Original Article

Characteristics of Young-Onset Hypertension Identified by Targeted Screening Performed at a University Health Check-Up

Yutaka EJIMA[1),2),*], Yoko HASEGAWA[3),*], Satoru SANADA[1)], Noriyuki MIYAMA[1),4)], Ryo HATANO[1)], Tomohiro ARATA[1)], Michiko SUZUKI[1)], Itsuro KAZAMA[1)], Akira SATO[4)], Susumu SATOMI[4)], Wataru HIDA[3)], and Mitsunobu MATSUBARA[1)]

Since the prevalence and clinical characteristics of young-onset hypertension are still to be elucidated, we performed targeted-screening at an annual university health check-up for two consecutive years. Out of 16,464 subjects in 2003 and 17,032 in 2004 that were aged less than 30 years, 22 and 26 students (all males) exhibited high blood pressure (BP), respectively, on three occasions during casual BP measurements at the Tohoku University Health Center (systolic and diastolic BP of 140 and/or 90 mmHg or greater, respectively). These students were asked to measure their BP at home, and 9 subjects in total were diagnosed as having essential hypertension (EH). The remaining students were diagnosed as having white coat hypertension (WCH). In 8 out of 9 EH students, their father and/or mother had also been treated with antihypertensive medication. Adjustment by attendance ratio for each BP measurement suggested that the incidence of EH was around 0.1% and that of hypertension (EH and WCH) was around 0.5% in university students aged less than 25 years, since most of the subjects and hypertensive students were between 18 and 24 years old. Body mass index of the EH, which was more than 25 kg/m^2 (overweight), was significantly higher than that with WCH. In conclusion, the combination of repeated casual BP measurements and home BP effectively identified young-onset EH. The clinical parameters indicated that male gender, genetic background, and excessive weight were risk factors for young-onset hypertension. (*Hypertens Res* 2006; 29: 261–267)

***Key Words*: home blood pressure, white coat hypertension, overweight, genetic background, male gender**

Introduction

The number of young patients (less than 30 years old) with essential hypertension (EH) is small (*1*), and most of them are not identified due to the lack of clinical symptoms other than a relatively small elevation of blood pressure (BP) and/or the limited opportunities for BP measurement. Recently BP measurement was added to the regular check-up at high schools and universities in Japan, and the results of this initiative indicated that up to 20% of young subjects have elevated BP (*2*, *3*). Follow-up studies have suggested that BP elevation at the school check-up is closely associated with the onset of EH and/or EH-related cardiovascular complications later in life

From the [1)]Division of Molecular Medicine, [2)]Division of Anesthesiology and Perioperative Medicine, and [4)]Division of Advanced Surgical Science and Technology, Tohoku University School of Medicine, Sendai, Japan; and [3)]Health Administration Center, Tohoku University, Sendai, Japan.

The present study was supported by a Grant-in-Aid for Scientific Research (17590815) from the Ministry of Education, Culture, Sports, Science and Technology of Japan, 2005.

*These authors contributed equally to this work.

Address for Reprints: Mitsunobu Matsubara, M.D., Ph.D., Division of Molecular Medicine, Center for Translational and Advanced Animal Research on Human Diseases, Tohoku University School of Medicine, 2–1 Seiryo-machi, Aoba-ku, Sendai 980–8575, Japan. E-mail: mmitsu2i@mail.tains.tohoku.ac.jp

Received October 20, 2005; Accepted in revised form January 13, 2006.

(*2–5*). BP measurement at school also demonstrated that young subjects who were initially deemed hypertensive during the first check showed a decline in BP at the second medical check, suggesting a high incidence of white coat hypertension (WCH), and indicating the necessity for repeated BP measurements to evaluate the reliability and accuracy of elevated BP readings (*3*, *6*). This phenomenon indicates the additional difficulty of identifying the small number of EH patients among young subjects. Perhaps for this reason, none of the previous studies have examined a cohort of EH patients selected from a large group of young students examined at an annual health check-up (*2–5*). Thus, the prevalence and detailed characteristics of hypertension in young subjects both remain to be determined.

We have performed three separate casual BP measurements during a general check-up at Tohoku University, Japan, since 1994. We have noticed that, between the first two casual BP measurements, the number of students with high BP was markedly reduced, but the rate of decrease was much lower at a 3rd measurement that was conducted by a medical doctor. These results suggested that students with a high BP on three separate occasions of BP measurement could be considered to have high casual BP. The number of students who consistently exhibited elevated BP during three independent measurements was no more 30 among a total group of more than 18,000 students. Because additional BP measurement, such as self BP measurement at home (home BP), could be achieved with these students during the remainder of the school year, we designed a novel screening system consisting of three separate casual BP measurements and additional home BP. We utilized this novel system for two consecutive years, 2003 and 2004, and EH students requiring medical treatment were identified from more than 18,000 students each year. Analysis of these data from students aged less than 30 years provides important information for the estimation of the prevalence of hypertension, both EH and WCH, as well as demonstrating risk factors and specific characteristics of young-onset hypertension.

Methods

All students (18,456 in 2003 and 18,556 in 2004) at Tohoku University were asked to undergo a regular health check-up, including a BP measurement (1st BP) at Tohoku University Health Center. The BP was measured under the supervision of well-trained nurses using an automatic device (BP-203RVII; Nippon Colin Co., Ltd., Komaki, Japan) on the right upper arm with the subject in a sitting position after resting for at least 5 min. Repeated BP measurement was not performed for the hypertensive subjects, since the following additional arrangements were made for the BP measurement of these subjects. About 1 month later, we measured the BP of those students with a systolic BP of 140 mmHg or greater and/or a diastolic BP of 90 mmHg or greater (2nd BP). This 2nd BP measurement was performed under the same conditions described above. The students who again exhibited a high BP (based on the threshold values defined above) were asked to undergo a third BP measurement (1–2 months after 2nd BP) that was performed by a doctor after a resting period of more than 30 min and to respond to a questionnaire (3rd BP). The doctor also performed a physical examination, checked the chest X-ray, urinalysis, blood cell count, and electrocardiogram, confirmed the absence of clinical symptoms suggesting underlying systemic disease, and checked the history of familial hypertension. The doctor then selected students with high blood pressure as defined above, and requested that they measure their home BP, in the morning, using a fully automated, digital display device (HEM 747IC; Omron Life Science, Kyoto, Japan) that was provided by the health center. According to the guidelines of the Japanese Society of Hypertension, the first measurement in the morning was recorded for more than 2 weeks, and the mean BP values on different mornings (last 7 measurements) were calculated and used as the home BP. Finally, the students with a systolic home BP of 135 mmHg or greater and/or a diastolic home BP of 85 mmHg or greater were referred to the Tohoku University Hospital for a detailed examination. The students exhibiting lower home BP were diagnosed as having WCH, which was considered to have been the cause of their consistently increased BP during the school measurements. The results from students less than 30 years of age (16,464 in 2003 and 17,032 in 2004) were analyzed. The study protocol was approved by the Institutional Review Board of Tohoku University School of Medicine and performed during the Japanese school years for 2003 and 2004.

The differences between data were examined for statistical significance using the unpaired *t* test followed by Student's *t*-test. The results are expressed as the means±SD. p values <0.05 were considered statistically significant.

Table 1. Profiles of Students Aged Less than 30 Years at General Check-Up (1st Casual BP Measurement)

Variable	Male	Female
2003		
Number	9,664	2,899
Age	22.0±2.6	21.3±2.7
BMI	21.3±2.1	20.1±2.4
Casual BP		
Systolic	125.8±13.6	114.4±12.5
Diastolic	74.1±15.0	68.9±9.4
2004		
Number	9,562	2,741
Age	21.8±2.7	21.5±2.8
BMI	21.0±2.8	20.1±2.4
Casual BP		
Systolic	126.0±13.9	114.7±12.8
Diastolic	74.0±12.1	69.8±9.2

BP, blood pressure; BMI, body mass index. Data are mean±SD.

School year	2003 total (female)	attending ratio	2004 total (female)	attending ratio
Subject aged less than 30	16,464 (3,551)		17,032 (3,577)	
↓				
First health check up	12,563 (2,899)	76.10%	12,303 (2,741)	72.20%
High BP (≥140/90)	1,354 (92)		1,367 (81)	
↓				
Second BP measurement	789 (57)	58.30%	937 (58)	68.50%
High BP (≥140/90)	78 (2)		80 (6)	
↓				
Third BP measurement	55 (2)	70.50%	57 (4)	71.30%
High BP (≥ 140/90)	22 (0)		29 (0)	
↓				
HBP mesurement	22 (0)	100%	26 (0)	89.60%
HBP < 135/85 (White coat hypertension)	16 (0)		23 (0)	
HBP ≥ 135/85 (Essential hypertension)	6 (0)		3 (0)	

Fig. 1. *Process of targeted screening for hypertension in 2003 and 2004. The numbers of students at each step, and the percentage attendances for blood pressure (BP) measurements are shown. HBP, self BP measurement at home.*

Results

Clinical profiles of the subjects and BP values based on the general health check (1st casual BP measurement) are presented in Table 1. The numbers of students who underwent each step of the BP measurements during the 2003 and 2004 school years at Tohoku University are presented in Fig. 1. In both years, two independent measurements (1st and 2nd measurement) of casual BP markedly reduced the number of hypertensive subjects. A third BP measurement by medical doctors further decreased the number of hypertensive students to 22 and 26 in 2003 and 2004, respectively. All of the hypertensive students were males. Since the percentages of students attending the 1st, 2nd and 3rd BP measurements were 76.1%, 58.3% and 70.5%, respectively (Fig. 1), the incidence of hypertensive students in 2003 was estimated to be 0.43% following adjustment for the attendance. After performing a similar adjustment for attendance, the incidence of hypertension in 2004 was estimated to be 0.48%. Out of these hypertensive students, only 6 students in 2003 and 3 in 2004 demonstrated elevated BP during the home BP (Fig. 1). These 9 students subsequently underwent hospital examination and were diagnosed as having EH requiring antihypertensive medication. Two out of the three EH patients diagnosed in 2004 had also shown increased casual BP in 2003 and had been admitted to Tohoku University Hospital, but failed to complete the screening protocol that year. The remaining patient was newly admitted to Tohoku University in 2004. The students who exhibited normal range BP during the home BP measurements were diagnosed as having WCH. The numbers of WCH students were 16 and 23 during 2003 and 2004, respectively (Fig. 1). Since 5 WCH students in 2004 had already been diagnosed with WCH in 2003, 18 WCH students were newly diagnosed in 2004. Therefore, the total numbers of EH and WCH students during these 2 years were 9 and 34, respectively. The father and/or mother in 8 out of 9 EH students and 18 out of 34 WCH students had been identified as EH patients. Other EH and WCH students also exhibited a familial history of hypertension.

Although we analyzed the data from students aged less than 30 years, the average age of both male and female students was between 21 and 22 years (Table 1), suggesting that most of the subjects in the present study were in their early 20s. Thus, we examined the distribution of students according to age, and the results are presented in Fig. 2A. The number of EH or WCH students according to age is presented in Fig. 2B. These figures indicate that most of the subjects and hypertensive students were less than 25 years of age. In addition, the attendance percentage for the first health check was more than 65% in this age range (65–93 %), whereas it was less than 50% in subjects 25–29 years of age (25–48%). Therefore, the incidences of hypertension given above are considered to be representative of the incidence in young subjects aged less than 25 years.

The WCH students diagnosed in 2003 were expected to undergo a targeted screening protocol in 2004. Most of the WCH students that were diagnosed in 2004 had been entered into this screening system in 2003, although some of them had not yet completed the protocol. Figure 3 shows the differences in the screening outcome for these WCH students between 2003 and 2004. Thirteen out of 16 WCH students diagnosed in 2003 underwent the targeted screening again in 2004; none of them were reclassified as having EH. Eight of the WCH subjects exhibited a normal range of casual BP (transient WCH), and only 5 students were again diagnosed

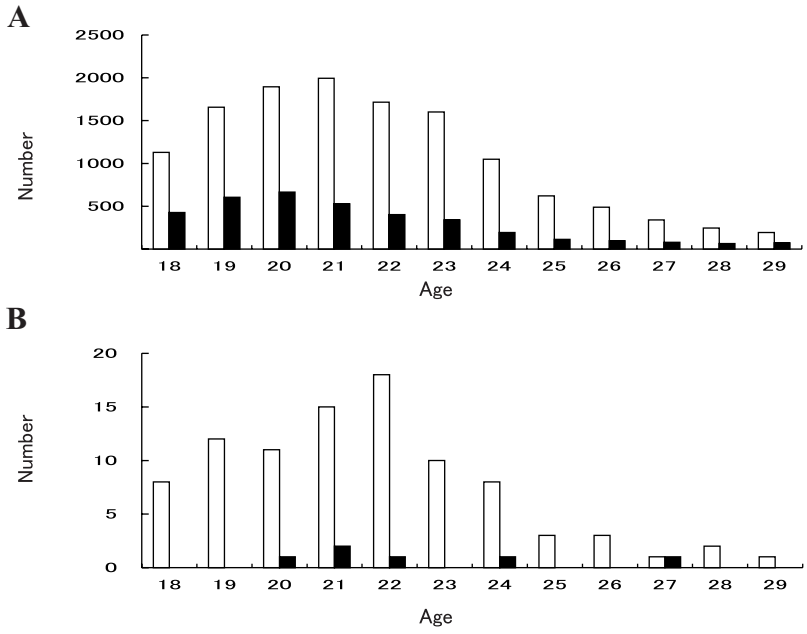

Fig. 2. *Age-dependent distribution. A: Students underwent the 1st BP measurement in 2004. The open columns represent the numbers of male students and the closed columns represent the numbers of female students. B: Students with hypertension between 2003 and 2004. The open columns represent the numbers of white coat hypertension (WCH) students and the closed columns represent the numbers of students with essential hypertension (EH).*

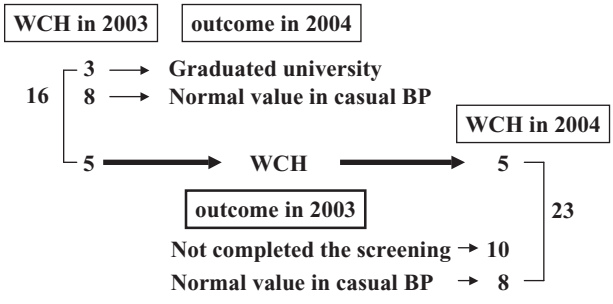

Fig. 3. *Diagnostic alteration of white coat hypertensin (WCH) between 2003 and 2004.*

with WCH (consistent WCH). Out of 18 WCH students that were newly diagnosed in 2004, 8 students were transferred from a group of subjects with normal casual BP. However, the diagnosis of the remaining 10 students in 2003 was absent due to novel admission or incomplete performance of the screening protocol in 2003.

To further investigate the clinical characteristics of EH and WCH in these young subjects, BP values (3rd casual BP and home BP), age, body mass index (BMI), presence of a strong genetic background (EH in parents), and smoking habit were examined, as presented in Table 2. Since 13 of the WCH students diagnosed in 2003 again underwent check-up in 2004, these students were divided into two subgroups, a transient WCH group and consistent WCH group, for comparison. The WCH students diagnosed in 2004 were included in one subgroup due to the lack of outcome in 2005. In BP values, there were no significant differences in casual systolic or diastolic BP values among the EH and 3 WCH subgroups, although the home BP values for the EH students were significantly higher than those for any of the WCH subgroups (Table 2). The mean BMI score in EH students was more than 25 kg/m^2, and this score was significantly higher than that of transient WCH or WCH students newly diagnosed in 2004, whereas there was no significant difference in age among these three groups (Table 2). However, the BMI score from the consistent WCH group was slightly elevated compared to that of the transient WCH group, but there was no significant difference between the EH and consistent WCH groups (Table 2). The incidence of smoking was quite low, even in EH students (Table 2).

Discussion

In both 2003 and 2004, the incidence of hypertensive students, identified by three separate casual measurements of BP, was estimated to be approximately 0.4–0.5% of all students aged less than 30 years. Although more than 10% of students receiving an annual check-up exhibited a high casual BP, additional casual BP measurements markedly reduced the number of students with high BP. The incidence of high BP at the 1st casual measurement was similar to the incidence of young-onset hypertension reported by several previous stud-

Table 2. Clinical Parameters of Hypertensive Students Defined by Casual BP

Variable	EH	Consistent WCH	Transient WCH	Newly diagnosed WCH in 2004
Number	9	5	8	18
Age	21.4±2.6	21.8±1.6	20.3±1.3	21.6±1.8
Casual BP				
Systolic	149.0±7.1	144.0±7.4	147.3±10.4	146.6±11.0
Diastolic	90.0±8.4	90.0±9.9	87.3±7.3	86.9±10.2
Home BP				
Systolic	142.8±5.7	123.0±3.5*	119.9±7.6*	122.3±6.4*
Diastolic	90.2±6.6	77.4±3.0*	72.8±7.0*	76.6±5.4*
BMI	27.8±4.3	24.5±4.1	21.8±3.0*	23.5±3.0*
EH in parents (%)	8 (89)	3 (60)	3 (38)	9 (50)
Smoking (%)	1 (11)	2 (40)	0 (0)	1 (6)

Values of consistent or transient WCH are those in 2003. BP, blood pressure; EH, essential hypertension; WCH, white coat hypertension; BMI, body mass index. Data are mean±SD. *$p<0.05$ *vs*. data of EH.

ies (*2*, 3). A marked decline in the number with subjects high BP following repeated BP measurements has also been reported previously (*3*, *6*). These findings indicate that the white coat response occurs quite often in young subjects, and thus the estimation of the incidence of hypertension in young subjects is largely influenced by the protocol of BP measurement. In the present study, the 3rd casual BP measurement was performed carefully by medical doctors, but the reduction in number of students with high BP was much lower than that following the 1st and 2nd casual measurements, both of which reduced the number by around one-tenth of the students. Thus, the students that exhibited high BP at each of the three casual BP measurements were considered to continuously exhibit high casual BP either by onset of EH or by a strong white coat reaction. The similar incidence of such hypertensive students between 2003 and 2004 confirms the consistent presence of hypertensive students by casual BP measurement, and also indicates the validity of three separate measurements of casual BP in young subjects to select patients requiring medical examination and treatment.

Home BP clearly classified the students with high casual BP into two groups, a group of WCH and another group of subjects requiring further evaluation, as we showed a significant difference in home BP values between these two groups of students. This supports the clinical importance of home BP as procedure for diagnosing hypertension, especially in young subjects, who have a high incidence of white coat reaction. The number of EH students identified in the present study varied between 2003 and 2004. The small incidence of EH in young subjects may limit the consistency of results from year to year, even in a population of more than 16,000. We found a total of 9 EH students and 34 WCH students over the 2 years of this study, and the incidence of hypertension either by EH or WCH was similar for each year, as mentioned above. Thus, the ratio of total numbers between EH and WCH in total is considered to be close to that of the incidence between them. Consequently, the incidence of EH might be around 0.1% in these young subjects. Because most of the subjects and hypertensive students were between 18 and 24 years of age, the incidence of EH or WCH may represent the prevalence in a very young population, aged less than 25 years. This study is limited in that the home BP was performed after casual BP measurements, and we may have failed to identify those students with isolated ambulatory hypertension, or elevated BP at home using normal casual BP. Recently, Palatini and coworkers reported a relatively high incidence of isolated ambulatory hypertension in a young population (*7*). However, home BP or ambulatory BP monitoring of more than 16,000 students at a general health check-up, which should be completed every year, requires much more medical staff, as well as more devices for BP measurement. Therefore, we intend to select students with normal casual BP for additional home BP, based on the clinical characteristics of young-onset hypertension that were demonstrated in the present study.

All hypertensive students selected by repeated casual BP measurement were males. The number of female students included in the present study was 3,551 in 2003 and 3,577 in 2004, and the attendance ratio for the 1st and 2nd BP measurements was greater than that of male students (data not shown). The absence of hypertensive students in the female population therefore indicates the extremely low incidence of hypertension in young female subjects. Sharabi and coworkers recently examined the casual BP levels in subjects from 25 to 45 years of age, and found a significantly higher BP for men than women in the population with normal BMI (*8*). When we compared the BP values during the 1st measurement of BP between male and female students, the BP of male students was significantly higher than that of female students. However, we have also demonstrated that BP values taken from a single occasion of BP measurement are not reliable due to the high incidence of WCH in these young subjects. Therefore, our present findings indicate that male gender is a

strong risk factor for young-onset hypertension, but BP values determined by repeated BP measurements are required to confirm the presence of gender-based differences in BP.

Since we performed a targeted screening for 2 consecutive years, we examined the alteration of diagnostic classification in individual WCH students. Thirteen WCH students that were diagnosed in 2003 underwent check-up again in 2004. In none of these cases was the diagnosis changed to EH, and 5 students were re-diagnosed with WCH (consistent WCH). By contrast, 8 of these 13 WCH students exhibited a normal casual BP (transient WCH). Frontini and coworkers examined the effect of awareness of hypertension in a large population of young adults (*9*), and reported that such awareness increased the proportion of subjects undergoing medical treatment. Our present findings suggest that the awareness of WCH may influence subsequent casual BP values in some of the young subjects with WCH. Continuous performance of the present screening system will further reveal the characteristics of young-onset WCH.

In the present study, we examined the effects of the presence of a strong genetic background, such as hypertension in the father and/or mother. This information is highly reliable in most university students, as their parents are in their 40s or 50s and undergoing general check-ups provided either by their employers or by the local government. Since BMI and smoking habits were also examined at our university check-up, we compared these clinical parameters between EH and various types of WCH. Although WCH students diagnosed in 2004 could not be divided into subgroups due to the lack of subsequent results, their data were also used for comparison (Table 2). EH students and all subgroups of WCH students demonstrated similar values of casual BP, indicating the absence of specific characteristics in BP levels except for increased home BP in EH students. The BMI score for the EH patients was more than 25 kg/m^2 (overweight) on average, and was significantly greater than that of students with transient WCH or the WCH students newly diagnosed in 2004. However, there was no significant difference in age or incidence of smoking among these three subgroups. The presence of a strong genetic background was also much higher in EH students when compared to the students with transient WCH or the WCH students newly diagnosed in 2004. These findings confirm that obesity (*8*) and a genetic background are risk factors for young-onset EH. Since the overweight could be treated by diet and exercise, the influence of body mass on young-onset hypertension could be further evaluated by controlling the body weight of EH or WCH students with high BMI score.

Identification of young EH patients at early stages of hypertension may reduce the incidence of later onset of cardiovascular diseases. Although the present targeted screening system is still incomplete due to several limitations, such as incomplete attendance and failure to find isolated cases of ambulatory hypertension, our present system assisted in the identification of 9 students with EH who exhibited no clinical manifestations other than hypertension over 2 years. This examination revealed several important characteristics of both young-onset EH and WCH in young subjects. Therefore, ongoing utilization of our present system, together with modifications based upon our present findings, may lead to better understanding of hypertension in young subjects, as well as further identification of young-onset EH at an earlier stage. Since the genetic investigations in the general Japanese population aged 40 years and over have as yet failed to identify significant genetic factors for EH (*10–16*), use of the present system could lead to an increase in the identification of cases of young-onset EH which may be associated with a strong genetic background for EH, and these cases could provide important genetic information for the study of hypertension. The low frequency of young-onset hypertension (both EH and WCH), however, indicates that most subjects who are going to show hypertension relatively late in life are not well identified by the present system. The threshold BP values, which are same as those used for general check-up for the general population, could be too high for young subjects. Therefore, a systematic prospective study following-up even students with normal-range BP is also required to determine the ideal threshold BP values for use at university check-ups.

Perspectives

We performed targeted-screening at an annual university health check-up for 2 consecutive years. The combination of three separate measurements of casual BP at a university health check-up and additional home BP measurements effectively identified the low frequency of young-onset EH. Repeated and ongoing utilization of this system suggests that male gender, strong genetic background, and obesity are risk factors for young-onset EH.

References

1. Kotchen JM, McKean HE, Kotchen TA: Blood pressure trends with aging. *Hypertension* 1982; **4**: III128–III134.
2. Kawabe H, Shibata H, Hirose H, Tsujioka M, Saito I, Saruta T: Determinants for the development of hypertension in adolescents. A 6-year follow-up. *J Hypertens* 2000; **18**: 1557–1561.
3. Kawasaki T, Uezono K, Sanefuji M, *et al*: A 17-year follow-up study of hypertensive and normotensive male university students in Japan. *Hypertens Res* 2003; **26**: 445–452.
4. Berenson GS, Wattigney WA, Webber LS: Epidemiology of hypertension from childhood to young adulthood in black, white, and Hispanic population samples. *Public Health Rep* 1996; **111** (Suppl 2): 3–6.
5. Clarke WR, Schrott HG, Leaverton PE, Connor WE, Lauer RM: Tracking of blood lipids and blood pressures in school age children: the Muscatine study. *Circulation* 1978; **58**: 626–634.
6. Weir MR: Impact of age, race, and obesity on hypertensive mechanisms and therapy. *Am J Med* 1991; **90**: 3S–14S.
7. Palatini P, Winnicki M, Santonastaso M, *et al*: Prevalence

and clinical significance of isolated ambulatory hypertension in young subjects screened for stage 1 hypertension. *Hypertension* 2004; **44**: 170–174.
8. Sharabi Y, Grotto I, Huerta M, Grossman E: Susceptibility of the influence of weight on blood pressure in men *versus* women: lessons from a large-scale study of young adults. *Am J Hypertens* 2004; **17**: 404–408.
9. Frontini MG, Srinivasan SR, Elkasabany A, Berenson GS: Awareness of hypertension and dyslipidemia in a semirural population of young adults: the Bogalusa Heart Study. *Prev Med* 2003; **36**: 398–402.
10. Matsubara M, Ohkubo T, Michimata M, *et al*: Japanese individuals do not harbor the T594M mutation but do have the P592S mutation in the C-terminus of the beta-subunit of the epithelial sodium channel: the Ohasama study. *J Hypertens* 2000; **18**: 861–866.
11. Matsubara M, Kikuya M, Ohkubo T, *et al*: Aldosterone synthase gene (CYP11B2) C−334T polymorphism, ambulatory blood pressure and nocturnal decline in blood pressure in the general Japanese population: the Ohasama Study. *J Hypertens* 2001; **19**: 2179–2184.
12. Matsubara M, Suzuki M, Fujiwara T, *et al*: Angiotensin-converting enzyme I/D polymorphism and hypertension: the Ohasama study. *J Hypertens* 2002; **20**: 1121–1126.
13. Matsubara M, Metoki H, Suzuki M, *et al*: Genotypes of the betaENaC gene have little influence on blood pressure level in the Japanese population. *Am J Hypertens* 2002; **15**: 189–192.
14. Matsubara M, Metoki H, Katsuya T, *et al*: T+31C polymorphism (M235T) of the angiotensinogen gene and home blood pressure in the Japanese general population: the Ohasama Study. *Hypertens Res* 2003; **26**: 47–52.
15. Kikuya M, Sugimoto K, Katsuya T, *et al*: A/C1166 gene polymorphism of the angiotensin II type 1 receptor (AT1) and ambulatory blood pressure: the Ohasama Study. *Hypertens Res* 2003; **26**: 141–145.
16. Matsubara M, Sato T, Nishimura T, *et al*: CYP11B2 polymorphisms and home blood pressure in a population-based cohort in Japanese: the Ohasama study. *Hypertens Res* 2004; **27**: 1–6.