Original Article

Blood Pressure Categories and Cardiovascular Risk Factors in Japan: The Jichi Medical School (JMS) Cohort Study

Shizukiyo ISHIKAWA[1], Yoshihiro SHIBANO[2], Yasuhiro ASAI[1], Kazuomi KARIO[3], Kazunori KAYABA[4], and Eiji KAJII[1]

Few studies have reported on risk factors by blood pressure categories based on antihypertensive treatment in the general population. We examined the associations between blood pressure categories and other risk factors in Japan. Cross-sectional study, multicenter population-based study was designed. A total of 11,302 men and women were eligible. Data were obtained from April 1992 to July 1995 in 12 rural districts in Japan. Subjects were divided into three categories: normotensives (with blood pressure <140/90 mmHg), treated hypertensives (antihypertensive treatment regardless of current blood pressure), and nontreated hypertensives (blood pressure ≥140/90 mmHg without hypertensive treatment). The proportions of normotensives, treated hypertensives, and nontreated hypertensives were 63%, 10%, and 27% among men, and 67%, 13%, and 20% among women, respectively. Total cholesterol, triglyceride, blood glucose, and body mass index were higher in treated or nontreated hypertensives than in normotensives. Fibrinogen, factor VIIc, and physical activity index were higher in treated hypertensives than in normotensives. High-density lipoprotein (HDL) cholesterol was higher in normotensives than in treated or nontreated hypertensives in women; but no tendency was shown in men. The proportions of dyslipidemia, impaired glucose tolerance, and metabolic syndrome were significantly higher in treated and nontreated hypertensives than in normotensive men and women. In conclusion, cardiovascular risk factors were higher in hypertensives with or without treatment than in normotensives in a general population in Japan. (*Hypertens Res* 2007; 30: 643–649)

Key Words: **hypertension, risk factors, Japanese, population, blood pressure category**

Introduction

Hypertension is an important condition affecting overall health, and the prevalence of hypertension is highest in Japan as well as other countries (*1–4*). Chronic high blood pressure (BP) increases the incidence of cardiovascular diseases (CVD) such as stroke, myocardial infarction (*5–10*), and mortality (*11*). Many studies, including randomized controlled trials, have shown that antihypertensive treatment reduces the risk of CVD. However, BP control among hypertensive patients is often insufficient, and a considerable proportion of treated hypertensive patients have not achieved target BP (*4*, *12–16*).

From the [1]Division of Community and Family Medicine, Center for Community Medicine and [3]Division of Cardiology, Jichi Medical University School of Medicine, Shimotsuke, Japan; [2]Saiseikai Iwaizumi Hospital, Iwate, Japan; and [4]School of Health and Social Services, Saitama Prefectural University, Saitama, Japan.

This study was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan; and grants from the Foundation for the Development of the Community, Tochigi, Japan.

Address for Reprints: Shizukiyo Ishikawa, M.D., Division of Community and Family Medicine, Center for Community Medicine, Jichi Medical University School of Medicine, Shimotsuke 329–0498, Japan. E-mail: i-shizu@jichi.ac.jp

Received September 6, 2006; Accepted in revised form March 15, 2007.

Table 1. General Characteristics of the JMS Cohort Study

	Men			Women		
	n	Mean	SD	*n*	Mean	SD
Age (years)	4,415	55.2	12.0	6,887	55.3	11.3
Systolic blood pressure (mmHg)	4,115	131.4	20.6	6,887	128.1	21.2
Diastolic blood pressure (mmHg)	4,115	79.2	12.3	6,887	76.3	12.2
Total cholesterol (mg/dL)	4,383	184.9	34.2	6,847	196.9	34.7
HDL-cholesterol (mg/dL)	4,384	48.9	13.4	6,847	52.7	12.5
Triglycerides (mg/dL)[§]	4,383	108.2	(62.7–186.8)	6,846	95.1	(57.5–157.2)
Lipoprotein(a) (mg/dL)[§]	3,801	12.4	(4.5–33.8)	6,118	14.6	(5.7–37.3)
Fibrinogen (mg/dL)	2,508	243.0	57.3	4,098	249.8	55.6
Factor VIIc (mg/dL)	2,243	108.8	19.8	3,337	114.8	21.3
Blood glucose (mg/dL)	4,384	105.5	30.9	6,836	100.6	22.5
Body mass index (kg/m^2)	4,370	23.0	2.9	6,816	23.2	3.2
Physical activity index	4,372	35.6	9.5	6,811	31.6	5.4

[§]Geometric mean (±SD). HDL, high-density lipoprotein.

Nevertheless, few studies have examined risk factors based on BP categories with or without hypertensive treatment. Here we examined the association between BP categories and cardiovascular risk factors in a population-based study in Japan.

Methods

Subjects

There were 11,302 subjects in the present study (4,415 men and 6,887 women) for whom information on BP. Data were obtained between April 1992 and July 1995 in 12 districts in rural areas of Japan as part of the Jichi Medical School (JMS) Cohort Study. Details of that project, which was a population-based prospective cohort study aiming to clarify the risk factors of CVD, were reported elsewhere (*17*, *18*).

The normotensives were defined as subjects with systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg, treated hypertensives were defined as subjects with antihypertensive treatment regardless of current BP, and nontreated hypertensives were defined as subjects with SBP ≥140 mmHg and/or DBP ≥90 mmHg without antihypertensive treatment. Dyslipidemia was defined as total cholesterol ≥220 mg/dL and/or triglyceride ≥150 mg/dL, and impaired glucose tolerance (IGT) was defined as fasting blood glucose (with no caloric intake for at least 3 h) of ≥110 mg/dL, or as casual blood glucose (for less than 3 h or without regard to time since last meal) of 140 mg/dL.

The diagnostic criteria of metabolic syndrome (MS) were decided in Japan in 2005. Although we used these criteria, waist circumference was not measured in most of the subjects, so instead we regard body mass index (BMI) ≥25 kg/m^2 as obesity according to the Japanese criteria of obesity. MS was defined by the following criteria: obesity (BMI ≥25 kg/m^2) as an essential component combined with two or more of the following components: triglycerides ≥150 mg/dL and/or high-densiy lipoprotein (HDL) cholesterol <40 mg/dL; SBP ≥130 mmHg and/or DBP ≥85 mmHg; fasting blood glucose ≥110 mg/dL or casual blood glucose ≥140 mg/dL.

The SBP and DBP were measured with a fully automated sphygmomanometer, BP203RV-II (Nippon Colin, Komaki, Japan) placed on the right arm of a seated subject who had rested in the sitting position for 5 min before the measurement. BMI was calculated as weight (kg)/height (m)^2.

Information about medical history and lifestyle was obtained by a questionnaire. Using the Framingham Study questionnaire, physical activity index (PAI) for a normal working day was estimated by calculating the weighted sum of hours spent at five levels: 1.0 for sedation including sleeping, 1.1 for quiet working such as that in a sitting position, 1.5 for a light level of working such as that in a standing position, 2.5 for a moderate level of working, and 5.0 for heavy work (*19*).

Total cholesterol and triglyceride were measured by an enzymatic method (Wako, Osaka, Japan; interassay coefficient of variation [CV]: 1.5% for total cholesterol and 1.7% for triglyceride). HDL cholesterol was measured using the phosphotungstate precipitation method (Wako; interassay CV: 1.9%). Blood glucose was measured *via* an enzymatic method (Kanto Chemistry, Tokyo, Japan; interassay CV: 1.9%).

Lipoprotein(a) (Lp(a)) levels were measured using an enzyme-linked immunosorbent assay (ELIZA) kit (Biopool, Uppsala, Sweden; interassay CV: 3.51%). The minimum detectable Lp(a) level was 1 mg/dL, and undetectable Lp(a) values were recorded as 0.5 mg/dL. Fibrinogen levels were determined with a one-stage clotting assay kit (Data-Fi, Dade Behring, Miami, USA; interassay CV: 2.5%). Factor VII activity was measured with a chromogenic assay using a human placenta–derived calcified thromboplastine reagent (Chromoquick, Behringwerke, Marburg, Germany), human factor VII–deficient plasma (Behringwerke), and a chro-

Table 2. Number of Blood Pressure Categories by Sex

	Normotensives (*n* (%))	Hypertensives (*n* (%))		Total (*n*)
		Treated	Nontreated	
Men	2,774 (62.8)	450 (10.2)	1,191 (27.0)	4,415
Women	4,620 (67.1)	860 (12.5)	1,407 (20.4)	6,887
Total	7,394 (65.4)	1,310 (11.6)	2,598 (23.0)	11,302

Normotensives: normal blood pressre without treatment. Treated hypertenives: subjects with treatment if any blood pressure. Nontreated hypertensives: hypertension without treatment.

mogenic assay autoanalyzer (Behringwerke; interassay CV: 3.8%).

We examined the association between BP categories and other risk factors in Japan.

Statistical Analysis

Analysis of variance (ANOVA) was used to calculate variance among BP categories, and mean values of lipids, fibrinogen, factor VIIc, BMI, and PAI were shown after age adjustment in each sex. Scheffe's test was used in comparison with the values of variables. The χ^2 test was used for BP categories and other categories such as lipid status, blood glucose status, MS, smoking status, and drinking status, and the Mantel-Haenszel test was used for adjustment for age. These analyses were done using SAS software version 8.2 (SAS Institute, Cary, USA).

Results

The general characteristics of the subjects are shown in Table 1. The mean ages were 55.2 years in men and 55.3 years in women. SBP and DBP were higher in men (131.4 mmHg and 79.2 mmHg) than in women (128.1 mmHg and 76.3 mmHg).

The proportions of the normotensives, treated hypertensives, and nontreated hypertensives were 62.8%, 10.2%, and 27.0% in men, and 67.1%, 12.5%, and 20.4% in women, respectively (Table 2).

Age-adjusted mean values of risk factors categorized by BP status were calculated using ANOVA. In both men and women, total cholesterol was lower in normotensives and higher in nontreated hypertensives, whereas triglyceride was lower in normotensives than in treated or nontreated hypertensives. Blood glucose, factor VIIc, and BMI were lower in normotensives than in treated or nontreated hypertensives in both men and women. As for HDL cholesterol, the mean value was higher in normotensives than in treated or nontreated hypertensives in women, but there was no tendency shown in men (Table 3).

In men, according to Scheffe's test, triglyceride, blood glucose, factor VIIc, BMI, and PAI were significantly higher in treated hypertensives than in normotensives; and total cholesterol, triglyceride, blood glucose, and BMI were significantly higher in nontreated hypertensives than in normotensives. In women, total cholesterol, triglyceride, blood glucose, fibrinogen, factor VIIc, BMI, and PAI were significantly higher in treated hypertensives than in normotensives; and total cholesterol, triglyceride, blood glucose, Lp(a), fibrinogen, factor VIIc, and BMI were significantly higher in nontreated hypertensives than in normotensives (Table 3).

Associations of BP categories with lipid status, blood glucose status, MS, smoking status, and drinking status are shown in Table 4. The proportions of dyslipidemia, IGT, and MS were significantly higher in treated and nontreated hypertensives than in normotensives in men and women using both the χ^2 test and the Mantel-Haenszel test adjusted for age. The same tendency was seen for smoking in men and women. The proportion of drinkers was lower in normotensives than in the treated and nontreated hypertensives in men, whereas in women the proportion of drinkers was lower in hypertensives with treatment than in normotensives and nontreated hypertensives.

Discussion

The JMS Cohort Study (*17*, *18*), a population-based cardiovascular cohort study using a mass screening examination system, was started in 1992 in a Japanese population. The study subjects were drawn from 12 rural districts in Japan, and the overall response rate was 63%. We examined cardiovascular risk factors in relation to hypertension categories in the present study using baseline data from the JMS Cohort Study.

There may be some bias in this study, such as detection bias, in that a single BP measurement may not reflect actual hypertension, and measurement bias, in that there is not enough information about antihypertensive treatment. Single measurement of BP is substantially considered to underestimate the strength of the relationship between BP and CVD. Single measurement of cholesterol has substantially underestimated the strength of the relationship between cholesterol and the risk of coronary heart disease (*20*), and the same framework might be applicable to BP. Single measurement of BP for epidemiological studies may markedly overestimate the true prevalence of hypertension, and a diagnosis of hypertension is difficult (*21*). However, in many epidemiological studies, single measurement of BP was used to determine hypertension.

Table 3. Age-Adjusted Means of Risk Factors

	Normotensives		Hypertensives				$p^{\#}$
			Treated		Nontreated		
	Mean$	SEM	Mean$	SEM	Mean$	SEM	
Men							
Total cholesterol (mg/dL)	183.1	0.7	186.6	1.6	188.4	1.0†	<0.01
HDL-chotesterol (mg/dL)	48.7	0.3	48.6	0.6	49.4	0.4	0.32
Triglyceride (mg/dL)§	102.5	(101.5–103.6)	122.1	(119.0–125.3)*	117.1	(115.3–119.0)†	<0.01
Blood glucose (mg/dL)	102.8	0.6	109.8	1.5*	110.2	0.9†	<0.01
Lipoprotein(a) (mg/dL)§	12.9	(12.6–13.2)	11.5	(10.9–12.1)	11.5	(11.1–11.8)	<0.01
Fibrinogen (mg/dL)	244.3	1.4	240.2	3.4*	241.0	2.2	0.32
Factor VIIc (mg/dL)	107.9	0.5	111.4	1.4*	109.9	0.8	0.02
Body mass index (kg/m^2)	22.4	0.1	24.2	0.1*	23.8	0.1†	<0.01
Physical activity index	35.8	0.2	34.9	0.5*	35.4	0.3	0.09
Women							
Total cholesterol (mg/dL)	194.3	0.5	200.9	1.2*	203.1	0.9†	<0.01
HDL-chotesterol (mg/dL)	53.2	0.2	51.9	0.4*	51.5	0.3†	<0.01
Triglyceride (mg/dL)§	90.0	(89.4–90.7)	108.3	(106.5–110.1)*	105.2	(103.8–106.6)†,‡	<0.01
Blood glucose (mg/dL)	98.9	0.3	105.2	0.8*	103.3	0.6†,‡	<0.01
Lipoprotein(a) (mg/dL)§	14.7	(14.5–15.0)	13.3	(12.8–13.7)	14.9	(14.5–15.3)†	0.01
Fibrinogen (mg/dL)	248.4	1.0	256.1	2.3*	250.5	1.9†,‡	0.01
Factor VIIc (mg/dL)	113.7	0.5	117.1	1.0*	117.0	0.8†	<0.01
Body mass index (kg/m^2)	22.6	0.0	24.8	0.1*	23.9	0.1†,‡	<0.01
Physical activity index	31.7	0.1	30.9	0.2*	31.5	0.1	<0.01

$Mean and SEM were shown with adjustment for age using ANOVA. §Geometric mean (±SEM). #$p<0.05$, ANOVA adjusted for age. *$p<0.05$, normotensives *vs*. treated hypertensives; †$p<0.05$, normotensives *vs*. nontreated hypertensives, ‡$p<0.05$, treated hypertensives *vs*. nontreated hypertensives. *, † and ‡ using Scheffe's test.

Hypertension is an important condition affecting health in Japan as well as in Western countries; hypertension contributes to CVD, such as stroke, ischemic heart diseases, heart failure, and high mortality. In prospective cohorts for the populations, there was a five-fold difference in stroke risk between the highest and lowest of the six BP categories, but relative stroke risks were greater in middle age than in old age even though absolute stroke risks were higher in old age (*8*). In other cohorts for a population in East Asia, BP was an important determinant of stroke risk, whereas cholesterol concentration was less important. The authors concluded that the association between BP and stroke seems stronger in East Asia than in Western populations, and a population-wide reduction of 3 mmHg in DBP eventually decreased the number of strokes by about one-third (*22*).

In case-control studies for the incidence of stroke in hypertensive patients, higher levels of BP were related to the onset of stroke (*7*, *23*, *24*) and myocardial infarction (*6*), and a considerable proportion of the stroke incidence among treated hypertensive patients may be prevented by achieving BP control (*7*). Bulpitt *et al*. reported that the optimal level of BP control for survival was treated SBP of <134 mmHg in men and <149 mmHg in women, and treated DBP of <95 mmHg in men and women in a prospective cohort study in hypertensive patients (*11*).

Many intervention trials have proven that antihypertensive drugs will help reduce the incidence of CVD. In a meta-analysis, the effect of antihypertensive drugs was significant for stroke and CVD in men and women; and, in terms of relative risk, the treatment benefit did not differ between men and women (*25–27*). Meanwhile, arterial stiffness increased with age according to the severity of hypertension, after adjustment for BP (*28*).

Even if hypertensive patients receive antihypertensive treatment, such treatment seems less effective if it does not achieve the target BP, for example 140/90 mmHg. In the present study, actually, elevation in treated hypertensives was seen in some cardiovascular risk factors, such as total cholesterol, blood glucose, fibrinogen, BMI, and PAI, in comparison with normotensives. Antihypertensive treatment does not modify the patient's physical condition and does not reduce BMI. A similar analysis of blood glucose in Japanese patients was performed in a previous study, and serum insulin and BMI were also higher in treated hypertensives than in normotensives, although hypertension was defined by SBP ≥160 mmHg and/or DBP ≥95 mmHg (*1*).

We found a different tendency between men and women with regard to HDL cholesterol. Although HDL was known to

Table 4. The Rates of Status Categorized with Metabolic Status, Smoking and Drinking

	Normotensives (*n* (%))	Hypertensives (*n* (%))		$p^{\#}$	p^{**}
		Treated	Nontreated		
Men					
Lipid status					
Dyslipidemia[†]	865 (31.2)	169 (37.6)	465 (39.0)	<0.01	<0.01
Nomal	1,909	281	726		
Blood glucose status					
IGT	671 (24.2)	143 (31.8)	397 (33.3)	<0.01	<0.01
Nomal	2,103	307	794		
Metablic syndrome					
MS[§]	141 (5.2)	94 (22.4)	246 (21.2)	<0.01	<0.01
Non-MS[§]	2,556	326	913		
Smoking status					
Current	1,494 (54.0)	161 (35.9)	565 (47.7)	<0.01	0.03
Ex-	706	185	355		
Non	565	103	265		
Drinking status					
Current	1,983 (73.3)	337 (78.6)	898 (78.4)	<0.01	<0.01
Ex-	93	28	34		
Non	630	64	214		
Women					
Lipid status					
Dyslipidemia[†]	1,345 (29.1)	404 (47.0)	646 (45.9)	<0.01	<0.01
Nomal	3,275	456	761		
Blood glucose status					
IGT	832 (18.0)	261 (30.0)	382 (27.7)	<0.01	<0.01
Nomal	3,788	599	1,025		
Metablic syndrome					
MS[§]	154 (3.4)	203 (24.8)	225 (16.4)	<0.01	<0.01
Non-MS[§]	4,371	616	1,149		
Smoking status					
Current	292 (6.4)	31 (3.7)	54 (3.9)	<0.01	0.04
Ex-	150	18	28		
Non	4,097	793	1,293		
Drinking status					
Current	1,192 (26.7)	151 (19.2)	325 (24.2)	<0.01	0.31
Ex-	63	12	27		
Non	3,217	625	990		

*χ^2 test, **Mantel-Haenzel test adjusted for age (10 years). [†]Dyslipidemia: total cholesterol ≥220 mg/dL and/or triglyceride ≥150 mg/dL. [§]Metabolic syndrome: BMI ≥25 kg/m^2 as an essential combined with 2 or more of the following components: triglycerides ≥150 mg/dL and/or HDL cholesterol <40 mg/dL; systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg; fasting blood glucose ≥110 mg/dL. IGT, impaired glucose tolerance; MS, metabolic syndrome; BMI, body mass index; HDL, high-density lipoprotein.

be affected by drinking alcohol (*29*, *30*), the results was identical after adjustment for age and alcohol drinking status. Higher HDL cholesterol in normotensives in women was due to a lower BMI level. That was because the difference in HDL cholesterol in women was not detected after adjustment for BMI in addition to age and drinking status. Yamamoto *et al*. reported that low HDL was related to high triglycerides and BMI in large-scale cross-sectional data, and this tendency was similar to ours (*31*). Serum insulin was higher in hypertensives with or without treatment in our data (data not shown because of the smaller number of subjects). Of course, lowering BP reduces the incidence of CVD, but it is more important to control BP or modify lifestyle. In a clinical setting, home BP has been used to evaluate BP control in recent years, but even now, neither home nor office BP values are adequately controlled (*32*).

We examined metabolic profiles such as dyslipidemia and IGT in relation to the different BP categories. In recent years it has been proposed that hypertension is part of a cluster of metabolic risk factors and is such as MS (*33*), and that MS is related to other CVD risk factors and manifestations, such as pulse wave velocity and sleep apnea syndrome (*34–37*). The Japanese criteria for MS were applied using BMI $\geq$25 kg/m^2 to define obesity in the present study, because waist circumference was not measured in most of the subjects. The proportion of hypertensive subjects with MS was also higher than that of normotensives with this syndrome. Even if we could have controlled BP, we could not control all other risk factors for CVD. Shapo *et al*. reported results similar to ours, *i.e.*, higher levels of total cholesterol, triglycerides, and glucose tolerance in hypertensives with or without medication than in normotensives, and higher levels in untreated than treated hypertensives. In our study, after adjustment for age, the findings were identical (*13*). In other studies, two-thirds of the hypertensive population were aware of the diagnosis, but only a quarter of the hypertensives were adequately controlled (*4*, *14*, *16*). Our data showed a similar tendency.

We thought a limitation of the present study was that only the relationship between BP categories and cardiovascular risk factors was investigated, and not the relationships between BP categories and CVD as true outcomes. We have been conducting a follow-up study for stroke and myocardial infarction, and some data will be shown in the future.

References

1. Ohmori S, Kiyohara Y, Kato I, *et al*: Hyperinsulinaemia and blood pressure in a general Japanese population: the Hisayama Study. *J Hypertens* 1994; **12**: 1191–1197.
2. Imai Y, Tsuji I, Nagai K, *et al*: Ambulatory blood pressure monitoring in evaluating the prevalence of hypertension in adults in Ohasama, a rural Japanese community. *Hypertens Res* 1996; **19**: 207–212.
3. Imazu M, Sumida K, Yamabe T, *et al*: A comparison of the prevalence and risk factors of high blood pressure among Japanese living in Japan, Hawaii, and Los Angeles. *Public Health Rep* 1996; **2**: 59–61.
4. Burt V, Whelton P, Roccella E, *et al*: Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988–1991. *Hypertension* 1995; **25**: 305–313.
5. Hansson L, Zanchetti A: The Hypertension Optimal Treatment (HOT) Study—patient characteristics: randomization, risk profiles, and early blood pressure results. *Blood Press* 1994; **3**: 322–327.
6. Kaplan RC, Psaty BM, Heckbert SR, Smith NL, Lemaitre RN: Blood pressure level and incidence of myocardial infarction among patients treated for hypertension. *Am J Public Health* 1999; **89**: 1414–1417.
7. Klungel O, Kaplan R, Heckbert S, *et al*: Control of blood pressure and risk of stroke among pharmacologically treated hypertensive patients. *Stroke* 2000; **31**: 420–424.
8. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450,000 people in 45 prospective cohorts. Prospective studies collaboration. *Lancet* 1995; **346**: 1647–1653.
9. Ueda K, Omae T, Hasuo Y, *et al*: Prevalence and long-term prognosis of mild hypertensives and hypertensives in a Japanese community, Hisayama. *J Hypertens* 1988; **6**: 981–989.
10. Kannel W: Blood pressure as a cardiovascular risk factor: prevention and treatment. *JAMA* 1996; **275**: 1571–1576.
11. Bulpitt C, Palmer A, Fletcher A, *et al*: Optimal blood pressure control in treated hypertensive patients. Report from the Department of Health Hypertension Care Computing Project (DHCCP). *Circulation* 1994; **90**: 225–233.
12. Banegas JR, Rodriguez-Artalejo F, de la Cruz Troca JJ, Guallar-Castillon P, del Rey Calero J: Blood pressure in Spain: distribution, awareness, control, and benefits of a reduction in average pressure. *Hypertension* 1998; **32**: 998–1002.
13. Shapo L, Pomerleau J, McKee M: Epidemiology of hypertension and associated cardiovascular risk factors in a country in transition: a population based survey in Tirana City, Albania. *J Epidemiol Community Health* 2003; **57**: 734–739.
14. Cifkova R, Skodova Z, Lanska V, *et al*: Prevalence, awareness, treatment, and control of hypertension in the Czech Republic. Results of two nationwide cross-sectional surveys in 1997/1998 and 2000/2001, Czech Post-MONICA Study. *J Hum Hypertens* 2004; **18**: 571–579.
15. Wang Z, Wu Y, Zhao L, Li Y, Yang J, Zhou B: Trends in prevalence, awareness, treatment and control of hypertension in the middle-aged population of China, 1992–1998. *Hypertens Res* 2004; **27**: 703–709.
16. Wolf-Maier K, Cooper RS, Kramer H, *et al*: Hypertension treatment and control in five European countries, Canada, and the United States. *Hypertension* 2004; **43**: 10–17.
17. Nago N, Kayaba K, Hiraoka J, *et al*: Lipoprotein(a) levels in the Japanese population: influence of age and sex, and relation to atherosclerotic risk factors. The Jichi Medical School Cohort Study. *Am J Epidemiol* 1995; **141**: 815–821.
18. Ishikawa S, Gotoh T, Nago N, Kayaba K: The Jichi Medical School (JMS) Cohort Study: design, baseline data and standardized mortality ratios. *J Epidemiol* 2002; **12**: 408–417.
19. Kannel W, Sorlie P: Some health benefits of physical activity. The Framingham Study. *Arch Intern Med* 1979; **139**: 857–861.
20. Davis C, Rifkind B, Brenner H, Gordon D: A single cholesterol measurement underestimates the risk of coronary heart disease. An empirical example from the Lipid Research Clinics Mortality Follow-up Study. *JAMA* 1990; **264**: 3044–3046.
21. Perry HJ, Miller J: Difficulties in diagnosing hypertension: implication and alternatives. *J Hypertens* 1992; **10**: 887–896.
22. Eastern Stroke and Coronary Heart Disease Collaborative Research Group: Blood pressure, cholesterol, and stroke in eastern Asia. *Lancet* 1998; **352**: 1801–1807.
23. Du X, Cruickshank K, McNamee R, *et al*: Case-control study of stroke and the quality of hypertension control in north west England. *BMJ* 1997; **314**: 272–276.
24. Makino Y, Kawano Y, Minami J, Yamaguchi T, Takishita

S: Risk of stroke in relation to level of blood pressure and other risk factors in treated hypertensive patients. *Stroke* 2000; **31**: 48–52.

25. MacMahon S, Peto R, Cutler J, *et al*: Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet* 1990; **335**: 765–774.
26. Gueyffier F, Boutitie F, Boissel J, *et al*: Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. *Ann Intern Med* 1997; **126**: 761–767.
27. Collins R, Peto R, MacMahon S, *et al*: Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990; **335**: 827–838.
28. Tomiyama H, Arai T, Koji Y, *et al*: The age-related increase in arterial stiffness is augmented in phases according to the severity of hypertension. *Hypertens Res* 2004; **27**: 465–470.
29. Steinberg D, Pearson TA, Kuller LH: Alcohol and atherosclerosis. *Ann Intern Med* 1991; **114**: 967–976.
30. Kiechl S, Willeit J, Poewe W, *et al*: Insulin sensitivity and regular alcohol consumption: large, prospective, cross sectional population study (Bruneck study). *BMJ* 1996; **313**: 1040–1044.
31. Yamamoto A, Temba H, Horibe H, *et al*: Life style and cardiovascular risk factors in the Japanese population—from an epidemiological survey on serum lipid levels in Japan 1990 part 2: association of lipid parameters with hypertension. *J Atheroscler Thromb* 2003; **10**: 176–185.
32. Ohkubo T, Obara T, Funahashi J, *et al*: Control of blood pressure as measured at home and office, and comparison with physicians' assessment of control among treated hypertensive patients in Japan: first report of the Japan Home *versus* Office Blood Pressure Measurement Evaluation (J-HOME) study. *Hypertens Res* 2004; **27**: 755–763.
33. Ishizaka N, Ishizaka Y, Toda E, Hashimoto H, Nagai R, Yamakado M: Hypertension is the most common component of metabolic syndrome and the greatest contributor to carotid arteriosclerosis in apparently healthy Japanese individuals. *Hypertens Res* 2005; **28**: 27–34.
34. Takeuchi H, Saitoh S, Takagi S, *et al*: Metabolic syndrome and cardiac disease in Japanese men: applicability of the concept of metabolic syndrome defined by the National Cholesterol Education Program–Adult Treatment Panel III to Japanese men—the Tanno and Sobetsu Study. *Hypertens Res* 2005; **28**: 203–208.
35. Tsubakimoto A, Saito I, Mannami T, *et al*: Impact of metabolic syndrome on brachial-ankle pulse wave velocity in Japanese. *Hypertens Res* 2006; **29**: 29–37.
36. Sasanabe R, Banno K, Otake K, *et al*: Metabolic syndrome in Japanese patients with obstructive sleep apnea syndrome. *Hypertens Res* 2006; **29**: 315–322.
37. Ishikawa S, Kayaba K, Gotoh T, Nakamura Y, Kajii E: Metabolic syndrome and C-reactive protein in the general population. *Circ J* 2007; **71**: 26–31.