Journal of Advances in Medicine and Medical Research

24(2): 1-8, 2017; Article no.JAMMR.36956
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Long-term Weight Changes and Subsequent Hypercholesterolemia in Chinese Population

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Authors' contributions

This work was carried out in collaboration between all authors. Authors Liancheng Zhao and YW designed the study, wrote the protocol and wrote the first draft of the manuscript. Author Long Zhou performed the statistical analysis. Authors YL and MG performed the laboratory tests. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2017/36956
Editor(s):
(1) Kate S. Collison, Department of Cell Biology, King Faisal Specialist Hospital & Research Centre, Saudi Arabia.
Reviewers:
(1) O. Sharaye Kolade, Ahmadu Bello University Teaching Hospital, Nigeria.
(2) Ngo Nonga Bernadette, University of Yaounde I, Cameroon.
Complete Peer review History: http://www.sciencedomain.org/review-history/21416

Original Research Article

Received 25th September 2017
Accepted 12th October 2017
Published 16th October 2017

ABSTRACT

Aims: To explore the relationship between long-term body weight changes and hypercholesterolemia in middle aged Chinese population.
Study Design: Population based cross-sectional study.
Place and Duration of Study: Department of Epidemiology, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, between August 1998 and December 1998.
Methodology: Data were from China Multicenter Collaborative Study of Cardiovascular Epidemiology which was conducted in 1998, including 15 population samples selected by random cluster sampling. Approximately 1000 men and women in each population were surveyed for CVD risk factors, including to asking participants' body weight at age 25. Weight change was the difference between the body weight at the age of 25 and at the survey. The association of long-term body weight change with hypercholesterolemia was examined by Logistic Regression models.
Results: A total of 13883 participants including 6603 men and 7280 women were enrolled. After adjusting for age, sex and other potential confounding factors, long-term weight gain since age 25

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was positively and weight loss negatively associated with the risk of hypercholesterolemia. In comparison with participants with a weight gain from − 2.5 to 2.5 kg since 25 years old, the ORs (95% CI) of developing hypercholesterolemia for other weight change categories of <− 7.5 kg, − 7.5 to − 2.6 kg, 2.6 to 7.5 kg, 7.6 to 12.5 kg, and >12.5 kg were 0.59(0.49-0.71), 0.90(0.78-1.03), 1.19(1.06-1.35), 1.39(1.23-1.57), and 1.72(1.53-1.93), respectively.

Conclusion: Long-term weight gain was independently associated with the marked increase in risk of hypercholesterolemia in middle-aged Chinese men and women. Weight loss may help to reduce the risk of hypercholesterolemia for people who were overweight or obese in early adulthood.

Keywords: Weight change; hypercholesterolemia; obesity; Chinese.

1. INTRODUCTION

Cardiovascular disease (CVD) remains a leading cause of death in the world [1]. Raised total cholesterol (TC) is a strong risk factor for CVD, especially for coronary heart disease (CHD). A recent study showed that the risk of CHD increased by 24% in men and 20% in women associated with a 1-mmol/L increase in total cholesterol [2]. Hypercholesterolemia confers more than 4 million deaths from ischemic heart disease and stroke, and 88 million disability adjusted life year (DALY) losses in 2015 according to the global burden of disease (GBD) study [3]. The relationship between obesity and risk of hypercholesterolemia has been well established in previous studies [4-7], and the Third National Cholesterol Education Program specifically recommends weight management for preventing hypercholesterolemia [8]. However, few studies estimated the effects of long-term weight changes from early adulthood to middle age on hypercholesterolemia, and there has been no research on the Chinese population. The present study aims to use cross-sectional survey data from the China Multicenter Collaborative Study of Cardiovascular Epidemiology (ChinaMUCA) to explore the relationship between long-term body weight changes and hypercholesterolemia in middle aged Chinese population.

2. MATERIALS AND METHODS

2.1 Study Populations

The participants were from the China Multicenter Collaborative Study of Cardiovascular Epidemiology, which was originally designed as a cross-sectional multicenter comparison of cardiovascular disease risk factors. The cross-sectional survey conducted in 1998 included 15 population samples, of which 9 were from rural residential areas and 6 from urban areas. These populations were selected on the basis of the main population characteristics, such as socioeconomic status and geographical location. Approximately one thousand participants with an age range of 35–59 years, of which half were men and half women, were included as a random cluster sample from each of the populations and were surveyed for risk factors of cardiovascular disease. Further details about the study populations have been reported elsewhere [9,10]. All participants signed consent forms.

2.2 Data Collection

The demographic information and lifestyle risk factors were collected through a standardized questionnaire that also asked participants to recall their body weight at age 25. All staff involved in administering the survey were trained and certified in advance of the survey according to a uniform protocol and operation manual. In addition to the survey items, body weight and height were measured. Height was measured to the nearest centimeter using a vertical ruler, and weight was measured to the nearest kilogram with a spring balance. When they were weighed, all participants were required to wear light clothing and no shoes. The body mass index (BMI) at age 25 was calculated as the recalled weight at age 25 (in kilograms) divided by the square of the height (in meters).

2.3 Laboratory Tests

Fasting blood specimens after an overnight fast were obtained from each participant for measurement of serum total cholesterol and the participants need to stay 12 h without eating before blood drawn [11]. Blood samples were centrifuged and serum were separated within 3 hours and samples were then transported to the laboratories for analyze. Total cholesterol was measured with high-performance enzymic reagent.

2.4 Statistical Analysis

All data were entered twice into the computers by trained staff at local centers and were then sent to the coordinating center of the Department of Epidemiology, Fuwai Hospital for final processing and analysis. Weight change was calculated as the difference between the measured weight during investigation and the recalled weight at age 25 and was grouped into six categories (<− 7.5 kg; − 7.5 to − 2.6 kg; − 2.5–2.5 kg; 2.6–7.5 kg; 7.6–12.5 kg and >12.5 kg); the − 2.5–2.5 kg group was defined as stable weight. We calculated the mean values and proportions with a one-way analysis of variance for continuous variables and with $\chi 2$-tests for categorical variables. In addition, multivariate non-conditional logistic regression models were used to assess the associations between weight change categories and the risk of hypercholesterolemia defined as serum total cholesterol ≥200 mg/dL according to the guideline on the treatment of blood cholesterol of the American College of Cardiology/American Heart Association Task Force [12]. To test for trends, we calculated the median values of weight change within each category and then modeled these median values as a continuous variable in all models. Potential covariates, such as age, sex, urbanization, education level, cigarette use and alcohol consumption, were included in the multivariate models. A two-tailed P-value <0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. RESULTS

3.1 Baseline Characteristics of the Study Population

A total of 15573 participants were included in this study, representing a response rate of 85.1%. One thousand six hundred and ninety participants were excluded, including 935 who could not provide the recalled body weight data at age 25, 3 whose body weight had not been measured during the investigation, and 752 who did not provide their blood specimens. In the present analysis, 13883 participants remained, including 6603 men and 7280 women. Participants had a mean age of 46.7±7.1 years and a mean weight change of +5.8 kg. The baseline characteristics of the study population according to weight change categories are shown in Table 1. Participants who had greater weight gain were more likely to be urban residents and have higher education levels, but they were less likely to be smokers than those who had moderate weight gain or weight loss. More importantly, serum TC level significantly increased with weight gain from age 25 years to middle age (P for trend <0.001).

3.2 Odds Ratios of Hypercholesterolemia Based on Weight Change Categories

Table 2 shows the ORs of hypercholesterolemia based on the weight change categories. In an age- and sex adjusted analysis (Model 1) and multivariate-adjusted analysis (Model 2), weight gain of 2.6 kg or more during adulthood was associated with a higher risk of hypercholesterolemia than that of the stable weight group. Weight loss more than 7.5 kg was significantly associated with low risk of hypercholesterolemia. When we additionally adjusted for BMI at age 25 as a continuous variable in Model 3, and the trend was consistent with the trends exhibited in Model 1 and Model 2. In comparison with participants with a weight gain from − 2.5 to 2.5 kg since 25 years old, the ORs (95% CI) of developing hypercholesterolemia for other weight change categories of <− 7.5 kg, − 7.5 to − 2.6 kg, 2.6 to 7.5 kg, 7.6 to 12.5 kg, and >12.5 kg were 0.59(0.49-0.71), 0.90(0.78-1.03), 1.19(1.06-1.35), 1.39(1.23-1.57), and 1.72(1.53-1.93), respectively. Results were not altered when we stratified by baseline age. The association between weight change and risk of hypercholesterolemia were consistent across the age groups (Fig. 1).

3.3 Stratified Analysis of the Association between Weight Change and Hypercholesterolemia

Table 3 shows the results of stratified analysis of the association between weight change and hypercholesterolemia by BMI at age 25. We found that weight gain of more than 7.5 kg in normal or higher BMI groups were consistently associated with a higher risk of hypercholesterolemia. We also found that weight loss more than 7.5 kg could significantly decrease the risk of hypercholesterolemia among participants with BMI≥24 kg/m^2, but weight loss was not significantly associated with the risk of hypercholesterolemia for participants with BMI<21 kg/m^2 at age 25.

Table 1. Characteristics of participants (n=13883) by categories of weight change since 25 years of age

	Weight change since 25 years of age (kg)						*P* value
	< -7.5	-7.5~-2.6	-2.5~2.5	2.6~7.5	7.6~12.5	> 12.5	
No. of participants	903	1883	2573	2786	2674	3064	
Age (years)	48.4±7.1	47.0±7.3	46.0±7.3	45.9±7.1	46.5±6.9	47.3±6.8	0.7
Men (%)	464(51.4)	945(50.2)	1251(48.6)	1205(43.3)	1219(45.6)	1519(49.6)	< 0.001
Urban (%)	166(18.4)	404(21.5)	915(35.6)	1321(47.4)	1410(52.7)	1726(56.3)	< 0.001
Education							< 0.001
Primary School or Below (%)	491(54.4)	939(49.9)	981(38.1)	869(31.2)	714(26.7)	787(25.7)	
Junior high school (%)	269(29.8)	575(30.5)	853(33.2)	930(33.4)	927(34.7)	1107(36.1)	
High school or equivalent (%)	113(12.5)	289(15.4)	551(21.4)	739(26.5)	720(26.9)	812(26.5)	
At least some college (%)	30(3.3)	80(4.3)	188(7.3)	248(8.9)	313(11.7)	358(11.7)	
Current smokers (%)	363(40.2)	694(36.9)	842(32.7)	731(26.2)	742(27.8)	833(27.2)	< 0.001
Current alcohol drinkers (%)	251(27.8)	508(27.0)	652(25.3)	670(24.1)	685(25.6)	836(27.3)	0.0445
BMI at baseline(1998)	20.2±2.2	20.9±2.1	21.8±2.3	23.2±2.3	24.8±2.3	27.6±2.9	< 0.001
BMI at 25 years of age	24.2±2.3	22.8±2.1	21.8±2.3	21.2±2.2	20.9±2.2	20.6±2.3	< 0.001
Total cholesterol (mg/dl)	176.9±36.7	180.6±37.0	181.7±36.7	184.0±38.5	187.7±37.9	192.2±38.9	< 0.001

Abbreviation: BMI, Body mass index

Table 2. Odds ratios of hypercholesterolemia by weight change since 25 years of age (N=13883)

Weight change	Cases (%)	Model 1[a]		Model 2[b]		Model 3[c]	
		OR	95% CI	OR	95% CI	OR	95% CI
< -7.5	192(21.3)	0.63	0.52-0.76	0.61	0.51-0.74	0.59	0.49-0.71
-7.5 to -2.6	510(27.1)	0.93	0.81-1.06	0.91	0.80-1.15	0.90	0.78-1.03
-2.5 to 2.5	709(27.6)	1.00	ref	1.00	ref	1.00	ref
2.6 to 7.5	850(30.5)	1.17	1.04-1.32	1.18	1.05-1.33	1.19	1.06-1.35
7.6 to 12.5	912(34.1)	1.34	1.19-1.51	1.37	1.21-1.54	1.39	1.23-1.57
> 12.5	1216(39.7)	1.65	1.47-1.85	1.68	1.50-1.89	1.72	1.53-1.93
P for trend		< 0.001		< 0.001		< 0.001	

Abbreviations: OR, Odds ratio; CI, Confidence interval.

a Model 1 adjusted for age and sex. b Model 2 additionally adjusted for urbanization (urban or rural),education level (primary school or below, junior high school, high school or equivalent, or at least some college),smoking status (current smoker or not),drinking status (current drinker or not),and family history of hypertension.

c Model 3 additionally adjusted for BMI at 25 years of age as a continuous variable

Table 3. Stratified analysis of relationship between weight change and hypercholesterolemia by BMI at 25 years (N=13883)

Weight change, kg	BMI at 25 years, kg/m^2							
	<18.5		18.5-20.9		21-23.9		≥24	
	Cases (%)	OR (95%CI)	Cases (%)	OR (95%CI)	Cases (%)	OR (95%CI)	Cases (%)	OR (95%CI)
<-7.5	0	-	18(29.5)	1.09(0.61-1.96)	79(20.2)	0.56(0.42-0.74)	95(21.1)	0.56(0.41-0.78)
-7.5~-2.6	6(25.0)	0.51(0.18-1.40)	90(25.5)	0.93(0.69-1.24)	250(25.3)	0.82(0.67-0.99)	164(31.6)	1.08(0.81-1.44)
-2.5~2.5	50(30.7)	1.00(ref)	199(24.4)	1.00(ref)	337(28.4)	1.00(ref)	123(30.1)	1.00(ref)
2.6~7.5	76(27.3)	0.91(0.59-1.42)	328(30.4)	1.39(1.13-1.72)	357(31.3)	1.15(0.96-1.38)	89(30.7)	1.05(0.75-1.46)
7.6~12.5	112(33.1)	1.15(0.75-1.74)	345(31.9)	1.42(1.15-1.75)	350(34.8)	1.33(1.11-1.61)	105(42.5)	1.86(1.33-2.60)
>12.5	210(39.8)	1.28(0.86-1.91)	494(38.0)	1.79(1.47-2.20)	419(42.0)	1.79(1.49-2.15)	93(39.2)	1.59(1.13-2.24)

Abbreviation: BMI, Body mass index; OR, Odds ratio; CI, Confidence interval

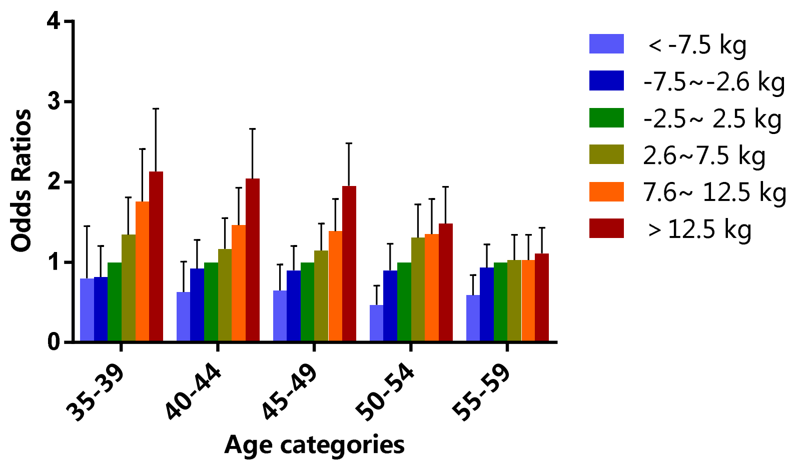

Fig. 1. Odds ratios for hypercholesterolemia according to weight change since age 25 in each age group. Results adjusted for age and sex, urbanization, education level, smoking status, drinking status, and BMI at 25 years of age as a continuous variable

4. DISCUSSION

4.1 Main Findings of this Study and Comparison with Other Studies

In this multicenter population study, we found that long-term weight gain from early adulthood to middle age were significantly associated with increased risk of hypercholesterolemia in middle-aged Chinese men and women. Even moderate weight gain from early adulthood to middle age was associated with a higher risk of hypercholesterolemia. These findings were consistent with the National Runners' Health Study conducted in United States, which found that the odds for developing hypercholesterolemia increased significantly in association with gains in BMI and waist circumferences in both male and female. A gain in BMI≥2.4 kg/m^2 significantly increased the odds for hypercholesterolemia by 94% in men and 129% in women compared to those whose BMI declined after 7 years follow up [13]. A cohort study conducted in Japanese population enrolled 4737 male employees showed that weight gain (more than 2 kg) was strongly related to an increased risk for hypercholesterolemia after being adjusted for possible confounding factors such as age, smoking status, alcohol intake [14]. The Coronary Artery Risk Development in Young Adults (CARDIA) Study erolled 3325 black and white men and women aged 18–30 y from four centers followed for 10 years, which found that a 9.1 kg weight increase in persons not overweight at baseline predicted an increase in LDL-C ranging from 0.23 mmol/l in black women to 0.28 mmol/l in black men [15]. However, these studies failed to further analyze the relationship between different degree of weight changes and hypercholesterolemia. In our study, even moderate weight gain (2.5 to 7.6 kg) was associated with a 19% higher risk of hypercholesterolemia in middle age compared with those with stable weight.

4.2 Stratified Analysis by Age Groups

Given the time between age 25 and the baseline survey varied greatly. Therefore, we stratified participants by age categories (Fig. 1). Notably, a positive association between weight change since age 25 and the risk of hypercholesterolemia was found in all age groups, indicating that the association between weight change and hypercholesterolemia remained regardless of the time between age 25 and the baseline survey.

4.3 Stratified Analysis by Body Mass Index at Participants' 25

We also found that weight gain of more than 7.5 kg in normal or higher BMI groups increased the risk of hypercholesterolemia and weight loss more than 7.5 kg could significantly decrease the risk of hypercholesterolemia among participants who were overweight or obesity, but weight loss was not significantly associated with the risk of hypercholesterolemia for participants who had lower weight at early adulthood. These findings suggested that weight loss is an obvious benefit for overweight or obese population, but not for normal weight and underweight population.

5. STRENGTHS

Our study has several strengths. First, to the best of our knowledge, this is the first study focusing on the relationship between long-term adult weight change and hypercholesterolemia in the Chinese population. Second, we enrolled a large population-based multicenter sample, including male and female participants from China.

6. LIMITATIONS

Our study also has several potential limitations. First, our analyses used self-reported and recalled weight at 25 years of age instead of measured values. Although some validation studies in other cohorts have shown that self-reported weights are highly correlated with measured weights [16,17], our results may be affected slightly for the existence of recall bias. Second, we could not provide the real cause-effect relationship between weight change and hypercholesterolemia since the cross-sectional design itself, long-term prospective study is needed in future.

7. CONCLUSION

In conclusion, long-term weight gain since age 25 was independently associated with the marked increase in risk of hypercholesterolemia in middle-aged Chinese men and women. Weight loss may help to reduce the risk of hypercholesterolemia for people with a higher BMI in early adulthood, but it did not reduce the risk of hypercholesterolemia for people who were underweight or had a lower normal BMI in early adulthood.

CONSENT

An informed consent form was provided to each participant before filling out the questionnaire. The study was conducted with the agreement from all participants based on their signed consent forms.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/21416