

RESEARCH ARTICLE

# Slightly increased BMI at young age is a risk factor for future hypertension in Japanese men

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## Abstract

### Background

Hypertension is developed easily in Asian adults with normal body mass index (BMI) (~23 kg/m<sup>2</sup>), compared with other ethnicities with similar BMI. This study tested the hypothesis that slightly increased BMI at young age is a risk factor for future hypertension in Japanese men by historical cohort study.

### Methods

The study participants were 636 male alumni of the physical education school. They had available data on their physical examination at college age and follow-up investigation between 2007 and 2011. The participants were categorized into six categories: BMI at college age of <20.0 kg/m<sup>2</sup>, 20.0–21.0kg/m<sup>2</sup>, 21.0–22.0kg/m<sup>2</sup>, 22.0–23.0kg/m<sup>2</sup>, 23.0–24.0kg/m<sup>2</sup>, and ≥24.0kg/m<sup>2</sup>, and the incidence of hypertension was compared.

### Results

This study covered 27-year follow-up period (interquartile range: IQR: 23–31) which included 17,059 person-years of observation. Subjects were 22 (22–22) years old at graduated college, and 49 (45–53) years old at first follow-up investigation. During the period, 120 men developed hypertension. The prevalence rates of hypertension for lowest to highest BMI categories were 9.4%, 14.6%, 16.1%, 17.5%, 30.3%, and 29.3%, respectively (p<0.001 for trend), and their hazard ratios were 1.00 (reference), 1.80 (95%CI: 0.65–4.94), 2.17 (0.83–5.64), 2.29 (0.89–5.92), 3.60 (1.37–9.47) and 4.72 (1.78–12.48), respectively (p<0.001 for trend). This trend was similar after adjustment for age, year of graduation, smoking, current exercise status and current dietary intake.

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## Conclusion

Slightly increased BMI at young age is a risk factor for future hypertension in Japanese men.

## Introduction

Overweight, defined by a body mass index (BMI) of 25.0 kg/m<sup>2</sup> or more, is recognized as a risk factor for mortality [1, 2], cardiovascular disease (CVD) [3, 4] and metabolic disorders, such as hypertension, type 2 diabetes, and dyslipidemia [5, 6]. In addition, it has been reported that overweight and obesity (BMI >30 kg/m<sup>2</sup>) at ~20 years of age are also risk factors for development of hypertension in middle aged Caucasians [7, 8]. For example, overweight and obesity at ~18 years of age increase the risk of hypertension at 25–45 years of age in Caucasians [9].

In contrast, in Asian countries, the prevalence of overweight subjects at young age is very low and most of patients with hypertension have normal weight [10]. However, metabolic disorders such as hypertension, type 2 diabetes, and dyslipidemia, and cardiovascular disease are easily developed in middle aged Asian with normal BMI, compared with BMI matched other ethnicities [11–13]. Thus, slightly increased BMI level (>23 kg/m<sup>2</sup>) in middle age (around 50 years old) is recognized as a risk for development of hypertension in Asians [13–15]. However, it is still unclear whether slightly elevated BMI at young age within normal BMI range (<25 kg/m<sup>2</sup>) also increases the risk of hypertension later in life.

Only two studies addressed this research question. Heianza et al. reported that a slight increase in BMI (~1 kg/m<sup>2</sup>) within the normal range at 20 years of age increased the risk of future hypertension in Japanese [16]. In their health study on nurses, Huang et al. also showed that a slight increase in BMI at 18 years of age even within the normal range was positively associated with future hypertension [17]. Thus, only a few longitudinal studies investigated whether the normal BMI at young age is a risk factor for future hypertension and more studies are required to confirm this association.

In the present study, we hypothesized that the BMI at young age is associated with the development of hypertension later in life. The study was historical cohort study of the Juntendo University Alumni Study, subjects were also participated in a similar study published previously by our group [18–20]. We used standardized physical examination data of the alumni recorded when they were college students, and medical examination of self-administered questionnaires at follow-up investigation to test the study hypothesis.

## Methods

### Study participants

The Juntendo University Alumni Study included male alumni of the Physical Education School of Juntendo University. In this cohort, we demonstrated previously that association between physical fitness and physical characteristics, such as cardiorespiratory fitness, at a young age and future disease [18–20]. The majority of the study subjects engaged in college sports clubs, such as track and field, gymnastics, soccer, and judo, and participated in training for competitions in their respective sport, and were competitive athletes at least while attending university. Between 2007 and 2011, 1,385 male alumni who participated at least once follow-up investigation were studied. This study excluded the female alumni because of small percentage before 1991. Of these, 37 male alumni did not answer appropriately the questionnaire and were therefore excluded. Five hundred and fifty-three alumni who graduated before

the standardized physical examination were excluded from this analysis. Thus, we finally included 636 male alumni in the current analysis.

The study protocol was approved by the Juntendo University Ethics Committee in 2007 (No.19-131). All data were anonymized before analysis to ensure privacy of the participants. Along with the questionnaire, we sent a letter of informed consent approving the collection and use of the athletic test data for research purpose. This study was carried out in accordance with the principles outlined in the Declaration of Helsinki.

### Assessment of BMI at college age

This college undergo standardized medical and physical examinations annually since 1971. We used the height and body weight recorded in the physical examination conducted at the college student. Then, average BMI during college student was calculated as weight in kilograms divided by the square of height in meters ( $\text{kg}/\text{m}^2$ ) and used for each analysis.

### Investigation for prevalence of hypertension

Incidence cases of hypertension were obtained from self-administered questionnaire between 2007 and 2011. In the survey, alumni were asked about their medical history whether they had ever been diagnosed with any disease, including hypertension, by a physician after graduation from college. Alumni were also asked about their current life-style, such as exercise, diet and smoking habits [18–20].

### Statistical analysis

For primary analysis, the participants were categorized for six categories (BMI at college age of  $<20.0 \text{ kg}/\text{m}^2$ ,  $20.0\text{--}21.0 \text{ kg}/\text{m}^2$ ,  $21.0\text{--}22.0 \text{ kg}/\text{m}^2$ ,  $22.0\text{--}23.0 \text{ kg}/\text{m}^2$ ,  $23.0\text{--}24.0 \text{ kg}/\text{m}^2$ ,  $\geq 24.0 \text{ kg}/\text{m}^2$ ). Before the primary analysis, we performed preliminary analysis after categorizing the participants into quartiles (Q1: lowest, Q2, Q3 and Q4: highest) by BMI at college age to see the rough trend of the association between BMI at young age and hypertension. We defined the lowest BMI group (Q1 or  $\text{BMI} < 20.0 \text{ kg}/\text{m}^2$ ) as the reference category. The cumulative incidence rate of hypertension according to the BMI categories was compared by  $\chi^2$  test. Hazards ratios and 95 percent confidence interval (95% CI) relating BMI to risk of hypertension were constructed with the Cox proportional hazards analysis. The unadjusted and multivariable-adjusted relative risks were computed. In the Model 1, the adjusted data included age (continuous variable, 1-year-old ticks), year of graduation (continuous variable, 1-year increments), and smoking (category, yes or no). In addition, several factors in middle age, such as low physical activity and over nutrition were reported as risk factor of elevated blood pressure [8, 21–26]. Thus, the model 2 further included current exercise status (continuous variable, 1-met\*hour/week increments) and current dietary intake (continuous variable, kcal/day increments) as confounding factor. The year of graduation was used as surrogate variables of economic status. All statistical analyses were conducted using SPSS version 23.0 for Windows software (SPSS Inc., Chicago, IL).

## Results

### Characteristics of study participants

Before the primary analysis, we performed preliminary analysis after categorizing the participants into quartiles (Q1: lowest, Q2, Q3 and Q4: highest) by BMI at college age (Table 1). Median age at graduated college were 22 (IQR: 22–22) years old. The median BMIs at college age were Q1:  $20.4 \text{ kg}/\text{m}^2$  (interquartile range: IQR: 19.7–20.7,  $n = 159$ ), Q2: 21.5 (21.3–21.8,

**Table 1. Baseline characteristics of study subjects according to BMI in former male college athletes.**

	Q1 (n = 159)	Q2 (n = 159)	Q3 (n = 159)	Q4 (n = 159)	All (n = 636)
Age, years	22 (22–22)	22 (22–22)	22 (22–22)	22 (22–22)	22 (22–22)
Year of graduation	1982 (1978–1985)	1982 (1978–1986)	1983 (1979–1986)	1982 (1978–1986)	1982 (1978–1986)
Body Mass Index, kg/m <sup>2</sup>	20.4 (19.7–20.7)	21.5 (21.3–21.8)	22.4 (22.2–22.7)	23.9 (23.4–25.0)	22.0 (21.1–22.9)
Body Height, cm	172.3 (167.6–175.8)	171.8 (167.6–177.9)	172.3 (168.2–177.5)	173.3 (168.4–178.0)	172.4 (168.0–177.0)
Body Weight, kg	59.9 (57.1–62.6)	63.5 (60.5–67.9)	66.5 (63.2–70.5)	72.6 (67.8–77.5)	65.1 (61.0–70.4)
Smoker, n (%)	74 (47.8)	77 (48.4)	83 (52.2)	73 (45.9)	309 (48.6)
College sports club participation, n (%)	158 (99.4)	154 (96.9)	156 (98.1)	158 (99.4)	626 (98.4)
Endurance sports, n (%)	32 (20.1)	10 (6.3)	8 (5.0)	6 (3.8)	56 (8.8)
Mixed sports, n (%)	109 (68.6)	126 (79.2)	140 (88.1)	97 (61.0)	472 (74.2)
Power sports, n (%)	2 (1.3)	7 (4.4)	3 (1.9)	46 (28.9)	58 (9.1)
No-participation / Unknown, n (%)	16 (10.1)	16 (10.1)	8 (5.0)	10 (6.3)	50 (7.9)

Data at time of college and are median (IQR: interquartile range), number (%), or column percentage.

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n = 159), Q3: 22.4 (22.2–22.7, n = 159) and Q4: 23.9 (23.4–25.0, n = 159). The median BMI for all study participants and for each category were within the normal range, while 36 participants (5.7%) were overweight (BMI  $\geq 25$  to  $< 30$  kg/m<sup>2</sup>) and only five (0.8%) were obese (BMI  $\geq 30$  kg/m<sup>2</sup>). Almost all of the participants had participated in a college sports club. Highest BMI group (Q4) was high percentage of individuals who participated in power sports, on the other hand, lowest BMI group (Q1) was high percentage of individuals who participated in endurance sports. The percentages of smokers was comparable among the groups.

### Association between BMI and incidence of hypertension

The follow-up period of this study was 27-year (interquartile range: IQR: 23–31 years), which included 17,059 person-years of observation. The median age at the time of the follow-up questionnaire was 49 years (IQR: 45–53 years), where 120 men had developed hypertension, with unadjusted cumulative incidence of hypertension of 18.9%.

To examine the relationship between BMI and development of hypertension, we evaluated the rate of incidence and hazard ratios in the Q1 (lowest BMI group; reference), Q2, Q3 and Q4 (highest BMI group). The prevalence rates of hypertension in Q1 to Q4 were significantly different among the groups, the highest BMI group included the highest rate of hypertension. Compared with men in the lowest group of BMI (Q1), men in the highest group of BMI (Q4) were at 2.5 times increased risk of hypertension (Table 2). The trend was persistently seen even after adjustment for age, year of graduation, smoking, current exercise status and current dietary intake (Table 2). In addition, the multivariable adjusted cumulative incidence rate of hypertension was associated with higher BMI throughout the follow-up (Fig 1). These results suggest a significant association between BMI at a young age and future development of hypertension in Japanese men.

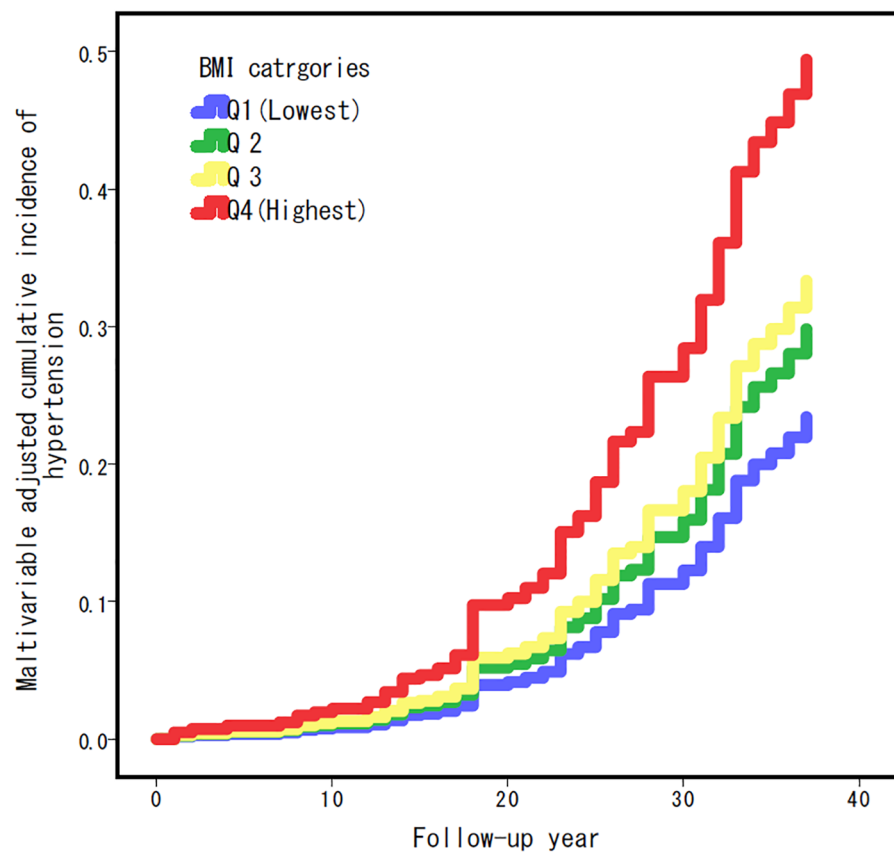
Then, we re-analyzed by six categories as primary analysis (Table 3). The incidence of hypertension per 10,000 person-years was associated with BMI at young age, the highest BMI category was highest incidence (Table 4). Compared with men in the lowest BMI category (BMI  $< 20.0$  kg/m<sup>2</sup>), men in the BMI category of 23–24kg/m<sup>2</sup> or over 24kg/m<sup>2</sup> had ~3 or ~4 times higher risk of hypertension, respectively (Table 4). The trend was persistently seen even after adjustment for age, year of graduation, smoking, current exercise status and current dietary intake (Table 4 and Fig 2).

**Table 2. Hazard ratio for hypertension according to BMI (quartiles).**

	BMI, quartiles				p for Trend
	Q1 (n = 159)	Q2 (n = 159)	Q3 (n = 159)	Q4 (n = 159)	
Follow-up year	28 (25–32)	27 (23–31)	27 (23–31)	27 (22–31)	
Person-years of follow-up	4435	4218	4248	4158	
Diagnosed with hypertension (n, %)	21 (13.2)	24 (15.3)	28 (17.6)	47 (29.6)	0.001
Incidence per 10,000 person-years	47.4	56.9	65.9	113.0	
Unadjusted hazard ratio (95% CI)	1.00	1.30 (0.72–2.33)	1.50 (0.85–2.64)	2.56 (1.53–4.29)	<0.001
Multivariable adjusted hazard ratio* (95% CI) Model 1	1.00	1.33 (0.74–2.39)	1.52 (0.86–2.68)	2.55 (1.53–4.27)	<0.001
Multivariable adjusted hazard ratio* (95% CI) Model 2	1.00	1.15 (0.63–2.11)	1.44 (0.81–2.55)	2.52 (1.51–4.22)	<0.001
Age, years	0.95 (0.62–1.47)				0.829
Year of graduation	0.99 (0.95–1.04)				0.756
Smoker (yes/no)	0.69 (0.47–0.99)				0.047
Current exercise status (mets*hour/week)	0.99 (0.98–1.00)				0.187
Current dietary intake (kcal/day)	1.00 (1.00–1.00)				0.988

\*Cox proportional hazards models adjusted for model 1: baseline characteristics (age, year of graduation and smoking), model 2: current exercise status and current dietary intake with model 1.

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**Fig 1. Multivariable adjusted cumulative incidence rate curve for hypertension during the follow-up, according to BMI (quartile).**

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**Table 3. Baseline characteristics of study subjects according to BMI in former male college athletes.**

	<20kg/m <sup>2</sup> (n = 53)	20-21kg/m <sup>2</sup> (n = 103)	21-22kg/m <sup>2</sup> (n = 163)	22-23kg/m <sup>2</sup> (n = 166)	23-24kg/m <sup>2</sup> (n = 76)	≥24kg/m <sup>2</sup> (n = 75)
Age, years	22 (22–22)	22 (22–22)	22 (22–22)	22 (22–22)	22 (22–22)	22 (22–22)
Year of graduation	1982 (1977–1985)	1982 (1979–1985)	1982 (1978–1986)	1982 (1979–1986)	1981 (1977–1985)	1983 (1979–1987)
Body Mass Index, kg/m <sup>2</sup>	19.4 (19.1–19.8)	20.6 (20.4–20.8)	21.5 (21.3–21.8)	22.4 (22.2–22.7)	23.5 (23.2–23.7)	25.2 (24.3–26.1)
Body Height, cm	171.6 (166.8–176.5)	172.6 (169.1–175.3)	171.8 (167.5–177.9)	172.4 (168.4–177.5)	173.4 (167.6–176.7)	173.3 (168.6–180.1)
Body Weight, kg	57.3 (53.2–60.3)	61.2 (58.7–63.4)	63.5 (60.3–67.9)	66.6 (63.4–70.6)	70.4 (65.7–73.1)	76.4 (70.8–83.0)
Smoker, n (%)	19 (35.8)	55 (53.4)	80 (49.1)	87 (52.4)	37 (48.7)	31 (41.3)
College sports club participation, n (%)	53 (100)	102 (99.0)	158 (96.9)	163 (98.2)	74 (100)	74 (98.7)
Endurance sports, n (%)	17 (32.1)	15 (14.6)	10 (6.1)	8 (4.8)	4 (5.3)	2 (2.7)
Mixed sports, n (%)	32 (60.4)	74 (71.8)	130 (79.8)	145 (87.3)	55 (72.4)	36 (48.0)
Power sports, n (%)	1 (1.9)	1 (1.0)	7 (4.3)	4 (2.4)	12 (15.8)	33 (44.0)
No-participation / Unknown, n (%)	3 (5.7)	13 (12.6)	16 (9.8)	9 (5.4)	5 (6.6)	4 (5.3)

Data at time of college and are median (IQR: interquartile range), number (%), or column percentage.

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## Discussion

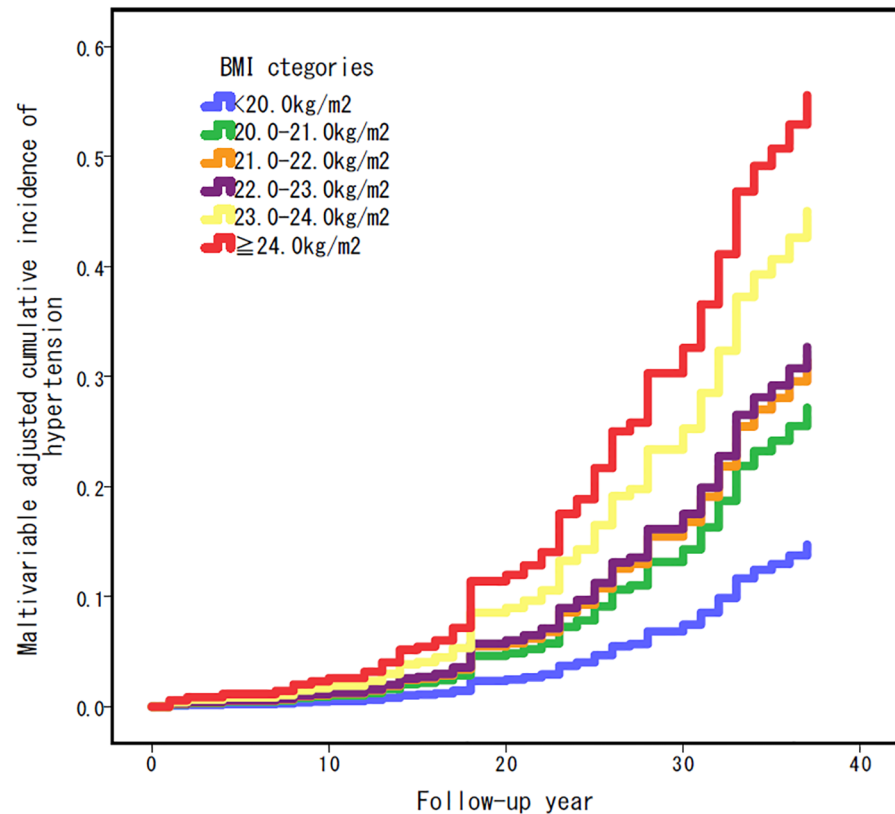
In the present study, we investigated the relationship between BMI at young age and future development of hypertension in University-educated Japanese men. After adjustment for potential confounding factors, the results identified BMI category of 23–24 kg/m<sup>2</sup> or over 24

**Table 4. Hazard ratio for hypertension according to BMI (six categories).**

	BMI at college age						p for Trend
	<20kg/m <sup>2</sup> (n = 53)	20-21kg/m <sup>2</sup> (n = 103)	21-22kg/m <sup>2</sup> (n = 163)	22-23kg/m <sup>2</sup> (n = 166)	23-24kg/m <sup>2</sup> (n = 76)	≥24kg/m <sup>2</sup> (n = 75)	
Follow-up year	29.0 (24.5–33.5)	28.0 (25.0–32.0)	27.0 (23.0–31.0)	27.0 (23.0–31.0)	28.0 (23.3–32.0)	24.0 (21.0–30.3)	
Person-years of follow-up	1542	2828	4306	4453	2099	1831	
Diagnosed with hypertension (n, %)	5 (9.4)	15 (14.6)	26 (16.1)	29 (17.5)	23 (30.3)	22 (29.3)	<0.001
Incidence per 10,000 parson-years	32.4	53.0	60.4	65.1	109.6	120.2	
Unadjusted hazard ratio (95% CI)	1.00	1.80 (0.65–4.94)	2.17 (0.83–5.64)	2.29 (0.89–5.92)	3.60 (1.37–9.47)	4.72 (1.78–12.48)	<0.001
Multivariable adjusted hazard ratio* (95% CI) Model 1	1.00	1.99 (0.72–5.51)	2.37 (0.91–6.20)	2.49 (0.96–6.44)	3.76 (1.43–9.89)	5.09 (1.92–13.51)	<0.001
Multivariable adjusted hazard ratio* (95% CI) Model 2	1.00	1.98 (0.72–5.49)	1.99 (0.75–5.27)	2.44 (0.94–6.32)	3.73 (1.42–9.83)	4.92 (1.85–13.04)	<0.001
Age, years	0.95 (0.62–1.46)						0.800
Year of graduation	0.99 (0.94–1.04)						0.668
Smoker (yes/no)	0.68 (0.47–0.99)						0.043
Current exercise status (mets*houre/week)	0.99 (0.98–1.00)						0.200
Current dietary intake (kcal/day)	1.00 (1.00–1.00)						0.992

\* Cox proportional hazards models adjusted for model 1: baseline characteristics (age, year of graduation and smoking and college sports club participation), model 2: current exercise status and dietary intake with model 1.

<https://doi.org/10.1371/journal.pone.0191170.t004>



**Fig 2. Multivariable adjusted cumulative incidence rate curve for hypertension during the follow-up, according to BMI (six categories).**

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$\text{kg/m}^2$  were ~3 or ~4 times high risk for hypertension compared with BMI category of under  $20 \text{ kg/m}^2$ . These data suggest that a slightly high BMI at a young age, even when within the "normal range", may influence future development of hypertension in Japanese men.

Our results demonstrated that for Japanese male college athletes, slightly increased BMI at young age is a risk factor for future hypertension. Median BMI of this study participants was  $22.0 \text{ kg/m}^2$  (IQR:  $21.1-22.9 \text{ kg/m}^2$ ), while only 37 participants (5.8%) were overweight (BMI  $\geq 25.0$  to  $< 30.0 \text{ kg/m}^2$ ) and only five (0.8%) were obese (BMI  $\geq 30.0 \text{ kg/m}^2$ ). In these subjects, we found BMI  $\geq 23 \text{ kg/m}^2$  at young age might be cut-off value of increased risk of future hypertension. This cut-off value was similar to previous report showing that subjects with BMI  $\geq 23 \text{ kg/m}^2$  at 20 years old have ~2 times higher risk of hypertension in middle age, compared with subjects with BMI  $< 23.0 \text{ kg/m}^2$  [16].

What is the mechanism through which the normal BMI at young increases the chance of hypertension in later life? Although our study did not investigate the exact mechanism, background data may help in the interpretation of our results. At least in adults, the body composition profile of Asians differs from that of Caucasians and African-Americans. Asians have a higher body fat content and more visceral adipose tissue, compared with Caucasians and African Americans of similar BMI [11, 27, 28]. Furthermore, previous studies reported the presence of muscle insulin resistance in non-obese subjects with one or more cardiometabolic risk factors [29]. It was also demonstrated that muscle insulin sensitivity is significantly associated with hypertension in non-obese subjects [29] and that insulin sensitivity is a risk factor for hypertension [30].



The present study has several limitations. First, the participants are not representative of all Japanese men and small cohorts. The study subjects were alumni of only one university department and almost all subjects were former college athlete, although they came from all over Japan. In addition, female alumni were not included because they were not registered at the college in 1971. Second, alumni without data of either the physical examination while at college or follow-up questionnaire were excluded. These exclusions limited the generalization of the results. Third, self-selection bias could have occurred because the participants who answered the follow-up questionnaires may have been those who were the healthiest. Finally, recall bias was possible because the questionnaire was cross-sectional and participants needed to recall their medical background. However, our previous studies have used the same method[18–20] and established the validity of the self-reports examination by re-examination[31]. In addition, in Japan, most people undergo free medical screening by a physician at least once annually at work or school.

## Conclusion

In conclusion, our data suggested that the slightly increased BMI at young age is a significant risk factor for future hypertension in Japanese men.

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## Author Contributions

**Conceptualization:** Yuki Someya.

**Data curation:** Yuki Someya.

**Formal analysis:** Yuki Someya.

**Funding acquisition:** Hiroyuki Daida.

**Investigation:** Yuki Someya, Yoshimitsu Kohmura, Kazuhiro Aoki.

**Project administration:** Sachio Kawai.

**Writing – original draft:** Yuki Someya.

**Writing – review & editing:** Yoshifumi Tamura.

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