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Associations of Overweight, Obesity, and Underweight With High Serum Total Cholesterol Level Over 30 Years Among the Japanese Elderly: NIPPON DATA 80, 90, and 2010

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ABSTRACT

Background: The trend of association between overweight and high serum total cholesterol (TC) among the elderly is unclear. In addition, there is little evidence of risk of underweight for high TC. Therefore, we examined the trend of association of overweight or underweight with high TC among Japanese elderly people using nationwide population-based data.

Methods: Data of the National Survey on Circulatory Disorders and National Health and Nutrition Survey for 1980, 1990, 2000, and 2010 were used in the analysis. High TC was defined as 220 mg/dL and above. For participants aged ≥ 50 years, sex-specific odds ratios (ORs) of overweight or underweight compared with normal body mass index participants for high TC were calculated using a logistic regression model adjusted for age, smoking, drinking, exercise, food, and treatment of hyperlipidemia.

Results: A total of 5,014, 4,673, 5,059, and 2,105 participants enrolled in these surveys in 1980, 1990, 2000, and 2010, respectively. Although overweight was positively and significantly associated with high TC in 1980, the association has gradually weakened since (ORs in 1980 and 2010 were 2.44; 95% confidence interval [CI], 1.83–3.24 and 0.92; 95% CI, 0.66–1.27 among men and 1.43; 95% CI, 1.18–1.72 and 1.08; 95% CI, 0.81–1.44 among women, respectively). While underweight was inversely and significantly associated with high TC in 1980, the association also gradually weakened among women (ORs in 1980 and 2010 were 0.28; 95% CI, 0.12–0.60 and 0.37; 95% CI, 0.10–1.28 among men and 0.39; 95% CI, 0.26–0.57 and 0.96; 95% CI, 0.58–1.57 among women, respectively).

Conclusions: These findings provide evidence that high TC prevention efforts must expand the target to not only overweight but also to normal and underweight people.

Key words: body mass index; overweight; thinness; hyperlipidemias; Japan

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INTRODUCTION

Prevalence of obesity has increased globally. Nearly one-third of the world population is obese or overweight.¹ Over the past three decades, the proportion of overweight has increased from 19.0% to 28.7% among Japanese men.² Among Japanese women, the proportions of overweight were 20.1% and 21.3% in 1984 and 2014, respectively.² However, the proportion of overweight is still higher among the elderly than young participants; the

proportion of overweight in participants at 20–29 years and 60–69 years of age was 20.9% and 31.2% among men and 10.4% and 24.0% among women, respectively.² The aging rate of the population in Japan is the highest in the world. Therefore, overweight in the elderly is an important public health issue in Japan.

Many studies reported high serum total cholesterol (TC) to pose a higher risk of coronary heart diseases than other measures of dyslipidemia.^{3–5} Although numerous cross-sectional studies

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have established that overweight and obesity are risk factors for high TC,^{6–12} the longitudinal change of the associations is controversial.^{10,11} For example, a cross-sectional study showed the odd ratios (ORs) for high TC (overweight vs normal) were 1.5 and 1.9 among men and women, respectively.¹⁰ The study targeted American subjects aged 50–76 years at 2000–2002 and defined high TC from self-report data. On the other hand, another survey reported the ORs for high TC (overweight or obesity vs normal) were 0.9 to 1.2.¹¹ The study analyzed the National Health and Nutrition Examination Survey with stratified sampling, multistage, probability cluster design among American women aged ≥ 55 years at 1988–1994 and defined high TC as measured serum blood lipid levels exceeding 220 mg/dL. Thus, it is unclear whether the change of associations is due to different protocols, such as sampling, high TC definitions, and others, or due to actual change. A unified protocol is needed to conduct a longitudinal analysis.

Limited data have been published on the association between underweight and high TC.^{11,13} A cross-sectional study showed underweight inversely and significantly associated with high TC.¹³ Underweight might be a protective factor for high TC, despite a high mortality risk.^{14,15} However, the longitudinal change of the association between underweight and high TC is also unclear. The long-term trends on the impact of overweight and underweight on high TC have not been studied. Therefore, we evaluated the trend of association of overweight or underweight with high TC in a Japanese elderly population using the unified national-wide population-based data set in 1980, 1990, 2000, and 2010.

MATERIALS AND METHODS

Study design

We performed a panel data analysis of information from 1980, 1990, 2000, and 2010.

Setting

The present study used data from the National Integrated Project for Prospective Observation of Non-communicable Disease And Its Trends in the Aged (NIPPON DATA), which is supported by the Ministry of Health and Welfare of Japan and consists of ongoing cohort studies conducted using the National Survey on Circulatory Disorders (NSCD) and National Health and Nutrition Survey (NHNS) in 1980, 1990, and 2010. Details of NIPPON DATA have been previously reported.^{16–19} Data of the NSCD and NHNS in 2000 were additionally obtained with permission from the Ministry of Health and Welfare of Japan. The NSCD was conducted every decade from 1960 and the NHNS was conducted annually and called the National Nutritional Survey (NNS) until 2002. The NSCD was integrated into the NHNS as of 2010. Participants were selected from 300 districts throughout Japan who were aged ≥ 30 years. Medical examination, blood tests, and a self-administered questionnaire about lifestyle were conducted among 10,546 participants aged ≥ 30 years in 1980, among 8,383 participants aged ≥ 30 years in 1990, among 5,565 participants aged ≥ 30 years in 2000, and among 2,898 participants aged ≥ 20 years in 2010.

Variables

Serum TC was measured using the Lieberman-Burchard direct method in 1980 and measured enzymatically in 1990, 2000, and

2010. Measuring instruments and reagents of blood tests are unified in each year. Previous study confirmed high validity between the Lieberman-Burchard direct and enzymatically method.²⁰ High TC was defined as 220 mg/dL and above. Public health nurses measured height and weight and calculated body mass index (BMI) as weight (kg) divided by the square of height (m). Overweight and underweight were defined as BMI ≥ 25.0 kg/m² and < 18.5 kg/m², respectively.²¹ We combined obesity (BMI ≥ 30.0 kg/m²) into the overweight category because of a lower prevalence of obesity in Japan. The prevalence of obesity was only 2.1% in 1980 and 3.4% in 2010.² Public health nurses obtained information about smoking, drinking, regular exercise, and treatment histories. A dietary survey was carried out employing the weighing record method in each household.²² Total energy intake, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), and polyunsaturated fatty acid (PUFA) were calculated.

Statistical analysis

For participants aged ≥ 50 years, sex-specific ORs and 95% confidence intervals (CIs) of overweight or underweight compared with normal BMI for high TC were calculated using a logistic regression model. Model 1 was adjusted for age. Model 2 was adjusted for age, smoking status, drinking status, regular exercise, total energy intake, SFA, MUFA, PUFA, and treatment of hyperlipidemia. Statistical significance was defined as a *P*-value of < 0.05 . All analyses were performed using IBM SPSS Statistics 22 for Windows (SPSS Inc, Chicago, IL, USA).

Ethics

The institutional review board of Shiga University of Medical Science approved this study (No. 12-18, 2000, No. 22-29, 2010).

RESULTS

A total of 5,014, 4,673, 5,059, and 2,105 participants aged ≥ 50 years were enrolled in the NSCD and NHNS in 1980, 1990, 2000, and 2010, respectively. The number of participants in 2010 was about half that of other periods because the sample size was designed to be small when the NSCD was integrated into NHNS in 2010. The distribution of the characteristics by periods is shown in Table 1.

The ORs of overweight for high TC are shown in Table 2. Interestingly, although a significantly positive association between overweight and high TC was observed in 1980, it was not noted in 2010.

In order to confirm the changes, analyses by treatment of hyperlipidemia were performed because of the common use of drug therapy for hyperlipidemia since the 1990s. Both non-treatment and treatment participants showed a decreased trend; ORs among non-treatment participants in 1980 to 2010 were 2.50 to 1.00 among men and 1.44 to 1.02 among women, and those among treatment participants decreased from 1.84 to 0.81 among men and from 1.51 to 0.91 among women (eTable 1).

The ORs of underweight for high TC are shown in Table 2. Although underweight was inversely and significantly associated with high TC in 1980, the relationship had weakened among women but not among men in 2010. In treatment-specific analysis, ORs among non-treatment and treatment women in 1980 to 2010 were 0.39 to 0.88 and 0.86 to 1.51, respectively. Among men, ORs in non-treatment participants remained,

Table 1. Characteristics of subjects aged 50 years and above in the study

	1980	1990	2000	2010
Men				
<i>n</i>	2915	2004	2313	942
Age, years, mean (SD)	61.7 (8.8)	63.2 (8.9)	63.7 (9.5)	67.2 (9.1)
TC, mg/dL, mean (SD)	185.0 (33.5)	196.9 (37.2)	197.9 (35.2)	201.0 (33.1)
High TC ^a , <i>n</i> (%)	314 (14.3)	488 (26.4)	359 (24.7)	253 (27.4)
BMI, kg/m ² , mean (SD)	22.1 (2.9)	22.8 (3.0)	23.3 (3.0)	23.9 (3.0)
Underweight ^b , <i>n</i> (%)	198 (9.0)	152 (7.7)	105 (5.2)	30 (3.2)
Normal ^b , <i>n</i> (%)	1639 (74.7)	1396 (70.7)	1356 (66.6)	591 (62.7)
Overweight ^b , <i>n</i> (%)	357 (16.3)	426 (21.6)	574 (28.2)	321 (34.1)
Smoking status				
Current and Ex-smoker, <i>n</i> (%)	1819 (83.1)	1539 (77.8)	1121 (64.8)	690 (73.6)
Never smoker, <i>n</i> (%)	371 (16.9)	438 (22.2)	609 (35.2)	247 (26.4)
Drinking status				
Current drinker, <i>n</i> (%)	1454 (66.4)	1076 (54.4)	920 (53.2)	670 (71.5)
Ex-drinker, <i>n</i> (%)	199 (9.1)	197 (10.0)	201 (11.6)	37 (3.9)
Never drinker, <i>n</i> (%)	537 (24.5)	704 (35.6)	609 (35.2)	230 (24.5)
Regular exercise ^c , <i>n</i> (%)	—	495 (25.0)	638 (36.9)	398 (42.4)
Food				
Total energy intake, kcal, mean (SD)	2318.3 (525.2)	2258.4 (474.8)	2168.9 (600.6)	2131.7 (540.6)
SFA, %E, mean (SD)	5.2 (1.4)	5.5 (1.4)	6.6 (2.5)	5.9 (2.3)
MUFA, %E, mean (SD)	6.9 (1.9)	7.4 (1.8)	7.6 (2.7)	7.5 (2.6)
PUFA, %E, mean (SD)	5.1 (1.4)	5.4 (1.4)	6.1 (2.0)	5.3 (1.9)
Treatment of hyperlipidemia, <i>n</i> (%)	—	73 (3.7)	165 (7.1)	140 (14.9)
Women				
<i>n</i>	2819	2669	2746	1163
Age, years, mean (SD)	61.9 (8.7)	63.5 (9.2)	64.7 (10.2)	66.8 (9.2)
TC, mg/dL, mean (SD)	202.1 (34.1)	218.7 (38.7)	216.1 (35.1)	216.3 (35.0)
High TC ^a , <i>n</i> (%)	814 (28.9)	1145 (47.2)	859 (44.2)	482 (42.3)
BMI, kg/m ² , mean (SD)	23.0 (3.5)	23.3 (3.4)	23.2 (3.4)	23.1 (3.4)
Underweight ^b , <i>n</i> (%)	236 (8.4)	175 (6.7)	165 (6.6)	77 (6.6)
Normal ^b , <i>n</i> (%)	1844 (65.4)	1685 (64.3)	1652 (66.3)	770 (66.4)
Overweight ^b , <i>n</i> (%)	739 (26.2)	761 (29.0)	676 (27.1)	313 (27.0)
Smoking status				
Current and Ex-smoker, <i>n</i> (%)	361 (12.8)	283 (10.8)	184 (8.3)	108 (9.3)
Never smoker, <i>n</i> (%)	2455 (87.2)	2342 (89.2)	2043 (91.7)	1051 (90.7)
Drinking status				
Current drinker, <i>n</i> (%)	454 (16.1)	115 (4.4)	156 (7.0)	341 (29.4)
Ex-drinker, <i>n</i> (%)	52 (1.8)	26 (1.0)	28 (1.3)	9 (0.8)
Never drinker, <i>n</i> (%)	2306 (82.0)	2484 (94.6)	2043 (91.7)	810 (69.8)
Regular exercise ^c , <i>n</i> (%)	—	572 (21.8)	740 (33.2)	429 (37.0)
Food				
Total energy intake, kcal, mean (SD)	1863.1 (424.3)	1803.6 (381.4)	1762.3 (503.4)	1759.4 (424.3)
SFA, %E, mean (SD)	5.6 (1.5)	5.9 (1.5)	7.1 (2.6)	6.5 (2.4)
MUFA, %E, mean (SD)	7.4 (2.1)	7.9 (1.9)	7.9 (2.8)	8.2 (2.9)
PUFA, %E, mean (SD)	5.5 (1.6)	5.8 (1.5)	6.5 (2.1)	5.7 (2.0)
Treatment of hyperlipidemia, <i>n</i> (%)	—	164 (6.3)	351 (12.8)	252 (21.7)

BMI, body mass index; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SD, standard deviation; SFA, saturated fatty acids; TC, total cholesterol.

^aHigh TC was defined as ≥ 220 mg/dL.

^bBMI was categorized into underweight (< 18.5 kg/m²), normal (18.5–25.0 kg/m²), overweight (≥ 25.0 kg/m²).

^cRegular exercise was defined as exercise ≥ 2 times/week and ≥ 30 min/session.

ranging from 0.29 to 0.30 from 1980 to 2010. In treatment participants, the sample size was too small for analysis. (eTable 1).

DISCUSSION

In this large population-based study, we found that the association between overweight and high TC was gradually weakened over time, although a positive and significant association was observed in 1980. Whereas underweight was

inversely and significantly associated with high TC in 1980, it was also gradually weakened among women but not men.

Numerous studies showed that overweight is positively associated with high TC.^{9–11,14,19,23} The analysis of the third National Health and Nutrition Examination Survey 1988–1994 with American participants aged ≥ 60 years, the ORs of BMI ≥ 30 kg/m² versus BMI < 25 kg/m² were 1.5 and 1.8 among men and women, respectively.²³ In another study, the proportion of high-TC participants was increased following weight gain in a Dutch population in 1974–1980.¹⁴ Our results were consistent

Table 2. Odds ratios and 95% confidence intervals for high TC^a

		1980	1990	2000	2010
Men					
Normal ^b		1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Underweight ^b	Crude	0.29 (0.13–0.59)	0.77 (0.49–1.18)	0.53 (0.26–1.09)	0.40 (0.13–1.18)
	Model 1 ^c	0.31 (0.15–0.64)	0.81 (0.52–1.26)	0.59 (0.29–1.23)	0.49 (0.16–1.45)
	Model 2 ^d	0.28 (0.12–0.60)	0.80 (0.51–1.25)	0.63 (0.3–1.3)	0.37 (0.10–1.28)
Overweight ^b	Crude	2.50 (1.89–3.29)	2.10 (1.65–2.66)	1.51 (1.17–1.95)	0.93 (0.68–1.26)
	Model 1 ^c	2.44 (1.85–3.21)	2.07 (1.62–2.62)	1.46 (1.13–1.88)	0.90 (0.65–1.22)
	Model 2 ^d	2.44 (1.83–3.24)	2.01 (1.57–2.56)	1.43 (1.10–1.86)	0.92 (0.66–1.27)
Women					
Normal ^b		1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Underweight ^b	Crude	0.39 (0.26–0.57)	0.64 (0.45–0.90)	0.64 (0.42–0.97)	1.01 (0.62–1.62)
	Model 1 ^c	0.39 (0.26–0.57)	0.65 (0.45–0.91)	0.65 (0.43–0.99)	1.03 (0.63–1.66)
	Model 2 ^d	0.39 (0.26–0.57)	0.68 (0.47–0.96)	0.63 (0.41–0.96)	0.96 (0.58–1.57)
Overweight ^b	Crude	1.44 (1.20–1.72)	1.30 (1.08–1.55)	1.13 (0.93–1.38)	0.89 (0.67–1.16)
	Model 1 ^c	1.43 (1.19–1.72)	1.29 (1.08–1.54)	1.15 (0.94–1.40)	0.91 (0.68–1.19)
	Model 2 ^d	1.43 (1.18–1.72)	1.33 (1.10–1.59)	1.14 (0.93–1.40)	1.08 (0.81–1.44)

TC, total cholesterol.

^aHigh TC was defined as ≥ 220 mg/dL.

^bBMI was categorized into underweight (<18.5 kg/m²), normal (18.5–25.0 kg/m²), overweight (≥ 25.0 kg/m²).

^cModel 1 adjusted for age.

^dModel 2 adjusted for age, smoking status, drinking status, regular exercise, total energy intake, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, and treatment of hyperlipidemia.

with these previous studies and revealed that these associations weakened in a later period. The reason for the weakened associations is still unknown, but three reasons may partly explain the trend. First, high-TC participants increased among the normal BMI population (eTable 2). The proportion of high TC among normal BMI participants increased by about twofold over 3 decades (12.8% to 29.2% and 28.1% to 46.9% among men and women, respectively), whereas it only slightly increased among obese participants. In Japan, a high-fat westernized diet became increasingly popular over the study period.²⁴ Fat intake increased regardless of BMI categories (Table 1). The northern Sweden MONICA study revealed that dietary factors mainly contribute to the TC level.²⁵ Second, the proportion of participants who have protective factors for TC elevation has increased more among the obese compared with normal BMI participants (eTable 2). Although the differences in total energy intake between normal BMI and overweight participants were 147.6 kcal among men and 9.1 kcal among women in 1980, they became 56.8 kcal among men and –97.6 kcal among women in 2010. Furthermore, the proportion of current drinkers decreased among the overweight compared with normal BMI participants in men. In Japan, overweight has drawn much attention in the past few decades; for example, a new health examination focusing on metabolic syndrome started in 2008. The second reason reflects the spread of knowledge of the harm of being overweight. Finally, the proportion of overweight participants with well-controlled TC values in the treatment population greatly increased in spite of the fact that the proportion of treatment participants had increased by about 4 times over 3 decades (eTable 3). The proportion of high-TC participants among the overweight population decreased from approximately 60% to 20% over 2 decades. One reason is that the total energy intake among overweight persons was relatively decreased. Total energy intake declined to low or equal in 2010, whereas it was high in 1990. The final reason, perhaps, may be the development of drug therapy. These explanatory mechanisms

mean not only that the proportion of high-TC participants had increased among those with normal BMI but also that the proportion of such participants had relatively decreased among overweight participants.

Limited studies have reported that underweight is inversely associated with high TC. The proportion of high TC was one-fourth to one-half among underweight compared with normal BMI participants in the United States during 1988–1990.¹¹ A cross-sectional study in 1998 in Korea found that the OR of BMI <18.5 kg/m² versus BMI 18.5–22.0 kg/m² for high TC was 0.58 (95% CI, 0.40–0.85) among women.¹³ The present study was consistent with these previous studies and revealed that the association had weakened among women. A possible explanation for the findings is that high-TC participants had increased among underweight participants, and the proportion of high TC among underweight participants at 1980 to 2010 was 13.1% to 43.7% (eTable 2). It is well established that the proportion of underweight Japanese women is the highest among developed countries, at 11.6%.²⁶ A cross-sectional study report that participants low in weight were not satisfied with their body among Japanese women compared with findings in other Asian participants.²⁷ However, interestingly, underweight Japanese women increased their fat intake. Thus, the proportion of high-TC participants among underweight Japanese women has increased due to a fatty diet.

A main advantage of this study is the use of unified national population-based data in 1980, 1990, 2000, and 2010. Moreover, potential confounding factors, such as smoking,²⁸ drinking,²⁹ exercise^{30,31} and food,^{32,33} were adjusted. To our knowledge, this is the first study to reveal the change of associations between overweight or underweight and high TC over 30 years using a consistent protocol.

However, our study has limitations. First, the results were only from Japanese elderly. Several studies reported that body composition in Asia is largely different from a Western population.^{34–36} The proportion of body fat at any given BMI among Asian participants tends to be a higher than among caucasians.^{36,37} WHO mentioned that the population-specific cut-off point for BMI is necessary.³⁸ More studies are needed to clarify the association among young people or a Western population. Second, the response rate has been decreasing over time in national surveys in Japan. Selection bias might be possible. Third, the mean age has increased. Although we adjusted for age in each survey, the effect of age on health status might be included. Fourth, high TC was defined as 220 mg/dL and above. According to WHO categories, high TC was defined as 200 mg/dL and above. But the risk of coronary artery diseases is lower among Japanese than Western participants.³⁹ The Guidelines for the Diagnosis and Prevention of Atherosclerosis Cardiovascular Diseases by the Japan Atherosclerosis Society in 1997 have indicated that TC value for treatment was serum blood lipid levels ≥ 220 mg/dL.⁴⁰ Therefore, we defined high TC as measured serum blood lipid levels ≥ 220 mg/dL. Fifth, TC measurement methods differed across 1980, 1990, 2000, and 2010 because the method of enzymatically measurement was not popular in 1980. Finally, other serum lipids, such as low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride were not used for the outcomes. The TC value was only an item when the serum lipid profile was assessed in 1980. For the longitudinal association analysis, the TC value was used as an outcome in the present study.

Conclusions

The association between overweight and high TC was gradually weakened, although it was positively and significantly associated both in men and women. The association between underweight and high TC was also gradually weakened among women, whereas it was inversely and significantly associated both in men and women. These findings provide evidence that high TC prevention efforts, nowadays, must expand their target to not only overweight but also normal and underweight participants.

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Conflicts of interest: None declared.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.2188/jea.JE20170229>.

APPENDIX B.

The NIPPON DATA80/90/2010 Research Group

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