Effects of Short-term Variation in Body Mass Index on Blood Pressure in Middle-aged Japanese Male Workers

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We attempted to perform multilevel analyses to explore whether a year-to-year weight variation causes any corresponding effects on blood pressure (BP) among middle-aged Japanese workers. Subjects were 4547 healthy male workers 40–59 in age from whom serial data of systolic and diastolic BP were collected during health checkups conducted in the years 1997–2000. The effects on BP of a time-varying body mass index (BMI) that was rescaled to center around the individual-specific mean of 4 examinations on BP were investigated by statistical analysis with multilevel modeling to adjust for the wide variability among individuals. A significant relationship between the time-varying BMI and both systolic and diastolic BP was confirmed. None of the interaction terms for BMI × potential effect modifiers (smoking history, drinking status, leisure-time physical activity, and preference for salty taste) included in the subanalysis model showed any significant modifying effect. Our result indicated that the year-to-year weight variation, though usually in a much narrower range than the between-individual variation, has a strong impact on the corresponding BP. This result supports the public health significance of interventions in short-term weight control to prevent the development of hypertension among an otherwise healthy workplace population.

Key words —— longitudinal observation, random effect, weight variation, multilevel model, annual health checkup, workplace health promotion

INTRODUCTION

The relationship between weight and blood pressure (BP) has often been investigated. A screening of over 1 million people revealed those who were overweight had more than double the prevalence rate of hypertension.[1)] With respect to the relationship between weight change and BP, a previous study demonstrated that a 5-year intervention trial reduced the incidence of hypertension as a result of weight loss programs and improvements in other lifestyle habits.[2)] On the other hand, there has been substantial evidence indicating that weight gain is a major determinant of the rise in BP.[3, 4)]

In most healthy people, weight is predominantly determined by one's energy balance, which is modulated by calorie intake and expenditure. It is highly likely that a short-term weight variation reflects some recent modification, intentional or unintentional, of an individual's dietary or exercise habits, and we speculated that such a short-term weight variation causes corresponding changes in BP in each individual, *e.g.*, a mild weight loss (gain) achieved within a period of one year might result in a significant BP reduction (elevation). If this speculation is confirmed, we believe that our knowledge about the effects of weight variation on BP constitutes a basis for intervention programs involving diet and physical activity to improve health behaviors. However, few studies have explored this question; previous researchers have evaluated the beneficial effects of intensive intervention targeted at a high-risk population,[5)] or have focused on the association between long-term weight gain and endpoint BP in a general population.[4, 6)] Moreover, since annual workplace health checkups are mandated by the Industrial Safety and Health Law of Japan, a wealth of longitudinal BP and biochemical data are usually available. In this respect, a more effective

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use of those data to examine the relationship between year-to-year weight variations with BP is of great interest.

The present study was undertaken to examine the effects of BMI variations on repeatedly measured BP in a large sample of middle-aged Japanese male workers. However, data arising from a longitudinal observation have a complex, correlated structure entailing sources of random variability at multiple levels, which cannot be modeled well by relying on conventional methods for the analysis of data. To distinguish such multiple information levels, we used multilevel analysis which can be applied to situations with nested sources of random variability.[7,8]

MATERIALS AND METHODS

Study Population and Data Collection —— The study population was enrolled from male workers of a manufacturing company and Aichi Prefectural government in a central area of Japan, who agreed to participate in a cohort study of cardiovascular diseases. Women were excluded because they were so few in number. A total of 7800 men participated in an annual health checkup program conducted in the baseline year of 1997, and all gave written informed consent to answering a self-administered questionnaire and providing the results of routine biochemical analyses performed in internally and externally quality-controlled laboratories. Among them, 6261 men met our inclusion criteria as follows: aged 40–59 years at baseline; completion the questionnaire sheets covering the present history of diseases and such lifestyle characteristics as smoking status, drinking habits, leisure-time physical activity, and preference for salty taste; underwent anthropometric measurements of height and weight for calculation of body mass index (BMI, kg/m^2) along with measurements of systolic BP (SBP) and diastolic BP (DBP); and not taking medication for diabetes or hypertension. The further eligibility criterion of serial attendance at the annual health checkups until 2000 excluded 1714 men, leaving 4547 subjects for a total of 18188 observations available for the present analysis.

In about two-thirds of the subjects, BP was measured by auscultation using a mercury sphygmomanometer, and in the rest, by an automated sphygmomanometer (UM-15, Parama-Tech Co., Fukuoka, Japan), the accuracy of which had been previously confirmed.[9] As a rule, BP measurements were taken from the right arm with the subjects in a sitting position after a minimum of 5 minutes of rest. If the first measurement values were outside the normal range, the measurements were repeated after the subject sat quietly for several more minutes, and the resulting lower values were used for this study. More details of the BP measurements have been given in our previous study.[10] The current study protocol was approved by the Ethical Board of the Nagoya University School of Medicine.

Statistical Analysis —— Because the data used for this present study were regarded as forming a hierarchical structure with individual repeated BP measurements (level-1) nested within individuals (level-2), a general mixed model was chosen for the multilevel analysis.[7] Let the random variable Y_{ij} denote BP at the i^{th} examination for the j^{th} individual. We then assume that Y_{ij} satisfies the following general multilevel model:

Within-individual model (level-1)

$$Y_{ij} = \alpha_j + \beta_j(BMI_{ij} - \overline{BMI}_j) + \gamma_1 age_{ij} + \gamma_2 Covar_{2j} + \cdots + \gamma_k Covar_{kj} + \varepsilon_{ij}$$

where $i = \{1, 2, 3, 4\}$. Time-varying variables, BMI_{ij} and age_{ij}, are BMI and age at the i^{th} examination for the j^{th} individual, whereas $\overline{BMI}_j$ is the mean value across 4 examinations for the j^{th} individual. This rescaling of BMI designed to center around the individual-specific mean is performed to render the parameter more interpretable.[11] We treated this centered BMI (cBMI) as a main predictor. Age was calculated as 'age-40' according to the previous study in which the model was scaled to begin with measurements starting at 40 years of age.[12] $Covar_{kj}$ is the categorical variable created by dummy-coding of the selected baseline characteristics for the j^{th} individual. Multivariate adjustments were made for age and the following baseline variables: smoking status (current, former, never), drinking habits (none, light: daily ethanol consumption approximately less than 23 g; moderate: 23–46 g; heavy: 46 g or over), leisure-time physical activity (not very active, somewhat active, regularly active), preference for salty taste (yes but abstaining, yes and not abstaining, prefer bland taste, no special preference). We also adjusted for a family history of hypertension among siblings or parents. Approximation of the daily ethanol consumption was based on the product of daily alcohol consumption and the number of per-week drinking days.[13] The classification method for the intensity of leisure-time physical activity has been described in our previous paper.[14] The intercept α_j represents the average BP for the j^{th} individual with an average cBMI across all of his examinations, and ε_{ij} denotes the error components accounting for his within-individual variability. The regression coefficient β_j is used to model the linear rate of BP change to cBMI.

Random effects were added to reflect the natural heterogeneity of the population. In this model, both the intercept and the slope were allowed to vary across individuals, and the individual-specific regression coefficients were defined at the second level:

Subject random-intercept-slope model (level-2)

$$\alpha_j = \alpha + \upsilon_j$$
$$\beta_j = \beta + \omega_j$$

The random components, υ_j and ω_j, measure the variation in an individual's mean BP and slope, respectively, from their average in the whole sample.

For statistical software, we ran the Statistical Analysis Package (SAS) release 9.1 licensed to the Nagoya University Information Technology Center (Nagoya, Japan). Multilevel model fitting was performed using the procedure PROC MIXED, where we specified RANDOM statement and type = UNSTRUCTURED,[15] which does not assume that the random-effects covariance takes any specific form.[16] In the multivariate statistical analyses, we built mixed models including both level-1 and level-2 predictors.

Because a smoking history is likely to modify the effect of weight variation on BP, additional analysis was conducted to include an interaction term between cBMI and smoking history in the within-individual model (level-1). Likewise, an interaction term of cBMI with each of drinking status, leisure-time physical activity, or preference for salty taste was included in the mixed model to examine whether the modifying effect of those variables on the association between BP and cBMI are significant.

For statistical comparison between two independent samples, unpaired t-test was used for two sample means and chi-square test for contingency tables. In all statistical tests, a two-tailed p value of < 0.05 was regarded as significant.

RESULTS

Table 1 gives the distribution of baseline characteristics of our subjects. Those aged ≥ 50 years and those with BMI ≥ 25 kg/m^2 accounted for 40.3% and 20.9%, respectively. Current smokers accounted for a little more than half (53.2%), and drinking status almost evenly distributed over 4 categories. A small proportion (5.8%) indicated that they engaged regularly in leisure-time physical activity. Nearly 60% revealed that they had preferred a salty taste, half of whom intentionally abstained from salty meals, while the rest did not. Reports of a history of hypertension among siblings or parents were seen in 28.0% of subjects. The results of comparison between 4547 and 1714 excluded men were also summarized in Table 1. There were significant differences in baseline age, BMI, SBP, and DBP, with excluded men showing higher mean values of these characteristics. Those aged ≥ 55 years accounted for more than 40% of those excluded. Statistical comparison also indicated that those excluded were more likely to have quit smoking and eat low-salt meals than the eligible subjects. No statistical differences were found between the two groups regarding the distribution of high BMI (≥ 30 kg/m^2), low BMI (< 18.5 kg/m^2), drinking status, physical activity, family history of hypertension, or engagement in shiftwork.

Our study population consists of 3122 employees of the Aichi Prefectural government and 1425 employees of a manufacturing company, whose workstyle characteristics were summarized in Table 2. A statistical comparison revealed that the employees of the manufacturing company have been more often engaged in shiftwork or overnight shiftwork and have less often assumed a sedentary posture during their working time than the government employees.

Table 3 presents the year-to-year means of BMI, cBMI, SBP, and DBP of the study population. Across the 4-year measurements, BMI showed no statistically significant difference, whereas cBMI, SBP and DBP differed significantly. An apparent linear increase with time was noted in cBMI and DBP but not in either BMI or SBP. Distributions of yearly BMI and cBMI were depicted in Figs. 1 and 2, respectively, as a box-plot with histogram overlaid by normal-distribution curves, demonstrating a normality in the BMI distribution and some departure from normality in the cBMI distribution.

Table 1. Demographic and Lifestyle Characteristics of 4547 Eligible and 1714 Excluded Men at Baseline Year of 1997

	Eligible		Excluded		
	Average	(Min, Max)	Average	(Min, Max)	p for difference [a]
Age (y/o)	48.5	(40, 59)	51.8	(40, 59)	< 0.01
BMI (kg/m^2)	22.9	(14.2, 33.9)	23.1	(14.0, 33.3)	< 0.01
Systolic Blood Pressure (mmHg)	128.1	(77, 198)	129.9	(86, 200)	< 0.01
Diastolic Blood Pressure (mmHg)	78.9	(46, 128)	80.2	(50, 125)	< 0.01
	Frequency	%	Frequency	%	p for difference [b]
Age					
≥ 50 y/o	1831	40.3	1064	62.1	< 0.01
≥ 55 y/o	601	13.2	751	43.8	< 0.01
BMI					
≥ 25 kg/m^2	950	20.9	397	23.2	0.028
≥ 30 kg/m^2	32	0.70	13	0.76	0.82
< 18.5 kg/m^2	176	3.9	61	3.6	0.56
Smoking history					
Never	1746	38.4	356	20.8	
Former	382	8.4	832	48.5	< 0.01
Current	2419	53.2	526	30.7	
Drinking status					
None	1212	26.7	450	26.3	
Light	1081	23.8	400	23.3	0.79
Moderate	1056	23.2	419	24.4	
Heavy	1198	26.3	445	26.0	
Physical activity					
Not very active	3663	80.6	1378	80.4	
Somewhat active	621	13.7	247	14.4	0.53
Regularly active	263	5.8	89	5.2	
Preference for salty taste					
Yes (no abstaining)	1360	29.9	430	25.1	
Yes (abstaining)	1375	30.2	567	33.1	< 0.01
Prefer bland taste	1089	23.9	439	25.6	
No special preference	723	15.9	278	16.2	
Family history of hypertension					
Yes	1271	28.0	484	28.2	0.42
Engagement in shiftwork					
Yes	445	9.8	161	9.4	0.61

a) p value by two-sample t-test. *b*) p value by chi-square test.

Table 2. Workstyle Characteristics of 3122 Prefectural Government Employees and 1425 Manufacturing Company Employees at Baseline Year of 1997

	Prefectural Government		Manufacturing Company		
	Frequency	%	Frequency	%	p for difference [a]
Engagement in shiftwork					
Yes	212	6.8	233	16.4	< 0.01
Engagement in overnight shiftwork					
Yes	127	4.1	168	11.8	< 0.01
Major physical position during working					
Roaming	421	13.5	507	35.6	
Standing	117	3.7	179	12.6	< 0.01
Sedentary	2584	82.8	739	51.9	

a) p value by chi-square test.

Table 3. BMI and BP among 4547 Men in Years 1997–2000

	Average	(Min, Max)
BMI (kg/m^2)		
Year 1997	22.8737	(14.2, 33.9)
1998	22.8705	(14.8, 34.1)
1999	22.9133	(14.7, 35.1)
2000	22.9303	(14.5, 35.1)
p for difference[a)]	0.62	
p for trend[b)]	0.22	
cBMI[c)] (kg/m^2)		
Year 1997	−0.0230	(−2.35, 2.85)
1998	−0.0265	(−2.73, 2.35)
1999	0.0164	(−3.20, 2.03)
2000	0.0334	(−3.50, 2.95)
p for difference[a)]	< 0.01	
p for trend[b)]	< 0.01	
SBP (mmHg)		
Year 1997	128.1	(77, 198)
1998	129.0	(85, 202)
1999	129.3	(85, 210)
2000	128.4	(79, 228)
p for difference[a]	< 0.01	
p for trend[b]	0.29	
DBP (mmHg)		
Year 1997	78.9	(46, 128)
1998	79.3	(48, 130)
1999	80.3	(38, 138)
2000	80.1	(47, 130)
p for difference[a)]	< 0.01	
p for trend[b)]	< 0.01	

a) *p* value by analysis of variance. *b*) Test for trend was performed using linear contrast on assumption of equal spacing from 1997 to 2000. *c*) Rescaled variable so as to center around the subject-specific mean value across 4 examinations.

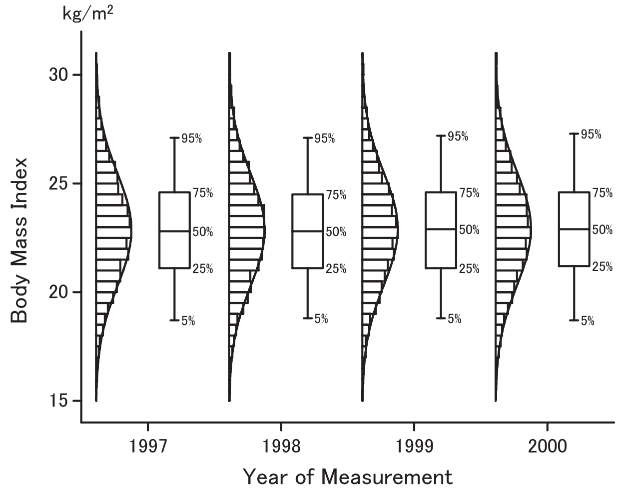

Fig. 1. Distribution of Body Mass Index by Year of Measurement

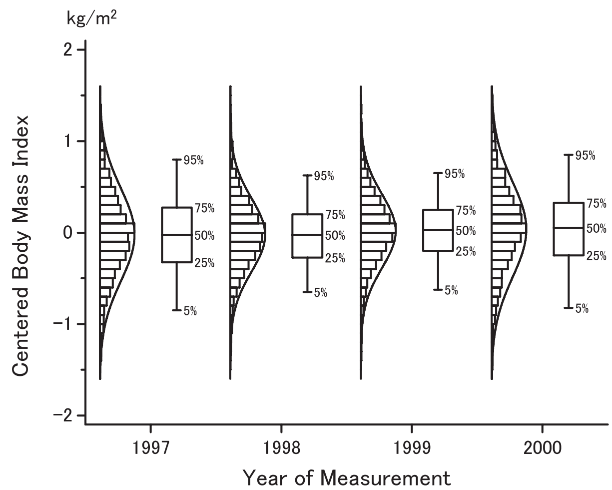

Fig. 2. Distribution of Centered Body Mass Index by Year of Measurement

The estimated fixed-effects of cBMI, age, and baseline lifestyle variables on BP are presented in Table 4. As cBMI increased, notable increases in both SBP and DBP were observed. With age, both SBP and DBP also increased significantly. With respect to the association with baseline lifestyle characteristics, former smokers showed no statistical difference in BP compared to never smokers, but both SBP and DBP in current smokers were found to be significantly lower than in never smokers. Either light, moderate, or heavy drinking status was associated with a significant increase in SBP and DBP compared with the reference category (no drinking habit). The linear trend that BP increased in proportion to the amount of daily ethanol consumption was also statistically significant. SBP showed no significant association with leisure-time physical activity, but an inverse association between DBP and physical activity was observed in a significant linear fit. Those who preferred a salty taste but were abstaining showed a significant increase in both SBP and DBP, whereas those who preferred a salty taste but were not abstaining had no significant BP increase in comparison with those who had no special taste preference. The relationship of a family history of hypertension with SBP or DBP was statistically significant. Table 4 also indicated that the variabilities in intercept and slope were highly significant between subjects.

Results of the subanalyses were given in Table 5, which revealed that neither smoking status, drinking habit, leisure-time physical activity nor preference for salty taste showed a significant interaction with cBMI to modify the association be-

Table 4. Mixed Models Describing Associations of SBP and DBP with BMI and Individual-level Covariates of 4547 Men

Parameter	SBP (mmHg)		DBP (mmHg)	
	Estimates	SE	Estimates	SE
Intercept	126.72	1.11**	77.22	0.74**
cBMI[a] (kg/m^2)	2.13	0.15**	1.54	0.11**
Covariates:				
Age (year)	0.200	0.034**	0.229	0.023**
Smoking history				
Never (reference)	—	—	—	—
Past	0.55	0.76	0.081	0.509
Current	−3.28	0.44**	−2.84	0.29**
Drinking status				
None (reference)	—	—	—	—
Light	2.06	0.56**	1.88	0.38**
Moderate	3.27	0.57**	2.65	0.38**
Heavy	6.62	0.56**	4.94	0.37**
p for trend[b]	$p < 0.01$		$p < 0.01$	
Physical activity				
Regularly active (reference)	—	—	—	—
Somewhat active	0.56	0.94	0.39	0.63
Not very active	1.41	0.87	1.26	0.58*
p for trend[b]	$p = 0.10$		$p = 0.03$	
Preference for salty taste				
No special preference (reference)	—	—	—	—
Yes (no abstaining)	0.90	0.62	0.54	0.42
Yes (abstaining)	2.37	0.62**	1.33	0.41**
Prefer bland taste	0.25	0.65	−0.22	0.43
Family history of hypertension				
Yes (*vs*. No)	4.86	0.45**	3.05	0.30**
Variance-covariance component:				
Intercept	163.10	3.82**	71.63	1.70**
Slope	8.24	1.70**	3.84	0.86**
Covariance	−4.47	2.04*	−1.24	0.95

a) Rescaled variable so as to center around the subject-specific mean value across 4 examinations. *b*) Test for trend was performed using linear contrast on assumption of equal spacing. $^{*}p < 0.05$, $^{**}p < 0.01$.

Table 5. Test of Fixed Effects of Terms for Interaction between BMI and a Selected Variable of 4547 Men in Each Mixed Model

	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
	F value	*F* value	*F* value	*F* value	*F* value	*F* value	*F* value	*F* value
cBMI[a]	87.4**	91.7**	199.3**	210.0**	70.0**	97.8**	177.8**	189.7**
Included interaction term:								
BMI × Smoking history	2.4#	1.8						
BMI × Drinking status			2.1#	1.3				
BMI × Physical activity					0.16	0.95		
BMI × Preference for salty taste							2.3#	0.39

a) Rescaled variable so as to center around the subject-specific mean value across 4 examinations. $^{\#}p < 0.1$, $^{*}p < 0.05$, $^{**}p < 0.01$.

tween BP and cBMI; however, a weak interaction of cBMI with smoking history, drinking status, and preference for salty taste was observed in the mixed model predicting SBP.

DISCUSSION

In this study of middle-aged men, longitudinally observed BP data with concurrent measures of obesity were analyzed using multilevel analysis. As is usual in repeated BP measurements, the between-individual variation is usually much wider than the within-individual one, which is likely to compromise statistical power when conventional regression analyses are applied to data from repeated measurements nested within individuals. The results of our study indicated a wide variation in individual-specific mean BP. The individual-specific slopes describing the rates of change in BP to cBMI were also found to vary widely from subject to subject. A strong point of the multilevel model is that it accounted for such between-individual heterogeneity in the intercept and slope of the regression line describing the association of cBMI and BP.[16)]

Regarding the effect of long-term weight variability on health outcome, we have already revealed that the root mean square error of variation (RMSE) as a measure of long-term weight fluctuation increased the risk of developing hyperinsulinemia in 1932 male Japanese workers aged 40–59.[17)] While that study focused on the deleterious effects of weight instability during the adult period between age 20 and middle-age, the results of some previous studies agree on the beneficial health effects of a modest weight loss in terms of the reduced cardiovascular or mortality risk.[18–20)] A recent systematic review of 25 randomized controlled trials comprising 4874 participants showed an estimated SBP/DBP reduction of −4.4/−3.6 mmHg for a ≈5-kg weight loss by means of energy restriction, physical activity, or both.[5)] Although the targeted populations in these trials had a high prevalence of hypertensive or overweight subjects under treatment, the BP reduction was achieved by a relatively short-term weight control intervention of an average 66.6 weeks. Furthermore, previous studies agreed that the BP response to weight loss was smaller in normotensive than in hypertensive populations.[5, 21, 22)]

Epidemiologic evidence in Japan indicated that obesity, which had played no important role in the development of hypertension in the 1950s through the 1970s when a high salt intake was the main contributor to BP elevation, has become an established risk factor contributing to hypertension with the increased consumption of animal food products and lifestyle changes. In line with this historic shift in risk factors related to hypertension, we have recently revealed a highly significant association of hypertension with obesity but not with a preference for salty taste in a study of middle-aged civil servant employees in Japan.[10)] However, that study was conducted using a cross-sectional design to uncover risk factors related to BP elevation, and did not consider the effect of year-to-year weight variation on BP. Thus, the present study was intended to follow and extend our previous one to evaluate the impact of weight change on the corresponding BP.

One of the most salient results of this study is that significant relationships of cBMI with both SBP and DBP were confirmed using data from longitudinal observations. Because the multilevel modeling accounted for the effect of wide between-subject variability in both the intercepts and slopes, the observed relationship implies that the year-to-year BMI variations have a significant impact on BP. As is shown in Table 1, the BMI varied in a relatively narrow range around one's average of 4 examinations from 1997 through 2000 within each individual of our study population. The results of our study may thus be interpreted to mean that prompt improvements in BP are expected to occur with mild weight control on the one hand, while poor weight control is likely to result in an immediate worsening of BP on the other. In the performance of subanalyses, we first considered smoking history as a potential effect modifier in that the effect of the BMI variation on BP differs with differences in smoking history. The interaction term between cBMI and smoking history included in the model, however, was not a significant contributor, suggesting that weight control is an equally important factor for optimal BP maintenance regardless of whether or not an individual smokes. Similarly, no significant interaction was found with the other potential effect modifiers, *i.e.*, drinking status, leisure-time physical activity, and preference for salty taste. We construed this lack of significant interactions to show that no differential approaches as to lifestyle differences should be given particular attention; *e.g.*, it should be noted that weight control in smokers is as effective as in non-smokers to achieve a comparable BP change.

Some considerations are required on the association with respect to lifestyle covariates in the analyses. Our result showing that current smokers are at a lower risk for BP elevation than never-smokers is seemingly contrary to common expectations, but is consistent with a number of previous studies.[10, 23, 24)] Differences between acute and habitual exposure to smoking in the effect on blood pressure may provide a partial explanation of this unexpected association.[25] Another possibility is that intensive advice by health care workers to those with high BP would have elevated their health awareness, thus resulting in a lower rate of smokers than in other groups. Moreover, a significantly high risk for BP elevation among those who prefer a salty taste but are abstaining *vs.* a lack of such an association among those who are not, might also result from the interventions targeted at high-risk subjects, motivating them to pursue a health-aware lifestyle.

Although the results of our study underscore the importance of short-term weight control for corresponding BP control, the underlying mechanism of the effect of weight variation on BP has yet to be elucidated. Until now, some plausible explanations have been proposed to explain the relevant biological pathway involved, including the overactivated renin-angiotensin-aldosterone system,[26] increased activity of the sympathetic nervous system,[27] an inhibited natriuretic peptide system,[28] or decreased insulin sensitivity in obese individuals.[5] Although we have presumed that a short-term weight variation reflects the relatively recent change in energy balance due to diet modification and physical activity, some have argued that aerobic exercise reduced BP independently of changes in body weight.[29] Since regularly active subjects comprised only a small part of our study population, the effect of intensive exercise on the mean BP of the study population was not indicated to be as significant as in the previous report,[29] and we have come to believe that energy restriction is definitely effective in reducing BP.

Our results should be interpreted with some precautions. First, we selected study subjects who annually continued to undergo 4 examinations during the years 1997–2000; the failure to participate was attributable largely to compulsory retirement, which explains the reason for the high proportion of those aged ≥ 55 (43.8%) among the excluded persons (Table 1). Although multilevel analysis allows all the available information of the incomplete data to be used without the need either to discard or to impute measurements whenever the missing-data mechanism is assumed to occur at random,[16] withdrawal due to compulsory retirement is not considered to be a random event. Such selection might have yielded biased inferences, the potential effect of which on the result would have been evaluated only by post-retirement follow-up. Second, with respect to the random effects, the component representing covariance between intercepts and slopes has taken negative values (Table 4). This result means that BP would be expected to decrease more among high baseline BP subjects than low baseline BP subjects, and we confirmed that the magnitude of such an uneven effect of weight changes on BP reduction was larger in subjects with BMI ≥ 25 kg/m^2 than in the others (data not shown). Taken together, our findings pointed to the relative importance of weight reduction interventions for high BP individuals in the overweight subpopulation. Third, our study was not designed to evaluate the risk of weight variation for the incidence of hypertension but focused on a linear relationship between BP and BMI, both of which varied in relatively narrow ranges within individuals. In this respect, a previous prospective study of Japanese male employees revealed a significant 1.2-fold elevation of the risk for incidence of hypertension associated with the weight gain of ≥ 2.0 kg during the 4-year follow-up period.[6]

A number of study limitations should be mentioned. Our reason for treating age and BMI as time-varying in the model was to better evaluate the patterns of BP changes with these predictors. However, we did not treat other covariates as time-varying, because information on such covariates was not available on a year-to-year basis. The possibility cannot be ruled out, therefore, that the classification of such lifestyle variables as smoking/drinking habits or physical activity could have changed in an individual during the period of serial data collection. Moreover, while those under medical treatment for diabetes or hypertension at baseline were excluded from the analyses, our study may have been affected by the cases who started to undergo medical treatment anew during the follow-up period. In our rough estimation based on the intermediate evaluation, 7–11% of our study population were newly diagnosed with hypertension during the years 1997–2004, indicating an annual incidence rate of about 1–2%. The influence of those cases also remains to be evaluated in any further analyses.

In conclusion, multilevel analyses of serial data provided evidence that year-to-year weight variations closely correlated with the corresponding BP within middle-aged healthy individuals. Even short-term weight control has a significant impact on BP change, though the change occurs in a narrow-range within an individual. Our results imply that the characterization of the relationship between BMI variation and BP has a public health significance from a practical point of view, since they can be incorporated into workplace health promotion programs to raise awareness of the importance of weight control.

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