Two-year change in BMI and subsequent risk of hypertension among men and women in a Taiwan community

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Objective **To examine the relationship between short-term changes in BMI and the development of hypertension in a cohort of ethnic Chinese men and women.**

Methods **BMI changes between the baseline survey in 1990–1991 and examinations in 1992–1993 were evaluated for 713 men and 853 women aged 35 years or above, free from hypertension, stroke, coronary heart disease and diabetes at the baseline. The incident hypertension and associated risks were assessed in follow-up visits in 2000.**

Results **Both men and women in the highest BMI change quartile had the highest adjusted mean blood pressures at the initial follow-up period. The differences in blood pressure between the extreme quartiles of BMI changes remained significant at the end of follow-up period in men but were notably reduced in women. The risk of incident hypertension increased as the BMI change quartile increased in men (multivariate-adjusted hazard ratio and 95% confidence interval for the highest quartile versus the lowest quartile: 1.81, 1.22–2.68, respectively, *P* for trend = 0.002). However, in women, the BMI gain effect on hypertension was not significant unless menopausal status was included in the adjustment (hazard ratio and 95% confidence interval: 1.46, 1.04–2.06, respectively). Stratified analyses showed that the BMI change effect was significant only in women in the premenopause or transition to menopause during their BMI change period.**

Conclusion **The 2-year substantial BMI gain is associated with a persistent risk for developing hypertension in men. The risk for women is influenced by their menopause status.** *J Hypertens* **27:000–000 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Abbreviations: CCC, cohort study, the Chin-Shan Community Cardiovascular Cohort Study; CI, confidence interval; P1, BMI change period; P2, follow-up period

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Introduction

Hypertension has been a persistent public health challenge because of its high prevalence rate in the middle-aged and elderly populations [1]. Obesity is a well known risk factor for hypertension. Weight loss is a critical lifestyle modification for overweight people to control hypertension [1–3]. Studies have shown that weight gain increases the risk for high blood pressure (BP) in population settings. However, these studies measured the effect of weight changes after a long study period [4–9] and concurrently evaluated changes in weight and BP during the same period [5,7–9]. The body weight may fluctuate during a long lag period. The development of hypertension may actually reflect the exposure in earlier years. Whether a short-term weight gain has a persistent adverse effect on BP during subsequent years in general populations has not been well documented.

Evidence has shown sex and ethnic differences in cardiovascular risks and levels of risk factors [10,11]. African–American women are over 1.5 times more likely than white women and African–American men to be overweight [11]. The Chinese population is in general characterized with a lower BMI but higher BP compared with whites [10]. Colin Bell *et al.* [12] also reported that the association between BMI and hypertension is stronger for Chinese people than for non-Hispanic white people. The effect of weight change on hypertension incidence has not been reported using prospective study for the ethnic Chinese population.

In the Chin-Shan Community Cardiovascular (CCC) Cohort Study, a study population homogeneous in Chinese ethnicity and culture was monitored for over 15 years and repeatedly examined approximately every other year. This longitudinal follow-up study provides a unique opportunity to observe short-term BMI changes and the effect on BP in successive years. The present study reports on the BMI change effect on the hypertension development 7 years after the initial 2-year

observation. Whether there are sex differences in the association was also assessed for this community cohort.

Methods and materials

Study design and study population

The CCC Cohort Study is a prospective study initiated in 1990 to investigate the trends and determinants of cardiovascular diseases. The cohort consisted of 1703 men and 1899 women aged 35 years or older (a response rate of 82.8%) residing in the Chin-Shan area, a township near Taipei city, Taiwan. At the baseline visit in 1990–1991 with follow-up visits approximately every other year, cardiologists and trained medical students conducted a structured questionnaire interview that included questions on family health history and lifestyle factors. The medical staff performed anthropometry, physical examinations and laboratory measurements with the consent of participants. The response rates in the follow-up visits were 86% or above. Study design and data collection details are published elsewhere [13,14]. The Institutional Review Board at National Taiwan University Hospital approved this study.

The change in BMI was calculated by subtracting the BMI measured in the baseline survey in 1990–1991 from that measured in 1992–1993 visits. The 2-year duration was defined as BMI change period. Individuals with stroke, coronary heart disease and diabetes at the baseline, or with hypertension before the 1992–1993 visits ($n = 1630$) or with incomplete data on BMI changes ($n = 406$) were excluded. Seven hundred thirteen men and 853 women remained for the prospective analyses to assess the association between BMI change and the incidence of hypertension during the follow-up period until the 1999–2000 visits.

Measurements

As described in previous reports [14,15], BP was measured using a mercury sphygmomanometer with a suitable cuff size adjusted to the arm circumference after patients had 5 min of rest in the supine position. SBP and DBP were defined by Korotkoff sounds I and V, respectively. Two measurements from the right arm were made with the arm supported and placed at the level of the heart. The mean of two measurements represented the BP level of a patient.

Hypertension was defined as the SBP higher than 140 mmHg, and/or the DBP higher than 90 mmHg and/or receiving antihypertensive medication. BMI was calculated as weight in kilograms divided by the square of height in meters. Individuals with a fasting serum glucose level higher than 126 mg/dl and/or a history of using hypoglycemic agents or insulin injections were considered as having diabetes mellitus. The metabolic syndrome was defined according to the criteria of the United States National Cholesterol Education Program Adult Treatment Panel III [16].

Serum lipid and fasting glucose levels were determined, as described elsewhere [13], in a central laboratory at the National Taiwan University Hospital. All blood samples were drawn from the antecubital vein of participants after a 12-h overnight fast and transported in an ice bath to the laboratory within 6 h.

Statistical analysis

All analyses were performed separately for men and women. Baseline characteristics were compared among groups of sex-specific quartile of BMI changes using analysis of variance (ANOVA) for continuous variables and χ^2 test for categorical variables. We estimated the adjusted means of SBP and DBP in each quartile group of BMI change using general linear models. Mean BPs at baseline were estimated adjusted for age and baseline BMI. Mean BPs at the end of BMI change period and at the end of follow-up period, baseline BP and medication on hypertension (yes or no) during the study period were additionally included for adjustment.

To evaluate the BMI change effect on subsequent hypertension during the follow-up period, we used Cox proportional hazard models to compute the hazard ratio and 95% confidence intervals (CIs) for BMI change groups. All potential confounding variables in the regression analyses were collected at baseline. Models were initially adjusted for the baseline age, BMI, SBP and DBP (model 1). To observe the influence of lifestyle factors and lipid markers, models were additionally adjusted for occupation, smoking, alcohol consumption and regular exercise (model 2), and further adjusted for levels of low-density lipoprotein cholesterol and triglycerides (model 3). Menopausal status was added to model 3 for adjustment for women (model 4). The linear trends across BMI change categories were examined by defining a median BMI change value within each quartile as a continuous variable. All models were repeated by treating the BMI change in its original scale instead of quartiles to examine the significance of the change across ranges including extreme values.

To evaluate the influence of menopause status on the association between BMI change and hypertension, we stratified women into two groups by their menstrual status during the BMI change period and repeated the Cox proportional hazard models. One group consisted of women that had menstruation (premenopause) and women experienced a transition to menopause. The other group included those that had spontaneously stopped menstruation before the BMI change period (postmenopause). We combined women in premenopausal and transition periods as one group because they had a similar U-shape relationship between hypertension

incidence and BMI change quartiles and because of a small size of patients in the transition group ($n = 71$). BMI changes were classified as a dichotomous variable using the highest quartile of BMI changes as the cut-off point in the analyses. A two-sided P value of less than 0.05 was considered statistically significant. All analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, North Carolina, USA).

Results

Baseline characteristics of participants

The medians of the 2-year BMI changes were 0.2 kg/m^2 in men and 0.3 kg/m^2 in women (interquartile ranges: −0.5 to 0.9 and −0.5 to 1.1 kg/m^2, respectively) (Table 1). Individuals had the BMI reduced for more than 0.5 kg/m^2 were more likely to have the highest BMI at baseline among the four quartile groups of BMI changes. Women with greater BMI reduction were older, exhibited higher levels of low-density lipoprotein cholesterol and were more prevalent in metabolic syndrome and postmenopause.

Blood pressure in BMI change period and follow-up period by sex

Figure 1(a) shows that in men, the adjusted mean SBP increased as the BMI change increased at both the 2-year change period (P1) and the subsequent 7-year follow-up period (P2) (P for trend across quartile: <0.001 and 0.007, respectively). The DBP trend showed a somewhat similar pattern, although individuals in the second BMI change quartile had slight higher BP than those in the third quartile at the end of the follow-up period. Overall, the differences in SBP and DBP between the highest and the lowest quartile of BMI change were parallel over time.

For women, individuals in the highest BMI change quartile had the highest adjusted-mean SBP, whereas the trend of BP across the other three quartiles fluctuated over time [Fig. 1(b), P for trend across quartile: 0.008 and 0.19 for P1 and P2, respectively]. The difference in SBP between the highest and lowest BMI change quartile appreciably reduced through the follow-up period. Similar patterns were observed for the adjusted mean DBP, of which the increasing trend across BMI change quartile became nonsignificant at the end of follow-up (P for trend: 0.008 and 0.077 for P1 and P2, respectively).

BMI change and later hypertension risk by sex

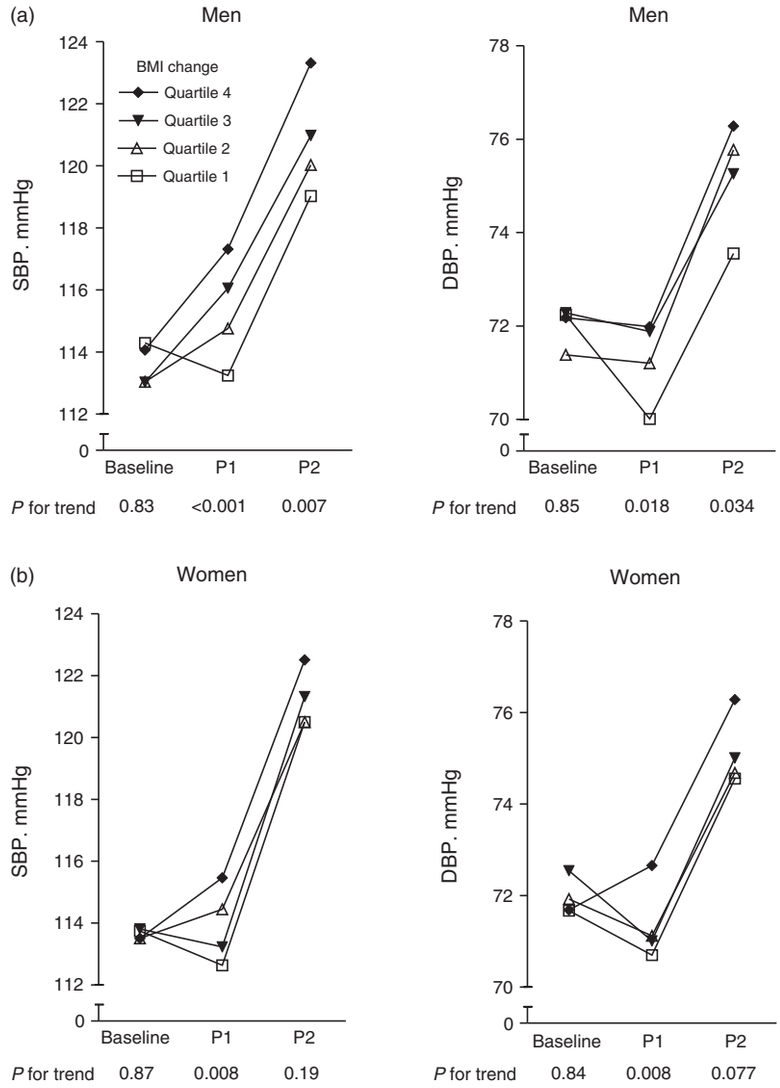
The overall incidence rates of hypertension were 63.5 per 1000 person-years in men and 59.7 per 1000 person-years in women during follow-up period (median 7.0 years). Compared with men with BMI reduction of −0.5 kg/m^2 or less (i.e. the lowest quartile of BMI changes), men with

Table 1 Baseline characteristics of participants by quartile of 2-year change in BMI from baseline

	Quartile of change in BMI				
	1	2	3	4	*P*
Men, *n*	179	177	178	179	
Change in BMI (kg/m^2)	≤−0.5	>−0.5 to 0.2	>0.2–0.9	>0.9	
BMI at baseline (kg/m^2)	23.1	22.7	21.8	22.2	<0.001
BMI at the end of BMI change period (kg/m^2)	21.7	22.6	22.4	24.0	<0.001
BMI at the end of follow-up period (kg/m^2)	22.9	23.4	23.1	23.8	0.16
Age (years)	54.9	52.9	53.6	52.0	0.15
SBP (mmHg)	114.9	113.1	112.7	113.7	0.19
DBP (mmHg)	72.6	71.6	71.9	72.0	0.62
Low-density lipoprotein cholesterol (mmol/l)	3.42	3.29	3.21	3.27	0.30
High-density lipoprotein cholesterol (mmol/l)	1.21	1.22	1.23	1.22	0.96
Triglycerides (mmol/l)	1.37	1.21	1.25	1.18	0.19
Current smoking, %	64.0	65.5	59.6	62.0	0.67
Current alcohol drinking, %	41.6	40.0	41.2	41.0	0.99
Regular exercise, %	12.3	17.5	15.2	13.4	0.53
Metabolic syndrome, %	12.6	8.0	7.0	5.9	0.12
Women, *n*	213	213	214	214	
Change in BMI, (kg/m^2)	≤−0.5	>−0.5 to 0.3	>0.3–1.1	>1.1	
BMI at baseline (kg/m^2)	24.1	23.1	22.7	22.7	<0.001
BMI at the end of BMI change period (kg/m^2)	22.5	23.0	23.3	24.8	<0.001
BMI at the end of follow-up period (kg/m^2)	24.0	23.6	23.9	24.9	0.008
Age (years)	51.4	48.2	48.7	49.0	0.011
SBP (mmHg)	115.1	113.1	113.3	113.1	0.14
DBP (mmHg)	72.2	71.8	72.3	71.5	0.64
Low-density lipoprotein cholesterol (mmol/l)	3.71	3.34	3.51	3.45	0.005
High-density lipoprotein cholesterol (mmol/l)	1.30	1.30	1.34	1.32	0.50
Triglycerides (mmol/l)	1.37	1.21	1.25	1.18	0.34
Current smoking, %	3.8	2.8	4.7	3.3	0.89
Current alcohol drinking, %	7.5	9.0	6.1	7.9	0.74
Regular exercise, %	8.9	16.9	14.6	11.2	0.069
Metabolic syndrome, %	13.3	8.5	8.6	4.4	0.015
Postmenopausal, %	51.7	45.5	47.3	40.7	0.18

Values are means or percentages.

Fig. 1



Adjusted mean blood pressure at baseline and at the end of BMI change period (P1) and follow-up period (P2) using the quartile change in BMI. Models for the estimation of mean blood pressure at baseline were adjusted for baseline age and BMI. For the estimation at P1 and P2, models were additionally adjusted for baseline SBP (for the SBP estimation) or DBP (for the DBP estimation) and medication on hypertension (yes versus no) during the study period.

a mild reduction or gain (the second quartile of BMI changes of −0.5 to 0.2 kg/m^2) had an increased risk for developing hypertension (hazard ratio and 95% CI: 1.55, 1.04–2.31, respectively) (model 3, Table 2). The risk for the third BMI change quartile rose to 1.81 (95% CI, 1.21–2.69), a magnitude similar to the highest quartile.

For women, the relationship between incident hypertension and BMI change quartiles exhibited a U shape with the lowest risk for hypertension in individuals in the third BMI change quartile. Women with a BMI gain of more than 1.1 kg/m^2 had the highest risk for incident hypertension, 69.7 per 1000 person-years, followed by women with the BMI reduction of 0.5 kg/m^2 or more. Regression analyses showed that hypertension was not significantly associated with BMI gain unless menopausal status was included in the model for adjustment (model 4, hazard ratio and 95% CI in the highest quartile versus the lowest quartile: 1.46, 1.04–2.06, respectively).

Stratified analyses by menopausal status

An increase in BMI was associated with hypertension development in women in premenopausal status and in transition during the BMI change period (Fig. 2, model 3,

Table 2 Hazard ratio (95% confidence interval) of incident hypertension during follow-up period in relation to BMI change

	Quartile of change in BMI					
	1	2	3	4	*P* for trend	Per unit increase
			Men ($n=713$)			
Range, kg/m^2	≤−0.5	>−0.5 to 0.2	>0.2–0.9	>0.9		
No. of events/participants	52/179	59/177	56/178	63/179		
Rate/1000 person-years	56.8	65.1	63.2	69.0		
Model 1[a]	1 (reference)	1.43 (0.98–2.08)	1.64 (1.11–2.41)	1.65 (1.13–2.41)	0.007	1.14 (1.02–1.27)
Model 2[b]	1 (reference)	1.49 (1.02–2.19)	1.68 (1.13–2.48)	1.70 (1.16–2.49)	0.005	1.13 (1.01–1.27)
Model 3[c]	1 (reference)	1.55 (1.04–2.31)	1.81 (1.21–2.69)	1.81 (1.22–2.68)	0.002	1.16 (1.03–1.30)
			Women ($n=853$)			
Range, kg/m^2	≤−0.5	>−0.5 to 0.3	>0.3–1.1	>1.1		
No. of events/participants	76/213	63/213	60/213	83/214		
Rate/1000 person-years	67.2	55.1	47.7	69.7		
Model 1[a]	1 (reference)	1.00 (0.72–1.41)	0.85 (0.60–1.20)	1.25 (0.91–1.72)	0.26	1.10 (1.02–1.19)
Model 2[b]	1 (reference)	1.01 (0.72–1.42)	0.85 (0.60–1.20)	1.25 (0.91–1.73)	0.25	1.10 (1.02–1.19)
Model 3[c]	1 (reference)	1.04 (0.73–1.47)	0.88 (0.62–1.26)	1.27 (0.91–1.76)	0.24	1.10 (1.01–1.19)
Model 4[d]	1 (reference)	1.10 (0.77–1.57)	0.94 (0.65–1.36)	1.46 (1.04–2.06)	0.058	1.12 (1.03–1.22)

[a] Adjusted for age, BMI, SBP and DBP at baseline. [b] Adjusted for variables in model 1 as well as occupation, smoking, alcohol consumption and regular exercise at baseline. [c] Adjusted for variables in model 2 as well as levels of low-density lipoprotein cholesterol and triglyceride at baseline. [d] Adjusted for variables in model 3 as well as menopausal status at baseline.

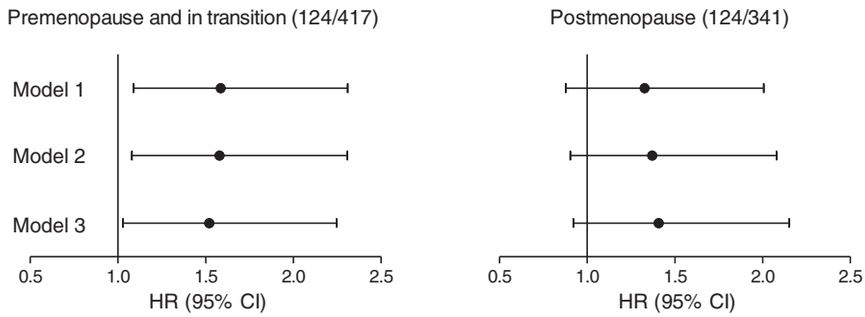
hazard ratio and 95% CI: 1.52, 1.03–2.25, respectively). No appreciable association was found in postmenopausal women.

Discussion

This study assessed the impact of the short-term BMI change on BP as both the short-term immediate effect and the long-term effect in later years. We observed a linear relationship between the 2-year BMI changes and hypertension development among men in a subsequent median 7-year follow-up period. In women, the association was unlikely to be linear, although, the short-term weight gain was slightly higher in women than in men.

Several studies have reported long-term weight gain and increased hypertension risk [4–8] or the beneficial effect on BP from weight reduction [17–19]. The Tromso Study [5] in Norway showed that the 9-year BMI changes affect the BP changes for all age groups and both sexes. However, younger patients, 20–39 years of age, have greater mean BMI increases but lower BP increases than older groups. A prospective study [6] in Japan found that the odds ratios for hypertension associated with the 5-year BMI changes were 2.48 for men and 2.19 for women. This strong association may be partly attributable to their defining hypertension using cut-off value of at least 160 mmHg for SBP and at least 95 mmHg for DBP. Consisting women 30–55 years of age at baseline, the United States Nurses' Health Study showed that the hypertension risk was linearly associated with 2–14 years weight changes [4]. They had much greater weight gains with a dose-response relationship, with the hypertension risk 2.85 times (95% CI, 2.44–3.33) greater for women with weight gains at least 25 kg than for those with loss or gains of 2.0 kg or less. The weight change effect was stronger in younger women.

Fig. 2



Hazard ratio and 95% confidence interval of incident hypertension in relation to the BMI change among women, stratified by menopause status during BMI change period. Model 1, adjusted for age, BMI, SBP and DBP at baseline; Model 2, adjusted for covariates in model 1 as well as occupation, smoking, alcohol consumption and regular exercise at baseline. Model 3, adjusted for covariates in model 2 as well as levels of low-density lipoprotein cholesterol and triglyceride at baseline. Values in parenthesis are number of patients of hypertension/number of patients in the categories. CI, confidence interval; HR, hazard ratio.

The above studies evaluated changes in weight and in BP over a long period. No information is available regarding the impact of short-term BMI change on long-term effect of BP. In our study, weight loss did not have appreciably benefit because the extent of weight loss was mild. Only 4.8% of women lost more than 5 kg. The potential benefit of major BMI reduction for women in our population cannot be fully excluded.

The present study showed that women with BMI gain of more than 1.1 kg/m^2 did not increase the risk for hypertension unless menopause status was included for adjustment. The univariate analyses showed that the postmenopausal women were less likely to have weight gain than premenopausal women (P for trend $= 0.048$) but tended to develop hypertension in the following years (37.1 versus 29.3%, $P = 0.019$; data not shown). The interrelationships between BMI, menopause and BP are debatable because body weight and BP usually change simultaneously as menopause occurs. In the Study on Hypertension Prevalence in Menopause in the Italian population (SIMONA) Study [20], BP in women has significant association with menopause independent of age and BMI. In contrast, two population studies [21,22] found that high BP associated with menopause was largely explained by BMI and age. In our study, menopause status negatively confounded the association between BMI change and hypertension. Both menopause status and BMI change may independently explain the variation in hypertension occurrence. Moreover, the relationship between BMI change and the future hypertension development was significant only in nonmenopausal women during the BMI change period. This finding suggests that the effects of other risk factors may dominate the BMI change on hypertension in postmenopausal women. Insulin resistance, cardiac output increase, blood viscosity increase, the sympathetic over activity and the increase in intravascular volume, all are associated with the elevation in BP [23–27].

Some limitations merit consideration in this study. First, this study did not distinguish people with involuntary weight loss due to illness such as cancer [28]. However, further multivariate analyses excluding people with cancer at baseline survey made no difference in our findings. In addition, people who had serious illnesses and were not able to present at the clinic themselves for a health checkup were excluded at the enrolment of this cohort. Second, information on menstrual cycle or estrogen level was not available in this study to address the estrogen role in the sex disparity. High estrogen concentration has been associated with obesity and insulin resistance [29]. Few women underwent hormone therapy in Taiwan. Additional regression analyses adjusting for menopause status through follow-up period did not alter the observed association.

Conclusion

Short-term substantial BMI gain increases the long-term risk for developing hypertension in middle-aged and older Chinese men and women. The long-term effect is weaker for women than for men. Monitoring weight changes over a 2-year interval is helpful in primary prevention of hypertension in a general population. The role of menopause is important in evaluating the weight change impact on hypertension among women.

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