



## Associations of body weight and weight change with cardiovascular events and mortality in patients with coronary heart disease



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### ARTICLE INFO

#### Article history:

Received 22 November 2017

Received in revised form

31 March 2018

Accepted 2 May 2018

Available online 5 May 2018

#### Keywords:

Coronary heart disease

Body weight

Obesity

Weight change

Mortality

Cardiovascular event

### ABSTRACT

**Background and aims:** It is recommended that patients with coronary heart disease (CHD) pursue a normal body weight, while the effects of body weight and weight change on prognosis are still controversial. The present study was to assess these effects using a large-scale population with CHD in China.

**Methods:** A total of 5276 patients with CHD were included from Jan 2000 to Dec 2014. Baseline and endpoint weights were measured. Outcomes including mortality and cardiovascular events were obtained.

**Results:** Relative to patients with normal weight, risks for adverse outcomes were lowest in overweight patients and similar in obese patients. Hazard ratios (HRs) and 95% confidence interval (95% CI) for all-cause death were 1.42 (1.06, 1.91) if overweight turned into normal weight and were 2.01 (1.28, 3.16) or 5.33 (2.81, 10.1) if obese turned into overweight or normal weight. Death risk increased with the extent of weight loss and moderate or large weight gain ( $p < 0.05$  for all). Similar results were found when risks for cardiovascular mortality and events were considered. Furthermore, these results remained significant when the patients were stratified by several covariates and even when several definitions of weight change were considered.

**Conclusions:** Obesity did not increase adverse outcome risks in patients with CHD. Both weight loss and weight gain increased adverse outcome risks regardless of baseline body weight. The findings suggest that maintaining a stable weight may be a better strategy for the reduction of risks for cardiovascular outcomes and all-cause death in patients with CHD.

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### 1. Introduction

Although cardiovascular disease (CVD) mortality declined dramatically over the past 2 decades in all high-income and some middle-income countries, CVDs remain the leading causes of premature death and chronic disability in the world [1,2]. The majority

of health lost to CVDs are attributable to coronary heart disease (CHD) and stroke [1]. It is concerning that trends in CHD mortality are no longer declining for many world regions, which may be due to rising rates of cardiovascular risk factors particularly obesity [1,3–5].

Previous studies reported that obesity increased risks for CHD [6,7], which was thought to result in an increase of adverse outcomes [8]. Based on these findings, guidelines recommend and the literature encourage patients with CHD to pursue a normal body weight, especially in overweight or obese patients [9–12]. However, in recent years, increasing efforts have been made to assess the potential effects of obesity and weight change on a variety of health outcomes, while the findings are controversial [13–17].

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Several studies have shown that overweight and obesity are related to better prognosis in patients with established CHD [18,19]. Other studies have shown that loss of weight in overweight or obese patients with CHD does not result in lower mortality and may even have worse prognosis [16,20]. These controversial findings raise questions regarding the effect of obesity on prognosis and the value of weight loss in patients with CHD. Furthermore, many of above studies had relatively small number of participants [16,17,19], and there are currently no large-scale studies involving the Asian population. Finally, data on analyses of associations between changes in body weight categories (i.e., body weight changes from normal weight to overweight) and prognosis in patients with CHD are limited.

Therefore, we investigated associations of body weight and weight change with outcomes using a large-scale population with CHD in China. We specifically explored how risks for adverse outcomes change with changes in body weight categories, and also decomposed changes in risks of weight change for deaths and cardiovascular events into the contributions of sex, age, and all other factors.

## 2. Patients and methods

### 2.1. Patients

The present study recruited the patients with established CHD who visited the Health Department of Agency for Offices Administration of PLA or the Chinese PLA General Hospital from Jan 2000 to Dec 2014. Eligible patients were men and women, 18–90 years of age, with clinically evident CHD, defined by one or more of the following: previous myocardial infarction (MI), the presence of angina pectoris with angiographic evidence of >50% stenosis in at least 1 major coronary artery, previous percutaneous coronary intervention (PCI), and a history of coronary artery bypass grafting (CABG). The exclusion criteria included a history of lung disease, kidney disease, liver disease, heart failure, mental illness, or cancer, or inability to participate in the study. After the exclusion of 104 patients who were lost to follow-up and 130 patients with missing data on covariates, complete data were obtained in 5276 patients. All known diseases were obtained from hospital medical records and confirmed by a medical record review. Written informed consent was obtained from all of the included patients. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Medical Ethics Committee of Chinese PLA General Hospital. The study population flow is explained in [Supplemental Fig. 1](#).

### 2.2. Body weight and weight change

Baseline and endpoint weights were obtained from hospital medical records. Self-reported endpoint weights through telephone visit were used in 185 participants because body weights at the endpoint were not able to be obtained from their hospital medical records. Baseline characteristics were comparable between these participants and the participants whose endpoint weights were obtained from hospital medical records. Body mass index (BMI) was calculated in  $\text{kg}/\text{m}^2$  and was categorized into: underweight,  $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$ ; normal weight,  $18.5\text{--}23.9 \text{ kg}/\text{m}^2$ ; overweight,  $24\text{--}27.9 \text{ kg}/\text{m}^2$ ; and obese,  $\geq 28 \text{ kg}/\text{m}^2$ , according to the recommendation by the Working Group on Obesity in China [21]. Weight change was defined by absolute weight change (kg). Absolute weight change was calculated by subtracting weight at baseline from weight at endpoint and were categorized into: weight stability ( $\leq 1 \text{ kg}$  loss or gain), small weight gain (1–5 kg gain), moderate weight gain (5–10 kg gain), large weight gain

(>10 kg gain), small weight loss (1–5 kg loss), moderate weight loss (5–10 kg loss), and large weight loss (>10 kg loss).

### 2.3. Covariates

Data on smoking status and family medical history were conducted via face-to-face interviews. Individual medical history and medication use were obtained from hospital medical records. Fasting glucose, serum lipids, serum creatinine, high-sensitivity C-reactive protein (CRP), and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were measured by routine laboratory methods.

### 2.4. Follow-up and adverse outcomes

Participants were followed until Dec 31, 2016. The follow-up protocol included a combination of hospital medical records, telephone contacts with patients or family members, and death certificates. The primary outcomes were all-cause mortality and cardiovascular mortality. Cardiovascular mortality was defined as death attributable to fatal myocardial infarction, sudden cardiac death, or stroke. The second outcomes were cardiovascular events, including myocardial infarction, stroke, and coronary revascularization (i.e., PCI and/or CABG). Patients with more than one event were assigned the highest-ranked event based on the previous list of cardiovascular events. The diagnosis of myocardial infarction was based on symptoms, elevated cardiac marker of myocardial necrosis, and the presence or absence of diagnostic electrocardiogram changes [22]. Sudden cardiac death was diagnosed as unexpected natural death due to cardiac causes within 1 h of onset of acute symptoms. Stroke included ischemic stroke and hemorrhagic stroke, which were diagnosed according to World Health Organization criteria [23]. All deaths were classified using the tenth revision of the International Classification of Disease and confirmed through death certificates using personal identity card number. All events were confirmed by hospital medical records and adjudicated by an event adjudication committee who were blinded to the measurements of body weight and weight change.

### 2.5. Statistics

Continuous variables are expressed as the mean  $\pm$  standard deviation (SD) or median (interquartile range) and categorical variables as percentages. Descriptive statistics were performed using one-way analysis of variance or chi-square tests. Non-normally distributed variables were log transformed before analyses. Age- and sex-standardized mortality and cardiovascular events per 1000 person years across BMI levels and weight change levels were calculated, respectively. Multivariate Cox proportional hazards models were used to assess associations of BMI levels and weight change with outcomes. Associations between changes in BMI levels and outcomes were also assessed. Hazard ratio (HR) and 95% confidence interval (CI) were shown.

In sensitivity analyses, associations of weight change with all-cause mortality were assessed in the patients stratified by baseline covariates. Furthermore, associations of the percentage of change in weight and average weight change per year with outcomes were assessed, respectively. Calculations and categories of the percentage of changing in weight and average weight change per year are described in the Supplemental material. Finally, the levels of baseline blood pressure, serum lipids, and fasting glucose were further adjusted in Cox models. All analyses were conducted using SPSS 18.0 (SPSS Inc., Chicago, Illinois), and a two-sided value of  $p < 0.05$  was considered statistically significant.

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