Original Article

Prevalence and Determinants of Prehypertension in a Japanese General Population: The Jichi Medical School Cohort Study

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It has been reported that subjects with prehypertension (pre-HT) (systolic blood pressure [SBP] 120–139 mmHg and/or diastolic blood pressure [DBP] 80–89 mmHg) have an increased risk of cardiovascular disease (CVD). We evaluated the prevalence and determinants of pre-HT in a Japanese general population. We enrolled 4,706 males and 7,342 females aged 18 to 90 years whose BPs were measured at baseline. The subjects' BPs were classified as follows: normotension (NT: SPB/DBP<120/80 mmHg), pre-HT (120/80–139/89 mmHg), and hypertension (HT: ≥140/90 mmHg or treated hypertension). The prevalence of pre-HT was 34.8% (males), and 31.8% (females). Body mass index (BMI) of more than 23.0 kg/m^2 was the strongest determinant of pre-HT (Males—BMI: 23.0–24.9 kg/m^2, odds ratio [OR]=1.47, 95% confidence interval [CI]=1.21–1.79; BMI: 25.0–26.9 kg/m^2, OR=2.20, 95% CI=1.68–2.87; BMI: 27.0–29.9 kg/m^2, OR=2.75, 95% CI=1.80–4.19; BMI: ≥30.0 kg/m^2, OR=3.39, 95% CI=1.21–9.46. Females—BMI: 23.0–24.9 kg/m^2, OR=1.67, 95% CI=1.42–1.95; BMI: 25.0–26.9 kg/m^2, OR=1.79, 95% CI=1.46–2.19; BMI: 27.0–29.9 kg/m^2, OR=3.65, 95% CI=2.73–4.89; BMI: ≥30.0 kg/m^2, OR=4.23, 95% CI=2.33–7.70). The other determinants of pre-HT were hyperlipidemia (Males: OR=1.25; Females: OR=1.43), and aging (by 10 years; Males: OR=1.12; Females: OR=1.48). Determinants of pre-HT in females were impaired glucose tolerance (OR=1.41, 95% CI=1.03–1.94), diabetes (OR=2.01, 95% CI=1.16–3.47) and a family history of HT in both parents (OR=1.90, 95% CI=1.38–2.62), whereas in males the only other predictor was alcohol drinking (OR=1.45, 95% CI=1.23–1.70). In conclusion, even subjects with a mild increase of BMI (23.0–24.9 kg/m^2) had an increased risk of pre-HT in a Japanese population, and the level of BMI associated with pre-HT was lower than that in Western countries. Additionally, there were gender differences in the determinants of pre-HT. (*Hypertens Res* 2008; 31: 1323–1330)

***Key Words*: prehypertension, Japanese, obesity, diabetes, cross-sectional study**

Introduction

Prehypertension (pre-HT) was defined as a systolic blood pressure (SBP) of 120–139 mmHg or a diastolic blood pressure (DBP) of 80–90 mmHg in the Seventh Report of the 2003 Joint National Committee (JNC 7) on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

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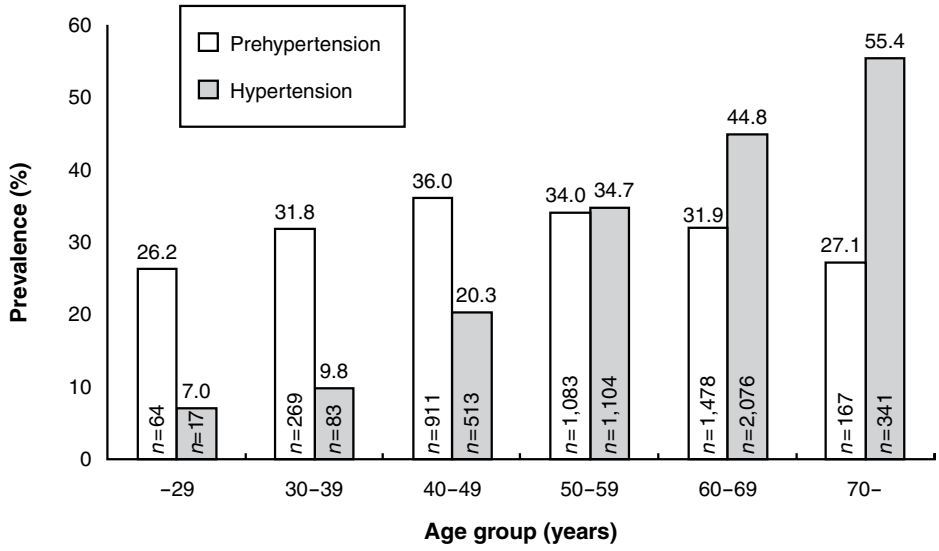

Fig. 1. *Prevalence of prehypertension and hypertension in different age groups.*

(*1*). The data from more than 1 million individuals indicated that death from ischemic heart disease and stroke increases progressively and linearly from BP levels as low as 115 mmHg in SBP and 75 mmHg in DBP (*2*), such that subjects with pre-HT have an increased risk for cardiovascular events in comparison with those with normotension (NT). Therefore, evaluation and modification of characteristics of subjects with pre-HT may help to prevent the evolution from pre-HT to hypertension (HT) and cardiovascular disease (CVD). The main determinants of pre-HT in the US and several Asian countries have been reported to be body mass index (BMI), diabetes mellitus, and hyperlipidemia, which together have been reported as risk profile for CVD (*3–6*), although there were some differences among the reports. In particular, BMI was the strongest determinant of pre-HT, but the definition of obesity is different between Japanese (BMI>25 kg/m^2) and Western people (BMI>30 kg/m^2) (*7*). Therefore, the magnitude of BMI associated with pre-HT in Japanese populations may be different from that of Western populations.

The purpose of this study was to clarify the prevalence and determinants of pre-HT in the Japanese general population.

Methods

Subjects

We used the baseline data of the Jichi Medical School (JMS) Cohort Study, a population-based prospective cohort study designed to quantify risk factors for CVD. The baseline data were obtained between April 1992 and July 1995 in 12 rural areas in Japan. Mass screening for CVD has been conducted in Japan since 1983 in accordance with the health and medical service law for the aged, and we used this system to collect the data for this study. The number of the subjects whose BP was measured for the present study was 12,048 (4,706 males and 7,342 females). Details of the JMS Cohort Study design and some descriptive data have been published previously (*8*). The Institutional Review Board of Jichi Medical University School of Medicine approved this study, and written informed consent was obtained from all subjects.

Variables

Health check-ups were carried out in each community. Body height was measured with the subjects in stockinged feet. Body weight was recorded with the subjects clothed, and 0.5 kg in summer and 1.0 kg in other seasons was subtracted from the recorded weight. BMI was calculated as weight (kg)/height (m)^2. BMI was categorized as <23.0 kg/m^2, 23.0–24.9 kg/m^2, 25.0–26.9 kg/m^2, 27.0–29.9 kg/m^2 and ≥30.0 kg/m^2. We used subjects whose BMI was less than 23.0 kg/m^2 as a reference when we performed multivariable logistic regression, because the World Health Organization (WHO) has recommended that the optimum BMI should be 18.5–23.0 kg/m^2 in Asian populations (*7*). In addition, we defined the subjects with a BMI of 23.0–24.9 kg/m^2 as overweight, and those with BMI of 25.0 kg/m^2 or greater as obese, following the recommendations of the WHO, the International Association for the Study of Obesity and the International Obesity Task Force (*9*). Blood pressures were measured using a fully automated device, BP203RV-II (Nippon Colin, Komaki, Japan), placed on the right arm of the subject after a seated 5-min rest. The subjects were classified as NT (SPB/DBP<120/80 mmHg), pre-HT (SBP 120–139 mmHg, and/or DBP 80–89 mmHg), and HT (SPB/DPB≥140/90 mmHg or medicated for HT). Total cholesterol levels were measured by an enzymatic method (Wako, Osaka, Japan; interassay coefficient of variation [CV]: 1.5% for total cholesterol and 1.7%). High-density

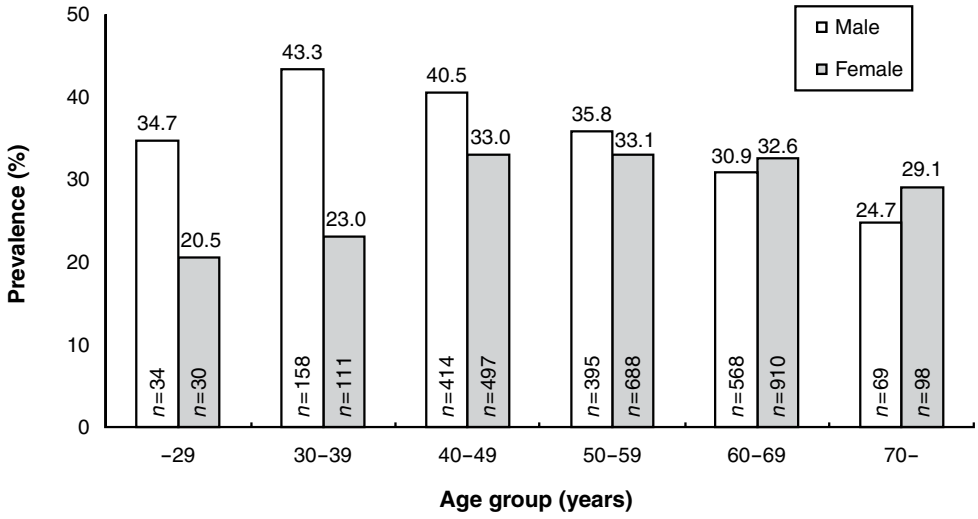

Fig. 2. *Prevalence of prehypertension in different sex and age groups.*

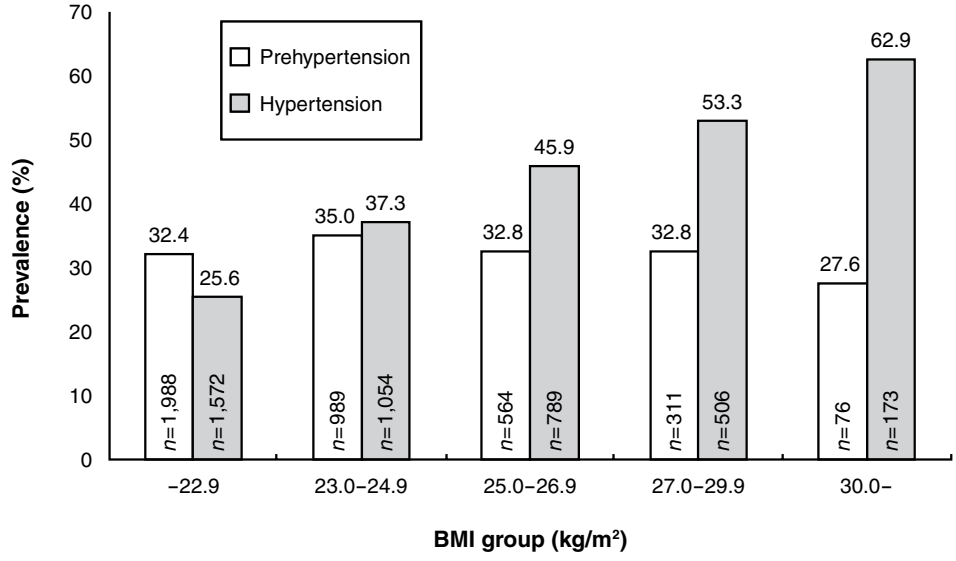

Fig. 3. *Prevalence of prehypertension and hypertension in BMI groups.*

lipoprotein (HDL) cholesterol was measured using the phosphotung state precipitation method (Wako; interassay CV: 1.9%). We defined hyperlipidemia as total cholesterol of ≥220 mg/dL or being medicated for hyperlipidemia. Blood glucose was measured using the enzymatic method (Kanto Chemistry, Tokyo, Japan; interassay CV: 1.9%). Diabetes mellitus was considered to be present when fasting blood glucose was more than 126 mg/dL or postprandial glucose was more than 200 mg/dL, or when subjects were being medicated for diabetes, and impaired glucose tolerance (IGT) was considered to be present when fasting blood glucose ranged from 110 to 125 mg/dL or postprandial glucose ranged from 140 to 199 mg/dL.

Information about medical history, family history and sociodemographic characteristics were obtained by trained interviewers using a standardized questionnaire. Smoking status was classified as current smoker or non-smoker. Alcohol drinking status was classified as drinking alcohol more or less than 20 g/d for 4 d in 1 week.

Statistical Analysis

Values are expressed as the mean±SD or a percentage. Differences in mean values among the NT, pre-HT and HT groups were calculated using ANOVA. Intergroup differences were calculated using Tukey's honestly significant test.

Table 1. Characteristics of the Subjects by Classification of Blood Pressure Level

	NT (n=3,942)	Pre-HT (n=3,972)	HT (n=4,134)	p
Male				
Number (%)	1,334 (28.3)	1,638 (34.8)	1,734 (36.8)	
Age, years	52.2±12.6	53.7±11.7**	59.1±10.3***	<0.001
Body mass index, kg/m^2	22.0±2.5	23.0±2.8**	23.8±3.0**	<0.001
Glucose, mg/dL	101.2±29.9	105.2±28.5**	110.6±34.7***	<0.001
Total cholesterol, mg/dL	180.3±33.0	185.6±34.0***	187.4±34.6***	<0.001
HDL cholesterol, mg/dL	48.7±12.9	48.5±13.4	49.1±13.7	0.419
Family history of HT, %	24.8	27.9	35.0	<0.001
Alcohol drinkers, %	42.5	49.5	54.6	<0.001
Current smokers, %	57.2	51.1	44.4	<0.001
Diabetes				
IGT, %	5.6	7.9	12.1	<0.001
Diabetes, %	3.6	4.2	7.1	<0.001
Hyperlipidemia, %	27.0	35.5	39.8	<0.001
Famale				
Number (%)	2,608 (35.5)	2,334 (31.8)	2,400 (32.7)	
Age, years	50.5±11.8	55.9±10.5***	60.1±8.7***	<0.001
Body mass index, kg/m^2	22.1±2.7	23.3±3.1***	24.3±3.4***	<0.001
Glucose, mg/dL	95.8±18.6	102.0±21.6***	105.7±26.3***	<0.001
Total cholesterol, mg/dL	187.1±34.0	198.1±34.2***	206.7±33.5***	<0.001
HDL cholesterol, mg/dL	53.9±12.4	52.5±12.5**	51.5±12.6***	<0.001
Family history of HT, %	26.7	26.5	62.1	<0.001
Alcohol drinkers, %	3.2	2.4	2.8	<0.001
Current smokers, %	8.1	4.3	3.8	0.207
Diabetes				
IGT, %	3.3	5.5	8.4	<0.001
Diabetes, %	1.0	2.4	4.7	<0.001
Hyperlipidemia, %	23.6	37.2	48.7	<0.001

Data were shown as mean±SD or %. NT, normotension; pre-HT, prehypertension; HT, hypertension; HDL, high-density lipoproteine; IGT, impaired glucose tolerance. Comparison between the subjects who were defined in NT, pre-HT and HT were calculated by ANOVA or χ^2 test. Intergroup differences were calculated by Tukey's honestly significant test. Probability <0.05 was considered significant. **p<0.01, ***p<0.001.

Differences in percentages among these groups were calculated using a χ^2 test and p<0.05 was considered significant. Odds ratios (OR) and 95% confidence intervals (CI) were calculated by multivariable logistic regression to evaluate determinants of pre-HT and HT. Statistical analysis was performed using the computer software package SPSS ver.11.0 (SPSS Inc., Chicago, USA).

Results

There were 4,706 males and 7,342 females in the present study. The mean ages were 55.3±11.5 years (55.3±11.9 years in males, 55.4±11.2 in females). In the total subjects, the prevalence of NT was 32.7%, that of pre-HT was 33.0% (34.8% in males and 31.8% in females), and that of HT was 34.3% (36.8% in males and 32.7% in females). The prevalence of pre-HT and HT in different age groups is shown in Fig. 1. The prevalence of pre-HT increased up to the age of 40 and then decreased, while the prevalence of HT increased progressively with age. The prevalence of pre-HT in different age groups in both males and females is shown in Fig. 2. In males, the prevalence of pre-HT increased up to the age of 30 and then decreased, while in females the prevalence of pre-HT increased up to the age of 40 and then stabilized. The prevalence of pre-HT and HT in BMI groups is shown in Fig. 3. The prevalence of pre-HT increased up to a BMI of 25.0 kg/m^2 and then decreased, while the prevalence of HT increased progressively with increased BMI.

Characteristics of subjects who were classified by hypertension groups (*i.e.*, NT, pre-HT, and HT) and sex are shown in Table 1. In subjects with pre-HT, the age, glucose, and total cholesterol levels were significantly higher than those in the NT group in both males and females. And the percentages of subjects with a positive family history of HT, IGT, diabetes, hyperlipidemia, and habitual alcohol drinking in the subjects with pre-HT were significantly higher than in those with NT

Table 2. Odds Ratios of Pre-HT *vs*. NT by Sex

Variables	Male			Female		
	OR	95% CI	*p*	OR	95% CI	*p*
Age, 10 years	1.12	1.05–1.20	0.001	1.48	1.39–1.57	<0.001
Body mass index, kg/m^2						
<22.9	1.00			1.00		
23.0–24.9	1.47	1.21–1.79	<0.001	1.67	1.42–1.95	<0.001
25.0–26.9	2.20	1.68–2.87	<0.001	1.79	1.46–2.19	<0.001
27.0–29.9	2.75	1.80–4.19	<0.001	3.65	2.73–4.89	<0.001
30.0–	3.39	1.21–9.46	0.020	4.23	2.33–7.70	<0.001
Family history of HT						
None	1.00			1.00		
Father or mother	1.09	0.89–1.32	0.406	1.12	0.95–1.31	0.168
Both	1.46	0.99–2.16	0.058	1.90	1.38–2.62	<0.001
Alcohol drinkers	1.45	1.23–1.70	<0.001	1.02	0.68–1.51	0.932
Current smorkers	0.82	0.69–0.96	0.016	0.67	0.50–0.88	0.005
Status of dysglycemia						
None	1.00			1.00		
IGT	1.26	0.91–1.73	0.162	1.41	1.03–1.94	0.034
Diabetes	1.22	0.80–1.85	0.363	2.01	1.16–3.47	0.012
Hyperlipidemia	1.25	0.99–1.57	0.058	1.43	1.22–1.67	<0.001

NT, normotension; pre-HT, prehypertension; HT, hypertension; IGT, impaired glucose tolerance. Odds ratio (OR), 95% confidence interval (CI), and *p* values were calculated using multiple regression analysis (*vs*. the subjects with normontension) after adjustment for age, classification of body mass index, family history, alcohol drinkers, current smokers, status of disglycemia and hyperlipidemia.

in both males and females. The HDL cholesterol level in pre-HT subjects was lower than that in NT subjects only in females. The percentage of habitual smoking in pre-HT subjects was lower than that in NT only in males. The differences of variables between HT and NT subjects were more significant than those between pre-HT and NT subjects.

Determinants of pre-HT (*vs*. NT) in males and females in multivariable logistic regression analysis are shown in Table 2. Overweight and obesity were the most significant determinants of pre-HT even at the level of more than 23.0 kg/m^2 in both males and females. The other determinants of pre-HT in both males and females were hyperlipidemia and age. The only other determinant in males was alcohol drinking, whereas in females IGT, diabetes, and a family history of HT in both parents were also determinants.

Additionally, when we analyzed determinants of pre-HT by dividing females into two groups, *i.e.*, above or below the age of 50 years, determinants of pre-HT in the older females were BMI≥23.0 kg/m^2 (BMI: 23.0–24.9 kg/m^2, OR=1.76; BMI: 25.0–26.9 kg/m^2, OR=1.73; BMI: 27.0–29.9 kg/m^2, OR=2.75; BMI: ≥30.0 kg/m^2, OR=4.08), hyperlipidemia (OR=1.50), aging (by 10 years, OR=1.53), IGT (OR=1.51), and diabetes (OR=1.83), while in the younger females the determinants were BMI≥23.0 kg/m^2 (BMI: 23.0–24.9 kg/m^2, OR=1.46; BMI: 25.0–26.9 kg/m^2, OR=1.96; BMI: 27.0–29.9 kg/m^2, OR=6.11; BMI: ≥30.0 kg/m^2, OR=4.55), aging (by 10 years, OR=1.83) and a family history of HT in both parents (OR=2.26).

Determinants of HT (*vs*. NT) in males and females are shown in Table 3. Overweight and obesity were the strongest determinants of HT in comparison with NT. Other determinants of HT were hyperlipidemia, age, a family history of HT in one parent, a family history of HT in both parents, IGT, and diabetes. Alcohol drinking was a determinant of HT only in males. Smoking was a negative determinant of HT in both males and females.

As the definition of obesity in Japanese subjects is different from that in Western countries, we analyzed the prevalence and determinants of pre-HT and HT using the two definitions of obesity level (*i.e.*, BMI≥25 kg/m^2 and BMI≥30 kg/m^2). The percentage of obesity in subjects with pre-HT was 24.1% when obesity was defined as BMI≥25 kg/m^2, and 1.8% when it was defined as BMI≥30 kg/m^2. The percentage of obesity in subjects with HT was 35.7% when obesity was defined as BMI≥25 kg/m^2, and 4.2% when it was defined as BMI≥30 kg/m^2. Additionally, we analyzed risks related to obesity for pre-HT and HT using logistic regression models after adjustment for age and sex, and the OR of pre-HT were 2.12 (95% CI=1.87–2.40) in subjects with BMI≥25 kg/m^2 and 2.95 (95% CI=1.84–4.73) in those with BMI≥30 kg/m^2. The OR of HT were 3.98 (95% CI=3.52–4.52) in subjects with BMI≥25 kg/m^2 and 8.27 (95% CI=5.30–12.90) in those with BMI≥30 kg/m^2 after adjustment for age and sex.

Table 3. Odds Ratios of HT *vs*. NT by Sex

Variables	Male			Female		
	OR	95% CI	*p*	OR	95% CI	*p*
Age, 10 years	1.84	1.70–2.00	<0.001	2.43	2.25–2.63	<0.001
Body mass index, kg/m^2						
<22.9	1.00			1.00		
23.0–24.9	2.15	1.74–2.66	<0.001	2.34	1.97–2.79	<0.001
25.0–26.9	4.23	3.19–5.60	<0.001	3.30	2.68–4.07	<0.001
27.0–29.9	7.44	4.86–11.40	<0.001	7.15	5.29–9.66	<0.001
30.0–	13.05	4.91–34.70	<0.001	13.14	7.26–23.80	<0.001
Family history of HT						
None	1.00			1.00		
Father or mother	1.50	1.21–1.85	<0.001	1.82	1.53–2.16	<0.001
Both	2.46	1.67–3.62	<0.001	3.75	2.67–5.28	<0.001
Alcohol drinkers	2.03	1.70–2.43	<0.001	1.43	0.92–2.21	0.111
Current smorkers	0.75	0.63–0.90	0.002	0.66	0.47–0.92	0.015
Status of dysglycemia						
None	1.00			1.00		
IGT	1.79	1.31–2.46	<0.001	2.05	1.49–2.83	<0.001
Diabetes	2.06	1.37–3.10	<0.001	3.37	2.00–5.70	<0.001
Hyperlipidemia	1.34	1.05–1.71	0.018	1.80	1.53–2.12	<0.001

NT, normotension; HT, hypertension; IGT, impaired glucose tolerance. Odds ratio (OR), 95% confidence interval (CI), and *p* values were calculated using multiple regression analysis (*vs*. the subjects with normontension) after adjustment for age, classification of body mass index, family history, alcohol drinkers, current smokers, status of disglycemia and hyperlipidemia.

Discussion

We have presented the prevalence and the determinants of pre-HT as defined by JNC 7 in a Japanese population (*3*, *4*, *6*). There have been few studies of pre-HT in Japanese subjects (*10*). In the present study, the prevalence of pre-HT was 34.3%, which indicated that pre-HT was very common in Japan just as in other countries. The prevalence of pre-HT in the US (from the National Health and Nutrition Examination Survey: NHANES 1999–2000), Korea, and Taiwan were reported as 31.0%, 31.6% and 34%, respectively. Our findings of the prevalence of pre-HT in Japan are thus consistent with other countries. In the present study, the main determinants of pre-HT in both males and females were increasing BMI, age, and hyperlipidemia, of which the most powerful determinant was BMI. Even being slightly overweight was positively associated with pre-HT, and obesity had an even stronger association. Alcohol drinking was important only in males, while in females diabetes and a family history of HT were determinants. Thus the determinants of pre-HT were mostly the traditional CVD risk factors, although smoking was a negative determinant, presumably because of its association with a lower BMI.

There are several notable points in our findings. The first is that the main determinants of pre-HT were metabolic factors that are risk factors for CVD. It has been reported in both Western and Asian countries that the main determinants of pre-HT are increasing BMI, aging, hyperlipidemia, and dysglycemia (*3*–*6*). A longitudinal study from the Strong Heart Study reported that pre-HT subjects had a 3.2 times higher risk of developing HT and 1.7 times higher risk for incidence of CVD than NT subjects (*11*). However, the 1992 NHANES II Mortality Study in the US with a 12-year follow-up reported that pre-HT was not independently associated with increased CVD mortality (*12*). In a Japanese study of subjects who underwent coronary angiography for suspected CVD, those with pre-HT had an increased risk of coronary atherosclerosis compared to the NT subjects, even after adjusting for other risk factors (*13*). As there are few population-based studies about pre-HT in Japanese populations, our study may provide important information for the management of pre-HT for preventing the development of HT and CVD in the Japanese general population.

The second point is that we determined the BMI threshold level that was associated with an increased risk of pre-HT in the Japanese population, and this BMI level was lower than that of the Western population. The prevalence of pre-HT in subjects whose BMI was ≥25 kg/m^2 and ≥30 kg/m^2 in the present study was lower than that in NHANES (24.1% and 1.8% *vs*. 63.9% and 31.6%, respectively) (*3*). After adjustment for age and sex, the relationship between obesity and pre-HT is somewhat steeper for the Japanese population (OR=2.12 for subjects with BMI≥25 kg/m^2; OR=2.95 for subjects with BMI≥30 kg/m^2) than for the U.S. population (OR=1.46 for subjects with BMI≥25 kg/m^2; OR=2.26 for

subjects with BMI≥30 kg/m^2). These findings indicate that the risk of pre-HT in Japanese subjects with a BMI≥25 kg/m^2 is similar to the risk in Americans with a BMI≥30 kg/m^2. Thus the BMI level which is associated with an increased risk of pre-HT in the Japanese population may be shifted lower by 5 kg/m^2 compared with that of the Western population.

The third point is that several sex-related differences were apparent in our findings. There was an age-specific difference in the impact of dysglycemia only in females. Dysglycemia was a determinant of pre-HT in older females, but not in young females. There was no age-specific difference in this impact in males. This finding may have been at least partly related to a decrease of estrogen production after menopause (*14*, *15*). In addition, endothelial dysfunction, oxidative stress, and activation of the renin-angiotensin system and sympathetic activity may all play a role in increasing diabetes and HT after menopause (*16*, *17*).

There was also a sex difference in the effects of alcohol drinking on the risk of pre-HT and HT, which was seen only in males. There have been few reports about the effects of alcohol on blood pressure in females in Japan (*18*). In a study about the relationships between alcohol drinking and HT in females in the UK, moderate alcohol consumption was associated with an increased risk of HT but lower amounts did not appear to increase the risk (*19*). Alcohol consumption is much less frequent in Japanese females than males, which may be one reason why alcohol drinking was not a risk factor for pre-HT and HT in females in the present study. The other sex difference of the determinants of pre-HT was a family history of HT in both parents, which was a determinant of pre-HT only in females. A family history of HT in one or both parents was a determinant of HT, which again was more apparent in females than in males. As expected, having two hypertensive parents was a stronger determinant of HT than just having one (especially in females). It is well-known that a family history of HT is a major risk factor for HT, but few studies have reported sex-related differences in the impact of family history (*20*). Hahn *et al*. reported that parental history was related to higher BP in females, but not in males, while Goldstein *et al*. reported that elevated SBP and DBP measured by ambulatory monitoring was related to a family history of HT in both parents in males, but there was no association in females (*21*, *22*). It has also been reported that females tend to have a better knowledge of their own and their family's health status than males (*23*). Our findings indicate that females with a family history of HT were more likely to have high BP than males with a family history of HT.

In addition, the Japanese Society of Hypertension Guidelines for the Management of Hypertension 2004 (JSH 2004) employ the concept of high-normal pressure, which they define as ranging from 130–139/85–89 mmHg, and which indicates the need for primary prevention of HT (*24*). In the present work, the prevalence of high-normal pressure was 15.9% (17.2% in males, 15.1% in females). The determinants of high-normal BP *vs*. optimal BP were similar to those of pre-HT *vs*. NT, and the relation between the former was stronger.

In conclusion, the risk factors of pre-HT in the present study included metabolic factors as well as the well-known risk factors for CVD. Increasing BMI was the most significant determinant of pre-HT, and even subjects with a BMI of 23.0–24.9 kg/m^2 had an increased risk of pre-HT in our Japanese population. The BMI level which was associated with an increased risk of pre-HT was almost 5 kg/m^2 lower than that of Western populations. Furthermore, we demonstrated that there were sex-related differences in the determinants of pre-HT. Drinking alcohol was more important in males, while dysglycemia and a family history of HT were more important in females. Our findings may be relevant for preventing the development of HT and CVD in the Japanese population

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