

## ORIGINAL ARTICLE

# Men who were thin during early adulthood exhibited greater weight gain-associated visceral fat accumulation in a study of middle-aged Japanese men

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## Summary

### Objective

This study aimed to assess the relationship between weight gain from early adulthood and visceral fat accumulation.

### Methods

The participants were 549 men aged 42 to 64 years who were randomly selected from the local resident registry for the National Institute for Longevity Sciences' neighbourhood. They were asked to recall their weight at 18 years of age, and then, post-18 weight-change values were calculated for each participant (their current weight minus their weight at 18). The participants were divided according to their median body mass index (BMI) at 18 years of age (initial BMI) ( $<20.14$  and  $\geq 20.14$  kg m<sup>-2</sup>). Visceral fat area (VFA) and subcutaneous fat area (SFA) were measured on computed tomography scans.

### Results

The participants with initial BMI of  $<20.14$  kg m<sup>-2</sup> exhibited greater post-18 weight changes than those with initial BMI of  $\geq 20.14$  kg m<sup>-2</sup>. The participants' post-18 weight-change values were negatively correlated with their initial BMI and positively correlated with both VFA and SFA. The slope of the regression line for the relationship between post-18 weight change and VFA was steeper in the participants with initial BMI of  $<20.14$  kg m<sup>-2</sup> ( $\beta = 4.36$ ) than in those with initial BMI of  $\geq 20.14$  kg m<sup>-2</sup> ( $\beta = 3.23$ ).

### Conclusions

Visceral fat accumulation is affected not only by an individual's post-18 weight gain but also by their initial BMI. Men who were thin in early adulthood experienced greater weight gain-associated VFA increases, but the same was not true for SFA.

**Keywords:** Visceral fat, weight at 18 years of age, weight gain.

## Introduction

Weight gain is commonly observed between early adulthood and middle age (1–4). According to the National Health and Nutrition Examination Survey in 2014 (a cross-sectional survey) (1), the mean body mass index (BMI) for Japanese men was 22.4 kg m<sup>-2</sup> in the 20 to 29 years age group, 24.0 kg m<sup>-2</sup> in the 40 to 49 years age group and 23.9 kg m<sup>-2</sup> in the 50 to 59 years age group. According to the National Health Examination

and the National Health and Nutrition Examination Surveys conducted in the USA from 1999 to 2002, the mean BMIs for men aged 20 to 29 years, 40 to 49 years and 50 to 59 years were 26.6, 28.4 and 28.7 kg m<sup>-2</sup>, respectively (2). In Norway, men aged 20–29 years exhibited a mean weight increase of 7.9 kg over 11 years (3). In a 14-year follow-up study conducted in South Wales, the mean BMI was 22.3 kg m<sup>-2</sup> at 18 years, and the mean weight gain during the study period was 11.2 kg (standard deviation [SD]: 11.2) (4).

There are several causes of weight changes, such as variations in food intake or physical activity (5), smoking habits (6–8), and genetic factors (9). In a study of middle-aged and elderly Japanese men, a combination of cholecystokinin 1 receptor and beta-3 adrenergic receptor polymorphisms was found to be associated with a weight gain of  $\geq 10$  kg after age 18 (9).

Marked weight gain is as harmful to health as being overweight or obese. In previous studies, weight gain from early adulthood to middle age was demonstrated to be closely associated with cardiovascular disease (10,11), coronary heart disease (4,12,13), and diabetes in men (5). Chei *et al.* found that weight gain was associated with a two-fold greater risk of coronary heart disease in Japanese men (11). Furthermore, the latter relationship was observed in men who had BMI of  $< 21.7$  kg m<sup>-2</sup> at 20 years of age but not in those with BMI  $\geq 21.7$  kg m<sup>-2</sup> at this age. They assumed that weight gain in initially lean men tends to favour upper abdominal fat accumulation over lower abdominal fat accumulation. Moreover, this tendency was weaker in men with higher BMI at 20 years of age. However, the latter study did not examine fat distribution, including visceral fat (VF) volume or area. Koh-Banerjee *et al.* found that weight gain was associated with the risk of diabetes (5), but they only measured waist circumference; i.e., they did not assess VF accumulation. However, waist circumference is not necessarily an accurate measure of VF accumulation, as it is influenced by

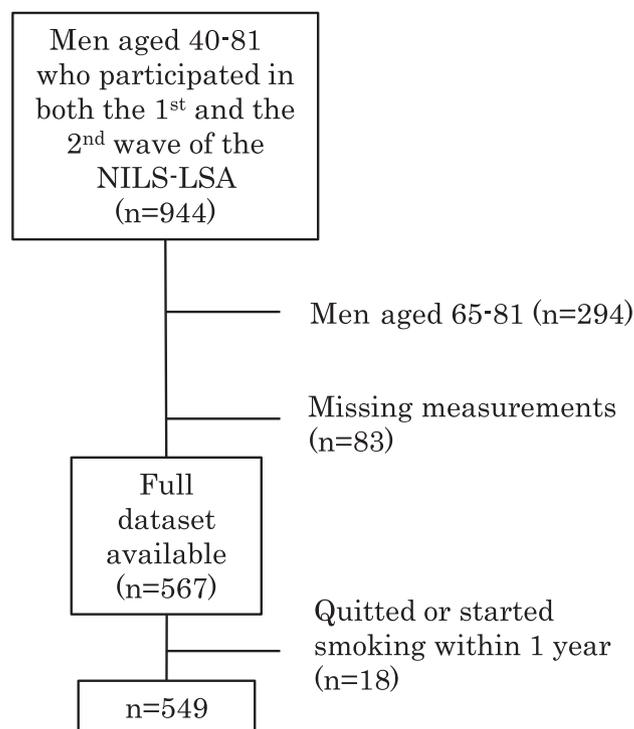
both VF and subcutaneous fat (SF). A previous study reported that VF accumulation was more strongly associated with numerous diseases than SF accumulation (14,15).

Thus, the weight gain seen from early adulthood to middle age might be strongly associated with VF accumulation, especially in lean young adults. However, little is known about the association between such weight changes and VF accumulation. Therefore, the purpose of this study was to investigate the association between the weight change from 18 years of age to the present day (post-18 weight gain) and VF area (VFA).

## Methods

### Participants

The participants were selected from among the 944 Japanese men (age range, 41 to 81 years) who participated in the first and second waves of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA) (16). The NILS-LSA involved gender-stratified and age-stratified samples from the neighbourhood of the NILS, who were randomly selected from the local resident registry in cooperation with the local government. The study participants were 549 men (age range, 42 to 64 years) for whom no measurements were missing (Figure 1). The participants who had quit smoking more



**Figure 1** Sampling procedure.

than 1 year ago after smoking for more than 1 year were also excluded because smoking habits also affect weight changes. Many studies have indicated that smokers tend to have lower body weights than non-smokers (7), and smoking cessation is known to be associated with substantial weight gain (6,8). Weight gain was associated with increases in total cholesterol, triglyceride and  $\beta$ -lipoprotein levels in men and women who ranged in age from 18 to 64 years but not in those who ranged in age from 65 to 88 years of age (17). Thus, men ranging in age from 65 to 82 years were excluded from this study.

## Measurements

The measurements were obtained in 1 d in the second wave of the NILES-LSA (April 2000 to May 2002). Body weight (kg) was measured in the morning after overnight fasting using digital scales while the participants were only wearing underwear. Waist circumference was measured at the level of the umbilicus with a fibreglass tape measure. VFA ( $\text{cm}^2$ ) and SF area (SFA;  $\text{cm}^2$ ) were measured on computed tomography scans of the abdomen taken at the umbilical level (L4 to L5). All of the computed tomography scans (SCT-6800TX; Shimadzu, Japan) were performed with the participants in the supine position. VFA and SFA were calculated using computer software (Fat Scan; N2 Systems, Japan) (18) in accordance with a previously described procedure (19). Percentage body fat was measured using dual energy X-ray absorptiometry (Hologic QDR-4500). The participants' weights at 18 years of age were self-reported via the first-wave questionnaires (November 1997 to May 2000).

## Data analysis

Body mass index at 18 years (the initial BMI) was calculated as the participant's weight (kg) at 18 years divided by their current height (m) squared. Post-18 weight-change values were calculated for each participant (the participant's current weight minus their weight at 18 years of age). Spearman's rank correlation coefficients were calculated for the relationships between post-18 weight gain and VFA or SFA. The participants were grouped into two categories based on the median initial BMI ( $<20.14$  and  $\geq 20.14$   $\text{kg m}^{-2}$ ). The unpaired Student's *t*-test was used to compare the post-18 weight changes seen in the two groups. In each group, two-way analysis of covariance (ANCOVA) was used to evaluate the effects of the interactions between (i) the initial BMI and post-18 weight gain and (ii) the initial BMI and current BMI on the participants' VFA and SFA after controlling for age. Regression lines were produced using multiple linear regression analysis, and the associated regression

coefficients were compared. Comparisons between frequencies were performed using the chi-squared test. The data were analysed using the SAS statistical software package (release 9.3; SAS Institute, Cary, NC, USA). Probability values of  $<0.05$  were regarded as significant.

## Ethics

This study was performed in accordance with the World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. The purpose of this study and the procedures for each examination were fully explained to the participants. All of the participants provided written informed consent. All data were analysed collectively, and the participants' privacy was protected. All of the procedures conducted in the NILES-LSA were approved by the committee of ethics for human research at the National Center for Geriatrics and Gerontology.

## Results

The participants' characteristics are shown in Table 1. Their mean initial BMI was 20.4 (SD: 2.3)  $\text{kg m}^{-2}$ , and their mean current BMI was 23.3 (SD: 2.8)  $\text{kg m}^{-2}$ . The mean post-18 weight change was 8.0 (SD: 7.9) kg. The participants with initial BMI of  $<20.14$   $\text{kg m}^{-2}$  exhibited a greater mean post-18 weight change than the participants with initial BMI of  $\geq 20.14$   $\text{kg m}^{-2}$  ( $p < 0.001$ ). The participants with initial BMI of  $<20.14$   $\text{kg m}^{-2}$  exhibited lower mean current BMI, VFA, SFA, and waist circumference values than the men with initial BMI of  $\geq 20.14$   $\text{kg m}^{-2}$ , but this was not true for percentage body fat. Table 2 shows data regarding post-18 weight changes. Post-18 weight increases of  $>10$  kg were seen in 39% of men, and such increases were significantly more common among the men with initial BMI of  $<20.14$   $\text{kg m}^{-2}$  (49.3%) than among those with initial BMI of  $\geq 20.14$   $\text{kg m}^{-2}$  (28.7%) ( $p < 0.001$ ).

The post-18 weight change was positively correlated with VFA, SFA, and waist circumference (after controlling for age and initial BMI), and it was negatively correlated with the initial BMI (after controlling for age) (Table 3). Two-way ANCOVA demonstrated that the interaction between the initial BMI ( $<20.14$  and  $\geq 20.14$   $\text{kg m}^{-2}$ ) and post-18 weight change was significantly associated with VFA ( $p = 0.026$ ), but not SFA ( $p = 0.554$ ), after controlling for age (Table 4). The regression coefficient for the relationship between post-18 weight change and VFA was significantly larger among the participants with initial BMI of  $<20.14$   $\text{kg m}^{-2}$  ( $\beta = 4.29$ , standard error [SE] = 0.24) than among those with initial BMI of  $\geq 20.14$   $\text{kg m}^{-2}$  ( $\beta = 3.60$ , SE = 0.31) (Figure 2). In the same way, two-

**Table 1** Participants' characteristics according to their BMI at 18 years of age

	All <i>n</i> = 549	BMI at 18 years of age		<i>p</i> -value
		<20.14 kg m <sup>-2</sup> <i>n</i> = 274	≥20.14 kg m <sup>-2</sup> <i>n</i> = 275	
Age (years)	53.7 (6.5)	53.4 (6.6)	54.0 (6.3)	0.331
BMI (kg m <sup>-2</sup> )	23.3 (2.8)	22.4 (2.6)	24.2 (2.6)	<0.001
BMI at 18 years (kg m <sup>-2</sup> )	20.4 (2.3)	18.7 (1.0)	22.1 (1.8)	<0.001
Post-18 weight change (kg)	8.1 (7.9)	10.3 (7.6)	5.8 (7.6)	<0.001
Visceral fat area (cm <sup>2</sup> )	92.0 (45.3)	86.8 (45.4)	96.9 (44.6)	0.009
Subcutaneous fat area (cm <sup>2</sup> )	114.6 (49.7)	106.4 (46.2)	122.4 (51.7)	0.001
Percentage body fat (%)	20.8 (4.3)	20.5 (4.3)	21.1 (4.2)	0.080
Waist circumference (cm)	85.2 (7.8)	83.8 (7.6)	86.6 (7.7)	<0.001

Data are shown as mean (standard deviation) values.

BMI, body mass index.

**Table 2** Frequency of weight change from 18 years of age to the present

	All		BMI at 18 years of age				<i>p</i> -value*
	<i>n</i>	%	<20.14 kg m <sup>-2</sup>		≥20.14 kg m <sup>-2</sup>		
Post-18 weight change (kg)	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
<0.0	80	14.6	20	7.3	60	21.8	<0.001
0–9.9	255	46.4	119	43.4	136	49.5	
≥10.0	214	39.0	135	49.3	79	28.7	

\*According to the chi-squared test.

BMI, body mass index.

**Table 3** Spearman's correlation coefficients for the relationships among the post-18 weight change, BMI at 18 years old, visceral fat area, subcutaneous fat area and waist circumference after controlling for age and BMI at 18 years of age

	Post-18 weight change (kg)	
BMI at 18 years of age <sup>†</sup>	-0.344	<i>p</i> < 0.001
Visceral fat area (cm <sup>2</sup> ) <sup>‡</sup>	0.691	<i>p</i> < 0.001
Subcutaneous fat area (cm <sup>2</sup> ) <sup>‡</sup>	0.781	<i>p</i> < 0.001
Waist circumference (cm) <sup>‡</sup>	0.851	<i>p</i> < 0.001

<sup>†</sup>After controlling for age.

<sup>‡</sup>After controlling for age and BMI at 18 years of age.

BMI, body mass index.

way ANCOVA demonstrated that the interaction between initial BMI (<20.14 and ≥20.14 kg m<sup>-2</sup>) and current BMI was not significantly associated with VFA (*p* = 0.584) or SFA (*p* = 0.436), after controlling for age (Table 4). However, the men with initial BMI of <20.14 kg m<sup>-2</sup> demonstrated significantly larger (98.3 and 120.0 cm<sup>2</sup>, respectively) least means square values for VFA and

SFA than the men with initial BMI of ≥20.14 kg m<sup>-2</sup> (85.9 and 108.2 cm<sup>2</sup>, respectively).

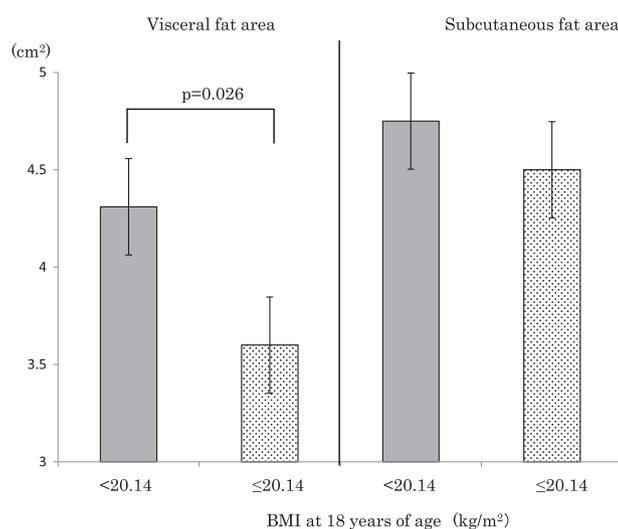
## Discussion

This study showed that the weight change that occurred in men during the period from 18 years of age to middle age (post-18 weight change) was positively correlated with the increases in both VFA and SFA during the same period. However, VFA differed depending on the participants' weight at 18 years of age. The slope of the regression line for the relationship between post-18 weight change (*x*) and VFA (*y*) was steeper in men with initial BMI of <20.14 kg m<sup>-2</sup> (*β* = 4.29, SE: 0.24) than in those with initial BMI of ≥20.14 kg m<sup>-2</sup> (*β* = 3.60, SE: 0.31). In other words, the VFA increase that accompanied the weight gain that occurred between the age of 18 and middle age was greater in men who were thin during early adulthood. Chei *et al.* found that weight gain of ≥10 kg was associated with a two-fold greater risk of coronary heart disease in men with BMI of <21.7 kg m<sup>-2</sup> at 20 years

**Table 4** Two-way factorial ANOVA results

		F-value	p-value
Visceral fat area	BMI at 18 years	61.67	<0.001
	Post-18 weight change	418.73	<0.001
	Age	28.99	<0.001
	BMI at 18 years * post-18 weight change	5.01	0.026
Subcutaneous fat area	BMI at 18 years	80.86	<0.001
	Post-18 weight change	598.39	<0.001
	Age	0.15	0.697
	BMI at 18 years * post-18 weight change	0.35	0.554
Visceral fat area	BMI at 18 years	0.00	0.967
	BMI	526.89	<0.001
	Age	19.12	<0.001
	BMI at 18 years * BMI	0.30	0.584
Subcutaneous fat area	BMI at 18 years	1.74	0.188
	BMI	1,103.38	<0.001
	Age	5.68	0.018
	BMI at 18 years * BMI	0.61	0.435

ANOVA, analysis of variance; BMI, body mass index.



**Figure 2** Estimated changes in visceral fat area and subcutaneous fat area according to each 1-kg weight change as determined by regression analysis. BMI, body mass index.

of age but not in men with BMI of  $\geq 21.7$  kg m<sup>-2</sup> at 20 years of age (11). This result can be explained by the findings of the present study. Individuals with BMI of  $< 21.7$  kg m<sup>-2</sup> at 20 years of age might possess more VF than those with BMI of  $\geq 21.7$  kg m<sup>-2</sup>. Furthermore, the post-18 weight change was found to be negatively correlated with the initial BMI ( $r = -0.338$ ) after controlling for age. This suggests that thin men are more likely to gain weight and accumulate VF during early adulthood than other men.

From the viewpoint of molecular biology, the total number of adipocytes increases in childhood and

adolescence and then levels off and remains constant in adulthood (20). Subcutaneous adipose tissue storage acts as a buffer for excessive energy intake (21). In men who are thin when they are young, the number of fat cells might be relatively low. Therefore, fat cannot accumulate in SF cells alone and so might also accumulate in the abdominal cavity.

In order to prevent VF accumulation, it is important that men are not too thin during early adulthood and that their weight does not increase markedly between age 18 and middle age. Smoking habits also affect weight changes. In the present study, 39.0% of the participants were

smokers, which was similar to the prevalence figure obtained in a national survey in 2016 (40 to 49 years of age: 41.1%; 50 to 59: 39.0%; 60 to 69: 28.9%) (1). Smoking might help to prevent weight gain or aid the maintenance of a low body weight (6–8). As a consequence, VFA might not increase in smokers. However, even if they exhibit little VF, smokers have higher blood haemoglobin A1c levels than those who do not smoke (22). Therefore, smoking in order to prevent weight gain is not advisable.

In this study, the association between VFA and current BMI was significantly stronger among the men with initial BMI of  $<20.14 \text{ kg m}^{-2}$  than among the men with initial BMI of  $\geq 21.14 \text{ kg m}^{-2}$ . In recent years, BMI and waist circumference have been used to diagnose obesity and abdominal adipose tissue accumulation. Post-18 weight change might be another useful parameter for diagnosing obesity and abdominal adipose tissue accumulation. This highlights the fact that BMI does not provide any information about body composition or body fat distribution.

This study had some limitations. First, the participants' weights at 18 years of age were not measured; rather, they were self-reported using a questionnaire. However, Tamakoshi *et al.* reported that individuals were able to recall their past weights with good accuracy over long periods (23). Casey *et al.* also detected strong correlations between measured weight at 18 years of age and self-reported recalled weight at 50 years of age (24). Second, the timing of the participants' post-18 weight changes was not examined. Previous studies have reported that weight fluctuations were associated with an increased risk of all-cause mortality. Zhang *et al.* found that among Japanese men aged 40–49 years, the development of metabolic syndrome might explain the increased risk of cardiovascular disease, not only in people with overweight or obesity but also in normal-weight people that exhibit large weight fluctuations (25).

In conclusion, in middle-aged men, the weight change that occurs between 18 years of age and middle age was found to be positively correlated with the increases in VFA and SFA observed during the same period. SFA might increase with weight in a uniform manner. However, VF accumulation was affected not only by an individual's post-18 weight gain but also by their initial BMI. Men who were thin in early adulthood experienced greater weight gain-associated VFA increases, but the same was not true for SFA. Moreover, although the men with initial BMI of  $<20.14 \text{ kg m}^{-2}$  exhibited lower current BMI, VFA, SFA and waist circumference values than the men with initial BMI of  $\geq 21.14 \text{ kg m}^{-2}$ , the association between VFA and current BMI was stronger among the men with initial BMI of  $<20.14 \text{ kg m}^{-2}$ .

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## Conflicts of Interest Statement

None declared.

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