Weight Trajectory Since Birth, Current Body Composition, Dietary Intake, and Glucose Tolerance in Young Underweight Japanese Women

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Abstract

Introduction: We studied weight trajectory since birth and dietary intake in Japanese female students majoring in nutrition sciences.

Materials and Methods: Birth weight, adolescent height and weight, current body composition by whole-body dual-energy X-ray absorptiometry, dietary intake, glucose tolerance, lipid profile, and adipokines were cross-sectionally compared between young underweight (body mass index [BMI] <18.5) and normal-weight (BMI ≥18.5 and <25.0) women with overweight (BMI ≥25.0) women as an internal reference.

Results: Serum adiponectin (leptin) was the highest (lowest) in 42 underweight women, intermediate levels in 251 normal-weight women, and the lowest (highest) levels in 14 overweight women. Compared with normal-weight women, underweight women had lower weight at birth, at age 12, 15, and 20 years, but comparable height, and hence lower BMI at three time points. Underweight women had higher gluteofemoral fat adjusted for total body fat and weight-adjusted skeletal muscle mass, although absolute and height-adjusted fat mass and skeletal muscle mass were lower. Glucose tolerance assessed by oral glucose testing, serum triglycerides, and high-density lipoprotein cholesterol did not differ between the two groups. Daily intake expressed per kg of body mass of energy and protein was the highest in underweight women, intermediate levels in normal-weight women, and the lowest levels in overweight women.

Conclusions: Some young Japanese women are underweight not because of a strong drive for thinness, but because they were born lighter and remained lean until young adults. Underweight was associated with higher gluteofemoral fat adjusted for total body fat and relative skeletal muscle mass.

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Introduction

Obesity has become a major health problem worldwide. Mean body mass index (BMI) was on the rise over time in Japanese men and older women.1,2 In contrast, BMI was on the decline in younger Japanese women.1–4 As a consequence, the prevalence of underweight or thinness (BMI <18.5 kg/m²) in young women increased from 15.8% in 1976–1980 to 22.9% in 1996–20003 and still remained high (21.7%) in 2016.1 The thinness prevalence rate in young women was higher in Japan compared to other countries. For example, it was 11.6% in Australian women 18–23 years of age (1996),5 and 11.4% (2000), 17.1% (2010), and 12.9% (2017) in female 1st-year university students in Lithuania.6

A higher thinness prevalence rate would be counterintuitive in the current obesity era. Although reasons of the increase in thinness in young Japanese women remain unclear, studies found a negative body image and weight-loss behaviors among a substantial proportion of normal-weight children and adolescents.7–9 This could manifest as a rising thinness prevalence. Indeed, some have suggested that programs to prevent overweight and obesity may actually cause unintended harm.10,11

It has recently demonstrated that the prevalence of presarcopenia (low muscle mass) was significantly elevated among the age group of 18–39 years from 11.3% in 1999–2000 to 14.1% in 2005–2006.12 Since skeletal muscle is a major site of insulin-mediated glucose disposal in the postprandial state,13 its decline could be associated with insulin resistance. Skeletal muscle mass can be evaluated by weight-adjusted relative skeletal muscle as the percentage of body mass and height-adjusted skeletal muscle mass. Although height-adjusted skeletal muscle mass is used in the diagnosis of sarcopenia,14 it has been shown that relative muscle mass is related inversely to insulin resistance, whereas absolute muscle mass is related positively.15,16 Studies found that low relative muscle mass was associated with an increased risk of type 2 diabetes independent of general obesity.17,18

To the best of our knowledge, studies are missing on weight trajectories since birth in underweight young women. In addition, studies are limited on detailed body composition and glucose tolerance in this population. In this study, we studied weight trajectory since birth and dietary intake in Japanese female students majoring in nutrition sciences because reasons of high prevalence of thinness in young Japanese women remain unclear, and because students majoring in nutrition sciences may be less likely to have unnecessary weight control.

Methods

For this open research for studying lifestyle-related diseases, briefing sessions on the study were held once or twice every year between 2004 and 2007 for female collegiate athletes (Department of Health and Sports Sciences), as well as students of Department of Food Sciences and Nutrition (nonathletes), Mukogawa Women's University. Written leaflets, which included aims, design, and exclusion criteria described below, were provided in each session. At the end of every year, participants were invited to a meeting, where study results were explained. In 2004, body composition, dietary intake, and cardiometabolic features were compared between female collegiate athletes and nonathlete students.

In 2005, similar study was done in nonathlete students and their biological mothers. In 2006 and 2007, a standard 75 g oral glucose tolerance test (OGTT), in addition to similar measurements done in 2004, was performed in two groups of students and their parents. Meal tests were also done in two groups of students in 2007. Although the number of nonathlete students totaled 318, who participated between 2004 and 2007, 7 students underwent both fasting blood sampling in 2004 and OGTT. Their data on OGTT were included in analyses and their fasting data were not included. Thereafter, data on 311 nonathlete students were used for all analyses.

Among 311 students,19,20 307 students21,22 whose genomic DNA was available were cross-sectionally studied in this study. They were recruited as volunteers. Subjects with clinically diagnosed acute or chronic inflammatory diseases, endocrine, cardiovascular, hepatic, or renal diseases, hormonal contraception, and unusual dietary habits were excluded. Nobody reported receiving any medication or having regular supplements. The study was approved by the Ethics Committees of the University (No. 07-28 on February 19, 2008).
to be in accordance with the Helsinki declaration. All subjects gave written consent after the experimental procedure had been explained.

Among 307 women, 226 and 198 women provided weight data since birth and dietary intake of the previous month, respectively. Weight at birth, and height and weight at age 12 and 15 were obtained either through maternal health check notes or child health notebook records (issued by each municipal office). Dietary intake was assessed using the self-administered diet history questionnaire.23 This has been widely used throughout Japan and its validity with respect to commonly studied nutrition factors has been confirmed. There was no significant difference in anthropometric and biochemical measurements between women who provided and those who did not provide data on weight trajectories and dietary intake (data not shown).

After a 12-hour overnight fast at 8:30 AM, participants underwent blood sampling and measurements of anthropometric indices and body composition as previously described.19,20 They were divided into three groups: underweight (BMI <18.5 kg/m²), normal weight (BMI ≥18.5 kg/m² and <25.0 kg/m²), and overweight (BMI ≥25.0 kg/m²). A subsample of 129 women underwent a standard 75 g OGTT. Blood was drawn at 0 (fasting), 30 minutes, 1 hour, and 2 hours for glucose and insulin measurements. In fasting blood samples, the following were also measured as previously reported: serum cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, glycated hemoglobin (HbA1c), adiponectin, leptin, and high-sensitivity C-reactive protein (hsCRP).19,20

Plasma glucose was determined by the hexokinase/glucose-6-phosphate dehydrogenase method (interassay coefficient of variation [CV] <2%). Serum insulin was measured by an enzyme-linked immuno sorbent assay method with a narrow specificity, excluding des-31, des-32, and intact proinsulin (inter-assay CV <6%). Impaired glucose tolerance (IGT) was defined as 2-hour glucose: 140–199 mg/dL.24 Insulin resistance and secretion were evaluated using homeostasis model assessment of insulin resistance (HOMA-IR) and secretion (HOMA-β), respectively.25

Fat mass, bone mass, and lean mass for arms, legs, trunk, and the total body were measured using whole-body dual-energy X-ray absorptiometry (DXA: Hologic QDR-2000, software version 7.20D, Waltham, MA) as previously reported.21 Muscle characteristics were relative lean mass (total body or appendicular lean mass [ALM] as percentage of body mass, %TBLM, and %ALM, respectively) and absolute lean mass (ALM/height² in kg/m² [ALM index] and total body lean mass). %ALM is suggested to be a better predictor of insulin resistance and diabetes risk than ALM or ALM index.15,16

Body fat mass was evaluated as either height-adjusted fat mass index (FMI) or weight-adjusted percentage body fat (% body fat). As the leg region included the entire hip, thigh, and leg, leg fat is referred to as gluteofemoral or lower-body fat. Leg (trunk) fat distribution was assessed by leg (trunk) fat relative to total fat mass and expressed as %LF (%TF). We have shown that %LF (%TF) was related to a favorable (unfavorable) cardiometabolic profile.26

Data were presented as mean± standard deviation unless otherwise stated. Due to deviation from normal distribution, hsCRP and HOMA-IR were logarithmically transformed for analysis. Comparisons between two groups were made with two-sample t-test or chi square test when appropriate. Differences among underweight, normal-weight, and overweight women were analyzed using analysis of variance and then Bonferroni’s multiple comparison procedure. Overweight women were included as the internal reference. A two-tailed value of p<0.05 was considered significant. Statistics were performed with SPSS system version 23 (SPSS Inc., Chicago, IL).

Results
Among 307 women, 42 (13.7%), 251 (81.7%), and 14 (4.6%) women were underweight, normal weight, and overweight, respectively (Table 1). The percentage of babies with low birth weight (<2500 g) was low in the total population (2.2%, 5/226).

Birth weight was lower in underweight compared to normal-weight women (Table 1). However, the percentage of babies with low birth weight did not differ significantly among the three groups (analysis of variance p = 0.229). Weight at age 12, 15, and 20 was also lower in underweight compared with normal-weight women, but height did not differ, and hence BMI at three time points was lower in underweight women.

As shown in Table 2, weight-adjusted lean mass (%TBLM and %ALM) and relative leg fat to total fat mass (%LF) were the highest levels in underweight women, intermediate levels in normal-weight women, and lowest levels in overweight women. In contrast, ALM index, FMI, % body fat, %TF, and trunk/leg fat ratio showed a graded increase, with the lowest levels
Table 1. Birth Weight and Trajectories of Body Mass Index of Underweight, Normal-Weight, and Overweight Japanese University Females Majoring in Nutrition Sciences

|                   | Underweight | Normal weight | Overweight |
|-------------------|-------------|---------------|------------|
|                   | n = 42      | n = 251       | n = 14     | #          |
| Birth weight <2500 g (n, %) | 2/32, 6.3   | 3/182, 1.6   | 0/12, 0   |
| Weight (kg) at birth | 2991 ± 369  | 3190 ± 388   | 3146 ± 306 |
| At age 12          | 37.5 ± 4.9  | 43.5 ± 6.4   | 56.2 ± 8.9 |
| At age 15          | 43.6 ± 4.7  | 49.5 ± 5.7   | 62.7 ± 9.9 |
| At age 20          | 44.4 ± 5.0  | 51.9 ± 4.9   | 67.6 ± 6.8 |
| Height (cm) at age 12 | 148.1 ± 63  | 151.0 ± 63   | 154.9 ± 7.5 |
| At age 15          | 155.9 ± 48  | 157.1 ± 50   | 159.1 ± 5.9 |
| At age 20          | 159.1 ± 5.1 | 158.9 ± 50   | 159.4 ± 5.6 |
| BMI (kg/m²) at age 12 | 17.1 ± 1.3  | 19.0 ± 2.1   | 23.3 ± 2.2 |
| At age 15          | 18.0 ± 1.7  | 20.0 ± 1.8   | 24.7 ± 2.8 |
| At age 20          | 17.5 ± 1.4  | 20.6 ± 1.4   | 26.6 ± 1.6 |

Mean ± standard deviation.
#: Significantly different at p < 0.05 or less. a and b: underweight versus normal weight and overweight, respectively, c: normal weight versus overweight.

BMI, body mass index.

Table 2. Body Composition of Underweight, Normal-Weight, and Overweight Japanese Female Students

|                   | Underweight | Normal weight | Overweight |
|-------------------|-------------|---------------|------------|
|                   | n = 42      | n = 251       | n = 14     | #          |
| Age (years)       | 20.5 ± 1.2  | 20.6 ± 1.2    | 20.7 ± 1.0 |
| BMI (kg/m²)       | 17.5 ± 1.4  | 20.6 ± 1.4    | 26.6 ± 1.6 |
| Waist (cm)        | 66.4 ± 3.6  | 71.5 ± 5.0    | 83.9 ± 4.6 |
| Height (cm)       | 159.1 ± 5.1 | 158.9 ± 5.0   | 159.4 ± 5.6 |
| Weight (kg)       | 44.4 ± 5.0  | 51.9 ± 4.9    | 67.6 ± 6.8 |
| BLM (kg)          | 32.1 ± 2.4  | 34.3 ± 3.0    | 36.8 ± 2.7 |
| ALM (kg)          | 13.6 ± 1.3  | 14.9 ± 1.5    | 17.2 ± 1.6 |
| %BLM (%)          | 73.1 ± 8.9  | 66.2 ± 4.6    | 57.3 ± 3.6 |
| %ALM (%)          | 30.8 ± 3.1  | 28.7 ± 2.1    | 25.5 ± 2.1 |
| ALM index (kg/m²) | 5.3 ± 0.4   | 5.9 ± 0.5     | 6.8 ± 0.4  |
| Total FM (kg)     | 9.5 ± 2.4   | 14.6 ± 3.3    | 25.0 ± 5.6 |
| %Total FM (%)     | 21.5 ± 4.4  | 28.3 ± 4.6    | 37.4 ± 4.9 |
| FM index (kg/m²)  | 3.7 ± 0.8   | 5.8 ± 1.3     | 9.8 ± 1.9  |
| Gluteofemoral/fat (%) | 42.6 ± 3.8  | 39.0 ± 4.0    | 35.3 ± 5.3 |
| Trunk/fat (%)     | 45.5 ± 3.7  | 48.3 ± 3.8    | 52.1 ± 5.1 |

Mean ± standard deviation.
#: Same as in Table 1.

ALM, appendicular lean mass; BLM, body lean mass; FM, fat mass.

Table 3. Glucose and Lipid Metabolism of Underweight, Normal-Weight, and Overweight Japanese Female Students Majoring in Nutrition Sciences

|                   | Underweight | Normal weight | Overweight |
|-------------------|-------------|---------------|------------|
|                   | n = 42      | n = 251       | n = 14     | #          |
| OGTT              |             |               |            |
| Age (years)       | 20.5 ± 1.2  | 20.6 ± 1.2    | 20.7 ± 1.0 |
| Fasting glucose   | 83 ± 8      | 83 ± 7        | 88 ± 7     |
| (mg/dL)           |             |               |            |
| 30-minute glucose | 122 ± 26    | 120 ± 22      | 120 ± 24   |
| (mg/dL)           |             |               |            |
| 60-minute glucose | 98 ± 24     | 104 ± 34      | 103 ± 37   |
| (mg/dL)           |             |               |            |
| 120-minute glucose| 94 ± 22     | 93 ± 23       | 90 ± 16    |
| (mg/dL)           |             |               |            |
| Fasting insulin   | 5.8 ± 2.9   | 6.0 ± 3.3     | 9.9 ± 5.2  |
| (µU/mL)           |             |               |            |
| 30-minute insulin | 50 ± 17     | 52 ± 34       | 68 ± 46    |
| (µU/mL)           |             |               |            |
| 60-minute insulin | 42 ± 24     | 43 ± 25       | 67 ± 39    |
| (µU/mL)           |             |               |            |
| 120-minute insulin| 39 ± 21     | 40 ± 25       | 44 ± 26    |
| (µU/mL)           |             |               |            |
| AUCg (mg/dL/2 hours) | 202 ± 35    | 205 ± 43      | 205 ± 45   |
| AUC (µU/mL/2 hours)| 77 ± 28     | 79 ± 38       | 108 ± 51   |
| Glucose and insulin and hence HOMA-IR were higher in overweight compared with underweight and normal-weight women, although HOMA-β did not differ (Table 3). Serum leptin showed a stepwise increase, whereas adiponectin showed a stepwise decrease from underweight to overweight women. However, underweight and normal-weight women did

and 0.14, respectively) and positive, not inverse, association with BMI (r = 0.662), FMI (r = 0.347) (both p < 0.001), and % body fat (r = 0.123, p = 0.03).

Among 129 women who underwent OGTT, one underweight and three normal-weight women had IGT, while no overweight women had. There was no difference in the proportion of women with IGT between underweight and normal-weight women (1/22 vs. 3/99, p = 0.78). Fasting glucose and insulin and hence HOMA-IR were higher in overweight compared with underweight and normal-weight women, although HOMA-β did not differ (Table 3). Serum leptin showed a stepwise increase, whereas adiponectin showed a stepwise decrease from underweight to overweight women. However, underweight and normal-weight women did
not differ in the area under the concentration curve of glucose and insulin, HbA1c, serum lipids, and lipoproteins. There was also no difference in blood hemoglobin and the prevalence of anemia (hemoglobin <12.0 g) among the three groups of women.

Daily dietary intake of energy, carbohydrate, fat, and protein did not differ among the three groups of women (Table 4). However, relative intake of energy and protein per kilogram of body mass was the highest in underweight women, intermediate levels in normal-weight women, and lowest levels in overweight women.

**Discussion**

As far as we know, this study is the first to show that young underweight women had lower weight at birth and age 12, 15, and 20 years. In addition, they had higher relative leg (gluteofemoral) fat to total fat mass (%LF) and weight-adjusted appendicular skeletal muscle mass (%ALM). Glucose tolerance and lipid profile did not differ between underweight and normal-weight women.

Reduced birth weight is a widely used indicator of retarded fetal growth and intrauterine malnutrition. Although the proportion of female infants with birth weight <2500 g has been reported to be increased from 4.8% in 1980 to 10.7% in 2012 in Japan,27 fetal malnutrition was not possibly the primary factor in this study since the percentage of infants with birth weight <2500 g was not high in underweight women (6.3%). Blood hemoglobin, anemia prevalence, and daily intake of energy and macronutrients did not differ among the three groups of women, suggesting that our underweight women were unlikely to be undernourished, but healthy.

Although reasons of the increase in thinness in young Japanese women remain unclear, studies found a negative body image and weight loss behaviors among a substantial proportion of normal-weight children and adolescents.7–9 This could manifest as a rising thinness prevalence. Indeed, some have suggested that programs to prevent overweight and obesity may actually cause unintended harm.10,11 Higher prevalence of underweight in young Japanese women may be, in part, due to unnecessary weight control in nonobese individuals as it has been shown that body dissatisfaction and desire for thinness are commonplace in high socioeconomic status settings across world regions in women in general,28,29 and in young Japanese women in particular.7,30 It may also be related to eating problems.31 Although we did not investigate eating behaviors, women with unusual dietary habits were excluded from the study and daily energy intake did not differ between underweight and normal-weight women.

A previous study suggested that the continuous increase in the smoking rate may be associated with an increase in thinness in Japanese women of childbearing age.3 However, this is not the case with our participants because no participant reported a smoking habit.21 Taken together, this study has clearly shown that in Japanese female students majoring in nutrition sciences, underweight is constitutional and is not due to calorie restriction. Although reasons why some Japanese female students majoring in nutrition sciences are underweight are not clear, a recent genome-wide association study identifies anaplastic lymphoma kinase as a thinness gene, which is involved in the resistance to weight gain.32

Skeletal muscle is a major site of insulin-mediated glucose disposal in the postprandial state.13 Disruption of glucose uptake by muscle directly contributes to the development of insulin resistance.33 In addition, in the fasting state, smooth muscle is a site of clearance of triglyceride in very low-density lipoprotein particles and production of HDL particles.34 Despite lower absolute ALM and ALM index in underweight women, glucose disposal rate during OGTT (area under the concentration curve of glucose) and lipid metabolism did not differ between underweight and normal-weight young women as previously reported.35 This may be explained, in part, by higher %LF associated with lower %TF and higher %ALM in underweight women.

We have shown that %LF (%TF) was related to a favorable (unfavorable) cardiometabolic profile.26 An
inverse association of relative muscle mass (%ALM) with fasting insulin and HOMA-IR was confirmed even in young Japanese women in this study as previously reported in elderly populations.15,16

Studies are limited on glucose tolerance in underweight and normal-weight people. We found two studies from the same Japanese laboratory.35,36 The former study found that although IGT was more prevalent in postmenopausal compared with young underweight women, glucose tolerance did not differ between 31 young underweight and 13 normal-weight women.35 The latter study found that IGT was more prevalent in 98 young underweight compared with 56 normal-weight women (13.3% vs. 1.8%).36

Although lower insulin secretion, lower muscle function, insulin resistance in muscle, and adipose tissue may contribute to elevated postload glucose values,35,36 a low carbohydrate intake before oral glucose testing is another forgotten factor, which is associated with elevated postload glucose values.37 As young underweight women in the latter study were underweight probably due to desire to be thin,36 young underweight women with IGT consumed, on average, 134 g of carbohydrate a day (46.7% of 1152 kcal), which is lower than the recommended daily carbohydrate intake (>150 g).37 In contrast, four underweight women with IGT in this study consumed, on average, 251 g a day (204–273 g).

Some studies38–40 examined the weight trajectory from birth in relation to type 2 diabetes, but not to underweight in young adulthood. As far as we know, this study may be the first to investigate weight trajectories since birth in underweight young women.

The strengths of this study include homogeneous study population with scarce confounding factors,19–21 and accurate and reliable measures of body composition by DXA, which provided direct measures of fat mass and skeletal muscle mass and their distribution. Several limitations of this study include the cross-sectional design, relatively small sample size, and a single measurement of biochemical variables. Students majoring in nutrition sciences may be more health conscious and diet aware. In addition, as the participation was voluntary, female students who pay more attention to health may be more likely to participate. Therefore, participants in this study may not be representative of the overall population of young healthy women in Japan. We used crude measures of insulin resistance/sensitivity, which may be less accurate. Menstrual cycles were not adjusted, and statistical power was not calculated. As we studied Japanese only, results may not be generalized to other races or ethnicities.

Conclusions

Some Japanese female students are underweight not because of a strong desire for thinness, but rather because they were born lighter and remained lean until young adults, that is, constitutionally thin. Underweight was associated with higher relative leg fat to total fat mass (%LF) and higher relative muscle mass, both of which may be related to glucose and lipid metabolism indistinguishable from normal-weight women.

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