declined to participate (16.1%), patients died rapidly before enrollment (1.5%), or for other reasons (1.5%). A total of 6508 patients were enrolled but 154 were excluded from analyses due to uncertainty of diagnosis and missing data. This resulted in 6354 cases consisting of 1572 patients with ICH and 4782 patients with ischemic stroke in the ChinaQUEST database. The diagnosis of ICH was confirmed by computerized tomography (CT) or magnetic resonance imaging (MRI) with the exception of one case.

After excluding 1 patient without record of BMI on admission, 1571 patients (mean age, 61.1 ± 12.9 years; male, 59.8%) with ICH were included in our analysis. The median time from stroke onset to hospital presentation of the 1571 patients was 3.8 h (interquartile range: 1.5–19.0 h). The average BMI was 23.3 ± 3.42 kg/m^2. A total of 109 patients (6.9%) were underweight, 657 (41.8%) had normal weight, 341 (21.7%) were overweight, and 464 (29.5%) were obese.

Baseline characteristics of the study population were shown in Table 1. As the severity of obesity increased, the prevalence of hypertension, diabetes, and hyperlipidaemia also increased, whilst patients' age and the proportion of low level of education decreased (all P for trend <0.05). Underweight patients and obese patients more often had a medical history of coronary artery disease than normal-weight patients. There was no significant difference in the distribution of other baseline variables among the BMI categories.

There were 412 patients who had died within 12 months after ICH. High dependency was found in 494 survivors at 3 months and in 369 survivors at 12 months. Unadjusted analysis showed, compared with patients of normal BMI, obese patients had decreased risks for death at 12 months (hazard ratio [HR]: 0.75, 95% confidence interval [CI]: 0.59–0.95) and death or high dependency at 12 months (odds ratio [OR]: 0.76, 95% CI 0.60–0.97). The proportion of death or high dependency at 3 months was lower but not statistically significant in obese patients than normal-weight patients (OR: 0.79, 95% CI 0.62–1.01; Table 2).

After adjustment of all covariates, the multivariable analyses indicated the significantly decreased risks for death at 12 months and for death or high dependency at 3 and 12 months in obese patients compared with normal-weight patients (HR:0.71, 95% CI 0.56–0.91; OR: 0.71, 95% CI 0.53–0.95; OR: 0.69, 95% CI 0.51–0.94, respectively). Neither underweight nor overweight was associated with these three outcomes significantly in unadjusted and adjusted analyses (Table 2).

The relationship between obesity and outcomes after ICH was consistent in sensitivity analyses (Table 3). Obese patients still carried improved survival and functional recovery compared with normal-weight patients when using another BMI classification criteria which defined obesity as BMI ≥ 28 kg/m^2, or excluding 201 patients who had died within 1 week after ICH, or excluding 137 patients who had received neurosurgical intervention, or excluding 210 patients who had prior dependency.

4. Discussion

The present study found a decreased mortality and better functional outcome associated with being obese at the time of experiencing an acute ICH. The risks of death and death or high dependency in