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Original Article

Long-term weight gain is related to risk of metabolic syndrome even in the non-obese

Akiko Suzuki, Rie Akamatsu *

Graduate School of Humanities and Sciences, Ochanomizu University, Japan

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ABSTRACT

Objective: To examine the relationship between long-term weight gain and risk of metabolic syndrome (MetS) in non-obese and obese subjects.

Methods: Cross-sectional data from 3342 participants (1614 men, 1728 women) were obtained from a Specific Medical Checkup and a self-reported questionnaire survey conducted by a health insurance society between April 2009 and March 2010. Subjects were divided into four groups based on body mass index (BMI) and experience of weight gain since the age of 20 years using a self-reported questionnaire: non-obese/non-gain, non-obese/gain, obese/non-gain, and obese/gain. Relationships between weight gain and risk of MetS were investigated using logistic regression analysis, with the four groups as a dependent variable.

Results: There were 2103 (62.9%) subjects in the non-obese/non-gain, 545 (16.3%) in the non-obese/gain, 125 (3.7%) in the obese/non-gain, and 569 (17.0%) in the obese/gain groups. The obese/gain group showed the highest risk of MetS in men (odds ratio [OR]: 37.45, 95% confidence interval [95% CI]: 25.32–55.40) and women (OR: 163.13, 95% CI: 56.22–473.32). Even the non-obese/gain group had an increased risk of MetS, in men (OR: 4.98, 95% CI: 3.47–7.15) and women (OR: 6.28, 95% CI: 1.53–25.83).

Conclusion: The data show that the obese/gain group had the highest risk of MetS, and that those who gained weight were at risk of MetS, even the non-obese.

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1. Introduction

Non-communicable diseases (NCDs), such as cardiovascular disease, cerebrovascular disease, cancer, and diabetes, are the leading causes of mortality in the developed world, representing 63% of all deaths [1]. Japan is no exception; according to a report released by the Ministry of Health, Labour, and Welfare (MHLW), the death rate due to NCDs is higher than the death rate due to other diseases [2]. Among the NCDs, it has been reported that the risk of developing cardiac and cerebrovascular diseases is increased by metabolic syndrome (MetS) [3,4]. According to the National Health and Nutrition Survey in 2010, more than 30% of men and women 20 years or older, and one in two men 40–74 years old are suspected to have MetS or preliminary MetS [5].

In recent years, it has been reported that the relationship between long-term weight gain from a young age that is self-reported by recall and actual weight values is strong. In long-term recall of past weight, accuracy is high according to previous studies [6–8]. It was shown that the value of weight that subjects self-reported and the actual value from a contemporaneous medical examination had a high correlation in men from 30 to 60 years old in Japan [6]. In studies targeting those from 60 to 80, results comparing recall of self-report weights with actual values by generation (e.g., those in their 20s, 30s, 40s, and 50s) showed high correlations [7,8].

Previous studies showed a strong relationship between long-term weight gain and risk of MetS [9–11]. Nishida et al. (2005) showed, targeting those who were 39–86 years old, that a person who gained weight since age 20 was at an increased risk of MetS, as compared to those who did not gain weight [9]. A study targeting middle-aged subjects examining the relationship between MetS and weight gain from 20 years old showed that those who gain weight by more than 10 kg had about an eight-fold increase risk in men and 12-fold in women [10]. Additionally, a longitudinal study running from 1985 to 2001 indicated that weight gain is an important risk factor for MetS [11].

Regarding biomarkers, few studies have examined the relationship with long-term weight gain. Some studies have shown that those who have weight gain since the age of 20 years are more

* Corresponding author at: Otsuka 2-1-1, Bunkyo-ku, Tokyo 112-8610, Japan. Tel.: +81 3 5978 5680; fax: +81 3 5978 5680.
E-mail address: akamatsu.rie@ocha.ac.jp (R. Akamatsu).

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likely to fulfill three or more of the criteria for a diagnosis of MetS [9,12]. Another study showed that BMI changes after the age of 25 years were significantly associated with biomarkers, such as HDL-cholesterol (HDL-C), and HbA1c [13].

In this way, long-term weight gain has been shown to be associated with the risk of MetS and biomarkers. However, few studies have examined the relationship between long-term weight gain and inspection values as biomarkers in non-obese and obese subjects. For example, Zhang et al. (2005) showed that long-term weight gain was associated with increasing risk for lipid abnormalities and hypertension. Additionally, when subjects were divided into obese and non-obese, the relationship was not seen in the obese (BMI $\geq$ 25) group [14]. Nishida et al. (2005) also showed that some people have a risk of MetS in the non-obese (BMI $<$ 25) and long-term weight gain group, not just the obese (BMI $\geq$ 25) and long-term weight gain group [9]. However, these studies did not compare the non-obese and obese subjects.

Therefore, non-obese subjects who show weight gain are also at risk of MetS along with those who are already obese. Nevertheless, in the criteria for diagnosing MetS in Japan, because abdominal circumference is a primary item [15,16], there is a high possibility of excluding the non-obese from MetS and various disease prevention efforts, even if they have long-term weight gain. Therefore, it is important to examine the risk of MetS in non-obese, as well as in obese.

This study examined the relationship between long-term weight gain and inspection values in non-obese and obese subjects. Furthermore, we examined the relationship between long-term weight gain and risk of MetS in non-obese and obese subjects.

2. Materials and methods

This study used cross-sectional data for 3879 participants (1764 men, 2115 women). The data were obtained from a checkup called the Specific Medical Checkup [17] and a self-reported questionnaire survey [17] conducted by a health insurance society at a financial enterprise between April 2009 and March 2010 in all parts of Japan (27 prefectural and city governments). The Specific Medical Checkup is a medical checkup used by the national insurance scheme to prevent lifestyle-related diseases, and is conducted by the health insurance society. The Specific Medical Checkup targets all public medical insurance subscribers from 40 to 75 years old in Japan [17].

This study was approved by the Ethics Review Committee of Ochanomizu University (No. 22-2).

2.1. Content of the questionnaire

2.1.1. Demographic characteristics

In this study, we used gender, age, and area of checkup (prefectural and city government) in statistical analyses. Body mass index (BMI) was calculated from height and weight (kg/m^2). Based on the criteria of the Japan Society for the Study of Obesity (JASSO) announced in 2000 [18], those with BMI $>$ 25 kg/m^2 were defined as obese.

2.1.2. Long-term weight gain

This item was included in the self-reported questionnaire [17], answered at the Specific Medical Checkup. To the question "I have gained weight by more than 10 kg from my weight at age 20 years old", the response was yes or no. Those who answered "yes" were defined as having long-term weight gain.

2.1.3. Inspection results

This study used eight items measured at the Specific Medical Checkup: abdominal circumference (AC); systolic arterial pressure (SAP); diastolic blood pressure (DBP); triglyceride (TG); HDL-cholesterol (HDL-C); LDL-cholesterol (LDL-C); fasting blood glucose (FBG; in Japan, the term generally conveys the same meaning as plasma glucose [19]); and HbA1c.

The diagnostic criteria used for MetS were the criteria that are appropriate for Japanese at MetS risk in Japan [15,20]. The AC was measured parallel to the navel of the subject in the upright position while exhaling lightly, according to the method of the "Standard Medical Checkup and Health Instruction Program" [17].

The AC was a required item (men: $>$85 cm, women: $>$90 cm). In addition to AC, those who had more than one of the three inspection risk items—blood pressure (SAP $>$ 130 mmHg or DBP $>$ 85 mmHg), lipids (TGs $>$ 150 mg/dL or HDL-C $<$ 40 mg/dL), and fasting blood glucose (FBG $>$ 110 mg/dL)—were diagnosed as having a risk of MetS. Those who did not fulfill the diagnostic criteria were considered to be at no increased risk of MetS (i.e., men with AC $<$ 85 cm or AC $\geq$ 85 cm and no inspection risk factors, and women with AC $<$ 90 cm or AC $\geq$ 90 cm and no inspection risk factors).

2.1.4. Physical activity and eating behaviors

This item was included in the self-reported questionnaire [17], answered at the Specific Medical Checkup. Physical activity: "Do you perform physical activity or the equivalent of walking for at least 1 hour a day?" Late dinner: "Do you eat dinner 2 hours before bedtime three or more times a week?" Midnight snacks: "Do you eat snacks after dinner three or more times a week?" Skipping breakfast: "Do you skip breakfast three or more times a week?" The above four items were answered "yes" or "no." Speed of eating: "Do you eat quickly in comparison with most people?" response "slow/medium" or "fast." Frequency of alcohol consumption per week was scored as "very rarely," "sometimes," and "every day." Responses to the amount of alcohol consumed per day were selected from "under 180 mL," "180–360 mL," "360–540 mL," or "over 540 mL." These items were used as covariates in multivariate logistic regression analysis.

2.2. Statistical analysis

Demographic characteristics, physical activity, eating behaviors, and the results of the Specific Medical Checkup were examined by gender. Based on BMI and long-term weight change, subjects were divided four groups: not obese and no weight gain (non-obese/non-gain), not obese and weight gain (non-obese/gain), obese and no weight gain (obese/non-gain), and obese and weight gain (obese/gain). The χ^2 test and the Kruskal–Wallis test were used to determine differences among each of the four groups in demographic characteristics and results from the Specific Medical Checkup. Additionally, the Bonferroni correction was used for multiple comparisons.

Abdominal circumference and inspection risk were examined in the four groups, and separately by gender. Based on the criteria, AC was used to divide subjects into two groups, with reference to 85 cm in men and 90 cm in women. In addition, the subjects were divided according to the number of inspection risk factors, i.e., 0 or 1–3.

Relationships between risk of MetS and the four groups were investigated with multivariate logistic regression analyses using MetS risk as a dependent variable. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated with "non-risk of MetS" and "non-obese and non-weight gain" as standards. Age, area of checkup, physical activity, and eating behaviors were used as covariates. For physical activity and eating behaviors, this study adjusted these items to analyze the association between weight gain and MetS, regardless of current physical activity and eating behaviors.

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