ASSOCIATION OF OBESITY WITH PREVALENCE OF WHITE-COAT AND SUSTAINED HYPERTENSION IN YOUNG ADULTS

Masao Kobayashi[1,2], Wakana Sato[2], Haruwo Tashiro[2], Ikuro Namura[1], Masahito Fushimi[1] and Hiroyuki Watanabe[2]

[1]*Health Administration Center of Akita University*
[2]*Department of Cardiovascular Medicine, Akita University Graduate School of Medicine*

(received 13 April 2020, accepted 8 May 2020)

Abstract

Purpose : This study was performed to determine whether obesity is associated with white-coat hypertension (WHT) and sustained hypertension (SHT) in young adults.

Methods : Blood pressure (BP) was measured at home by university students ($n=95$) who exhibited BP readings ≥ 140/90 mmHg during their annual health exam and post-exam measurements between 2005 and 2014. Subject characteristics and BP readings from the WHT and SHT groups were compared to those of normotensive (NT) subjects.

Results : The mean body-mass index (BMI) was higher in both the WHT ($p<0.05$) and SHT groups ($p<0.01$) compared to the NT group, and the mean BMI in the SHT group was higher ($p<0.01$) than the WHT group. The ratio of WHT to NT subjects in the obese group (BMI ≥ 30) was higher than in the normal weight group (18.5 ≤ BMI < 25) ($p<0.05$). The ratio of SHT to NT subjects in the obese group was higher than in the normal weight and overweight groups (25 ≤ BMI < 30) (each, $p<0.01$).

Conclusion : Obesity is associated with both WHT and SHT in university students, which suggests that maintaining a healthy weight is important for the management of WHT and SHT in young adults.

Key words : body-mass index, obesity, white-coat hypertension, sustained hypertension, young adults

Introduction

White-coat hypertension (WHT), in which individuals exhibit high blood pressure (BP) readings in a physician's office but normal BP readings at home, is common in young subjects[1-3]. The clinical consequences of WHT, including its prognosis, are controversial. Some evidence indicates that WHT is benign[4-8], whereas other data suggest that it increases the risk of developing sustained hypertension (SHT)[9] and cardiovascular disease[10-13].

Obesity is a well-known risk factor for hypertension, but the relationship between obesity and WHT is still under debate. Some studies have suggested that being overweight or obese is a risk factor for WHT[9,10,14-17] ; however, other studies have shown no association between BMI and WHT prevalence[18,19].

The association between obesity and WHT is a critical issue for young adults, because obesity in young adults increases the risk for hypertension[20], cardiovascular disease[21,22] and renal disease[23] later in life, suggesting that obese patients with WHT may need to undergo lifestyle changes and early interventions to prevent future dis-

Corresponding author : Masao Kobayashi, MD, PhD
1-1-1, Hondoh, Akita 010-8543, Japan
Tel : +81-18-884-6110,
Fax : +81-18-836-2612
E-mail : ninaika@doc.med.akita-u.ac.jp

ease.

To determine whether obesity is associated with WHT in young adults, we retrospectively examined annual health checkup data and follow-up exam results in students attending Akita University.

Methods

Subject data collection and BP measurements during an annual health exam and post-exam

The subjects in this study were retrospectively enrolled from a total population of 44,238 students who had undergone an annual health exam at Akita University between 2005 and 2014. The health checkup included measurements of body height and weight (while wearing light clothing) with an automatic electronic device (WB-510 ; Tanita, Tokyo, Japan) and BP. The body mass index (BMI) of each student was calculated as follows : weight in kilograms divided by the square of the height in meters (kg/m^2). The students were divided into the following four groups according to NIH criteria : underweight, BMI $<$ 18.5 ; normal weight, 18.5 $\leq$ BMI $<$ 25 ; overweight, 25 $\leq$ BMI $<$ 30 ; obese, BMI $\geq$ 30. The first BP reading was taken using an automatic electronic device (HBP-9020 ; Omron, Kyoto, Japan) with the subject in a sitting position. When the BP was $\geq$ 140/90 mmHg, a second BP reading was measured on the same day by a physician using a mercury sphygmomanometer during the physical examination, and the second BP reading was recorded as exam BP.

Home BP measurement

Students who had an exam BP $\geq$ 140/90 mmHg were asked to return to the health center at a later date, and a third BP reading (post-exam BP) was obtained by a trained nurse using a mercury sphygmomanometer in a sitting position after 3 min of rest. The student was diagnosed with official hypertension when their post-exam BP was still $\geq$ 140/90 mmHg, and others were diagnosed with normotension (NT). Students with official hypertension were advised to measure his/her BP at home using an automatic electronic device (ES-P101, ES-P110, or ES-P600 ; Omron), which was provided by the health center through an oral agreement. Based on the Japanese Society of Hypertension 2004 guidelines, the subjects were asked to measure their BP twice in the morning and twice before going to sleep at night for more than two weeks, and the mean values of the first measurements in the morning and at night were used in this study. WHT was defined as having an at-home BP $<$ 135/85 mmHg, both in the morning and at night ; all other subjects were defined as having SHT. The physician at the health center explained the at-home BP results to each subject, and the subjects were counselled on how to prevent hypertension with a healthy lifestyle. The students were also referred to a clinic for follow-up when needed. This study was approved by the Institutional Review Board of Akita University in 2015.

Avoidance of case overlap

Since students are required to have an annual health checkup every year at Akita University, the same student could potentially be classified into multiple groups based on their BP results from different years. To avoid enrollment overlap, the most severe post-exam BP readings were used.

Exclusion criteria

Students taking medication that might affect BP, those with a history of renal or endocrine disease, those with a positive urine protein test, and those who were more than 30 years old were excluded from the study.

Statistics

All values are expressed as the mean $\pm$ standard deviation. Significant differences among groups were examined using χ^2 tests for the number of subjects, and an analysis of variance (ANOVA) with a Scheffe's post hoc test for all other variables. A paired-t test, an unpaired-t test and a Pearson correlation analysis were also used when appropriate. Statistical analyses were performed using StatView 5.0 (SAS Institute Inc., Cary, NC, USA). A p value $<$ 0.05 was considered statistically significant.

Results

Number of subjects with NT, WHT and SHT

As shown in Figure 1, 1,161 students, all of whom met our inclusion criteria, had an exam BP ≥ 140/90 mmHg during their annual health exam. Post-exam BP monitoring was performed for 839 of 1,161 students, after which 588 cases were diagnosed with NT, and 251 were diagnosed with official hypertension. Home BP readings were obtained for 95 of 251 students, after which 58 were diagnosed with WHT, and 37 were diagnosed with SHT.

Anthropometric data, exam BP and post-exam BP

Subject characteristics and mean exam and post-exam BP readings from the NT, WHT and SHT groups are shown in Table 1. The male to female ratio, and the mean age and height of the students did not differ significantly between groups. The mean weight of the students in the WHT and SHT groups were significantly higher (each, $p<0.01$) than the NT group, and the mean weight of the students in the SHT group were higher (each, $p<0.01$) than in the WHT group. The mean BMI of the students in the WHT and SHT groups were significantly higher ($p<0.05$, $p<0.01$) than the NT group, and the mean BMI of the students in the SHT group were higher (each, $p<0.01$) than in the WHT group. The prevalence of individuals with NT, WHT and SHT in the underweight, normal weight, overweight, and obese groups is shown in Table 3 and depicted in Figure 2 (not including the underweight group). The ratio of subjects with WHT to those with NT in the obese group was significantly higher ($p<0.05$) than the normal weight group. The ratio of subjects with SHT to those with NT in the obese group was significantly higher than that in the normal weight and overweight groups (each, $p<0.01$).

The systolic and diastolic post-exam BP readings of the WHT and SHT subjects were significantly higher (each, $p<0.01$) than the NT group readings, and the diastolic post-exam BP readings of the SHT group subjects were higher ($p<0.01$) than the WHT group readings. In the NT group, the systolic and diastolic post-exam BP readings were significantly lower (each, $p<0.01$) than the exam BP values, while the systolic and diastolic post-exam BP readings did not differ from exam BP values in the WHT or SHT groups.

Home BP readings

Table 2 shows the characteristics and values of both exam and post-exam BP readings of the subjects that did not measure BP at home. The mean BMI of the subjects who measured BP at home did not differ from that of students who did not.

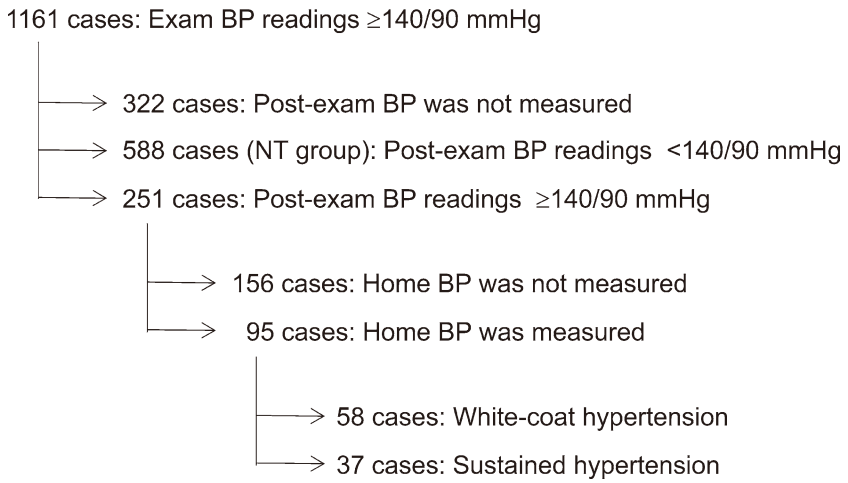

Figure 1. Schematic of the BP readings and relationships between each group. NT, normotension, BP, blood pressure.

Table 1. Characteristics of NT, WHT and SHT subjects

	NT (n = 588)	WHT (n = 58)	SHT (n = 37)
Sex (males : females)	537 : 51	53 : 5	35 : 2
Age	20.6±1.8	20.1±1.5	21.0±2.3
Height (cm)	171.7±7.3	173.6±5.7	173.1±6.1
Weight (kg)	73.2±14.4	80.1±17.7**	92.1±23.0**,##
BMI (kg/m^2)	24.8±4.4	26.5±5.3*	30.7±7.0**,##
Exam BP			
Systolic	145.2±7.9	153.2±11.4**	152.6±10.6**
Diastolic	85.2±9.6	83.8±10.8	90.2±11.6*,##
Post-exam BP			
Systolic	131.0±6.4++	154.2±10.3**	152.7±8.7**
Diastolic	74.6±8.4++	83.6±12.2**	91.9±11.4**,##

NT, normotension ; WHT, white-coat hypertension ; SHT, sustained hypertension ; BMI, body mass index ; BP, blood pressure. All values represent the mean SD.
*p<0.05 and **p<0.01 vs. NT ; ##p<0.01 vs. WHT ; ++p<0.01 vs. exam BP

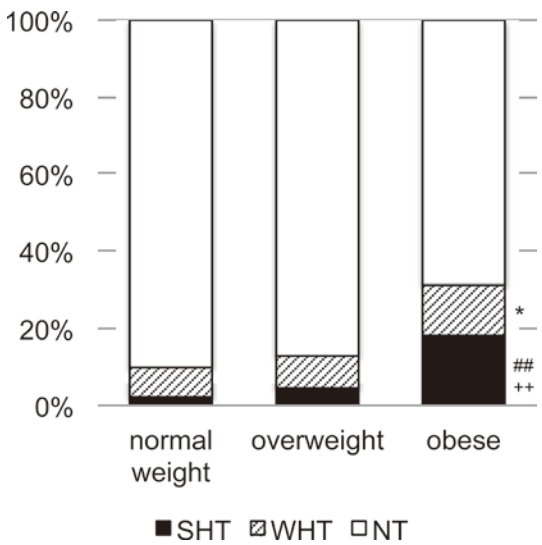

Figure 2. Prevalence of individuals with NT (normotension), WHT (white-coat hypertension) and SHT (sustained hypertension) in normal weight, overweight and obese subjects.
*p<0.05 vs. the ratio of WHT/NT subjects in the normal weight group ; ##p<0.01 vs. the ratio of SHT/NT subjects in the normal weight group ; ++p<0.01 vs. the ratio of SHT/NT subjects in the overweight group.

The mean home BP values are shown in Table 4. The systolic home BP readings taken at night in the WHT and SHT groups were slightly but significantly (p<0.01 and p<0.05) higher than those taken in the morning. The diastolic BP of the WHT group students was slightly but significantly (p<0.01) lower at night compared to the morning, while there was no difference in the diastolic BP of the SHT group students between morning and night. The at-home systolic and diastolic readings taken in the morning were highly correlated to those taken at night in both the WHT (r=0.800, p<0.0001 ; r=0.871, p<0.0001) and SHT (r=0.810, p<0.0001 ; r=0.888, p<0.0001) groups.

Discussion

The prevalence of WHT and SHT in university students was found to be associated with obesity.

For an appropriate diagnosis of WHT or SHT, obtaining stable official BP and at-home BP readings are essential. Since BP measurement occurs during annual health checkups, students with hypertension revealed by exam BP readings were asked to return to the health center, and a post-exam BP reading was taken after appropriate rest. As shown in Table 1, the post-exam BP

Table 2. Characteristics of subjects who did and did not measure home-BP

	Measured (n = 95)	Unmeasured (n = 156)	p value
Sex (males : females)	88 : 7	142 : 14	NS
Age	20.5±1.9	20.6±2.2	NS
Height (cm)	173.4±5.8	171.8±7.1	NS
Weight (kg)	84.8±20.7	80.6±18.9	NS
BMI (kg/m^2)	28.1±6.3	27.3±6.0	NS
Exam BP			
Systolic (mmHg)	153.0±11.0	151.5±12.0	NS
Diastolic (mmHg)	86.3±11.5	86.9±9.6	NS
Post-exam BP			
Systolic (mmHg)	153.6±9.7	145.8±9.6	<0.0001
Diastolic (mmHg)	86.8±12.5	83.1±10.4	0.0119

BP, blood pressure ; BMI, body mass index. All values represent the mean ± SD.

Table 3. Prevalence of NT, WHT and SHT in underweight, normal weight, overweight, and obese subjects

	Underweight (n = 18)	Normal weight (n = 365)	Overweight (n = 195)	Obese (n = 105)
NT	18 (100%)	328 (89.8%)	170 (87.2%)	72 (68.6%)
WHT	0 (0%)	28 (7.7%)	16 (8.2%)	14 (13.3%)
SHT	0 (0%)	9 (2.5%)	9 (4.6%)	19 (18.1%)

NT, normotension ; WHT, white-coat hypertension ; SHT, sustained hypertension.

Table 4. HBP readings of WHT and SHT subjects

	WHT (n = 58)	SHT (n = 37)
Systolic HBP (mmHg)		
Morning	121.2±7.1	136.6±11.1**
Night	123.9±7.1$^{\#\#}$	139.1±10.2**,$^{\#}$
Diastolic HBP (mmHg)		
Morning	73.1±7.5	84.0±10.4**
Night	71.0±8.1$^{\#\#}$	82.2±13.0**

WHT, white-coat hypertension ; SHT, sustained hypertension ; HBP, home blood pressure. All values represent the mean ± SD.
**p<0.01 vs. WHT ; $^{\#}p$<0.05 and $^{\#\#}p$<0.01 vs. morning.

of the NT group subjects was significantly lower than the corresponding exam BP, indicating that the post-exam BP readings were obtained in a well-rested state. However, despite the same protocols and rest periods, there were no significant differences between the exam and post-exam BPs of WHT and SHT subjects. Therefore, the post-exam BP readings were regarded as representative (official). The at-home BP readings taken in the morning were significantly correlated with those taken at night in both the WHT and SHT groups, indicating that the at-home BP readings were also stable. The mean official and at-home BP readings in this study are similar to a previous study of BP in university students[3].

Long-term follow-up studies have shown that being overweight or obese is a risk factor for hypertension at every age[24-26] ; however, WHT has not been separated from SHT in these studies. Since a large number of subjects with hypertension have WHT[1,2], it is reasonable to assume that being overweight or obese is associated with WHT across the age range considered in this study.

Other reports that considered WHT separately from

SHT indicate that being overweight is related to both WHT and SHT in middle-aged and older individuals[9,11,15], though little information is available for young adults. Helvaci *et al.*[17] reported that the prevalence of WHT among young overweight adults was higher than normal weight adults. Ejima *et al.*[3] showed that, in a university-age population, individuals with SHT were more likely to be overweight than individuals with WHT, but they did not include a comparison with NT subjects. In addition, Saito *et al.*[14] reported that weight control is important for the management of both WHT and SHT in young individuals. These findings, as well as the results of the present study, suggest that obesity is associated with both WHT and SHT in young adults.

Several previous studies showed no association between body weight and WHT[18,19]. Why these results differ from the results in the present study is not known ; however, the older age of the study populations, and a higher female to male ratio may account for some differences. In particular, the higher BMI of the NT group in their studies may have decreased the effects of obesity on WHT and SHT.

Although it is beyond the scope of this study to consider the mechanisms that connect obesity with WHT, previous studies have shown that subjects with WHT were more overweight and insulin-resistant than NT subjects[1,11]. Another study reported that WHT was associated with both autonomic dysregulation and a high BMI compared to NT[27]. These findings support the results of the present study.

Obesity in young adults is a growing concern in public health, since accumulating data suggest that obesity in young adults is associated with increased risk for hypertension, 20 cardiovascular disease[21,22] and renal disease[23] later in life. If obesity is also associated with WHT in young adults, patients with WHT should be recommended to maintain a normal weight, even though the long-term prognosis of WHT is unknown.

This study has some limitations. First, since this was a retrospective study, it may contain unknown selection biases. Second, not all cases were included. Post-exam BP measurements were obtained in only 72% of subjects with exam BP hypertension, but the mean BMI of subjects that took at-home BP readings did not differ from those that did not. Third, the number of subjects with WHT and SHT was not large, but few university students have hypertension after repeated BP measurements as previously reported[3], and the relatively homogeneous population in this study is still meaningful. Fourth, since the number of female subjects with WHT and SHT was small, our results cannot be extrapolated to draw conclusions about young adult females.

In conclusion, being obese was found to be associated with WHT and SHT in university students, suggesting that maintaining a healthy weight is important in the management of not only SHT, but also WHT in young adults.

Acknowledgments

We gratefully acknowledge the nursing support of Yukiko Fujiwara, Chiaki Anbo and MikakoTakaya to the students.

Conflict of interest

The authors have no conflicts of interest to declare.

References

1) Julius, S., Mejia, A., Jones, K., *et al.* (1990) "White coat" versus "sustained" borderline hypertension in Tecumseh, Michigan. *Hypertension*, **16**, 617-623.
2) Lurbe, E., Invitti, C., Torro, I., Maronati, A., Aguilar, F., Sartorio, G., Redon, J. and Parati, G. (2006) The impact of the degree of obesity on the discrepancies between office and ambulatory blood pressure values in youth. *J. Hypertens.*, **24**, 1557-1564.
3) Ejima, Y., Hasegawa, Y., Sanada, S., *et al.* (2006) Characteristics of young-onset hypertension identified by targeted screening performed at a university health check-up. *Hypertens. Res.*, **29**, 261-267.
4) Verdecchia, P., Porcellati, C., Schillaci, G., *et al.* (1994) Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. *Hypertension,* **24**, 793-801.
5) Khattar, R.S., Senior, R. and Lahiri, A. (1998) Cardiovascular outcome in white-coat versus sustained mild hypertension. A 10-year follow-up study. *Cir-*

culation, **98**, 1892-1897.

6) Ohkubo, T., Kikuya, M., Metoki, H., Asayama, K., Obara, T., Hashimoto, J., Totsune, K., Hoshi, H., Satoh, H. and Imai, Y. (2005) Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring. 10-year follow-up from the Ohasama study. *J. Am. Coll. Cardiol.*, **46**, 508-515.

7) Mancia, G., Facchetti, R., Bombelli, M., Grassi, G. and Sega, R. (2006) Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. *Hypertension,* **47**, 846-853.

8) McNiece, K.L., Gupta-Malhotra, M., Samuels, J., Bell, C., Garcia, K., Poffenbarger, T., Sorof, J.M. and Portman, R.J. (2007) Left ventricular hypertrophy in hypertensive adolescents. Analysis of risk by 2004 national high blood pressure education program working group staging criteria. *Hypertension,* **50**, 392-395.

9) Mancia, G., Bombelli, M., Facchetti, R., Madotto, F., Quarti-Trevano, F., Friz, H.P., Grassi, G. and Sega, R. (2009) Long-term risk of sustained hypertension in white-coat or masked hypertension. *Hypertension,* **54**, 226-232.

10) Glen, S.K., Elliot, H.L., Curzio, J.L., Lees, K.R. and Reid, J.L. (1996) White-coat hypertension as a cause of cardiovascular dysfunction. *Lancet,* **348**, 654-657.

11) Muldoon, M.F., Nazzaro, P., Sutton-Tyrrell, K. and Manuck, S.B. (2000) White-coat hypertension and carotid artery atherosclerosis. A matching study. *Arch. Intern. Med.*, **160**, 1507-1512.

12) Sega, R., Trocino, G., Lanzarotti., A., *et al.* (2001) Alterations of cardiac structure in patients with isolate office, ambulatory, or home hypertension. Data from the general population (Pressione Arteriose Monitore e Loro Associazioni [PAMELA] study). *Circulation,* **104**, 1385-1392.

13) Longo, D., Zaetta, V., Perkovic, D., Frezza, P., Ragazzo, F., Mos, L., Santonastaso, M., Garbelotto, R., Benetos, A. and Palatini, P. (2006) Impaired arterial elasticity in young patients with white-coat hypertension. *Blood Press. Monit.*, **11**, 243-249.

14) Saito, I., Murata, K., Tsujioka, M., Kawabe, H. and Saruta, T. (1998) Long-term changes in clinic blood pressure in patients with white-coat hypertension. *Blood Press. Monit*., **3**, 97-100.

15) Bjorklund, K., Lind, L., Vessby, B., Andren, B. and Lithell, H. (2002) Different metabolic predictors of white-coat and sustained hypertension over a 20-year follow up period. A population-based study of elderly men. *Circulation,* **106**, 63-68.

16) Kotsis, V., Stabouli, S., Bouldin, M., Low, A., Toumanidis, S. and Zakopoulos, N. (2005) Impact of obesity on 24-hour ambulatory blood pressure and hypertension. *Hypertension,* **45**, 602-607.

17) Helvaci, M.R., Kaya, H., Yalcin, A. and Kuvandik, G. (2007) Prevalence of white coat hypertension in underweight and overweight subjects. *Int. Heart J.,* **48**, 605-613.

18) Niiranen, T.J., Jula, A.M., Kantola, I.M. and Reunanen, A. (2006) Prevalence and determinants of isolated clinic hypertension in the Finnish population : the Finn-HOME study. *J. Hypertens,* **24**, 463-470.

19) Ben-Dov, I.Z., Mekler, J., Ben-Arie, L. and Bursztyn, M. (2007) Lack of association between body-mass index and white-coat hypertension among referred patients. *Blood Press. Monit.*, **12**, 95-99.

20) Suglia, S.F., Clark, C.J. and Gary-Webb, T.L. (2013) Adolescent obesity, change in weight status, and hypertension. Racial/ethnic variations. *Hypertension,* **61**, 290-295.

21) Silventoinen, K., Magnusson, P.K.E., Neovius, M., Sundstroem, J., Batty, G.D., Tynelius, P. and Rasmussen, F. (2008) Does obesity modify the effect of blood pressure on te risk of cardiovascular disease? A population-based cohort study of more than one million Swedish men. *Circulation,* **118**, 1637-1642.

22) Tirosh, A., Shai, I., Afek, A., *et al.* (2011) Adolescent BMI trajectory and risk of diabetes versus coronary disease. *N. Engl. J. Med.,* **364**, 1315-1325.

23) Silverwood, R.J., Pierce, M., Thomas, C., Hardy, R., Ferro, C., Sattar, N., Whincup, P., Savage, C., Kuh, D. and Nitsch, D. (2013) Association between younger age when first overweight and increased risk for CKD. *J. Am. Soc. Nephrol*., **24**, 813-821.

24) Skarfors, E.T., Lithell, H.O. and Selinus, I. (1991) Risk factors for the development of hypertension : a 10-year longitudinal study in middle-aged men. *J. Hypertens*., **9**, 217-223.

25) Kawasaki, T., Uezono, K., Sanefuji, M., Utsunomiya, H., Fujino, T., Kanaya, S. and Babazono, A. (2003) A 17-year follow-up study of hypertensive and normotensive male university students in Japan. *Hypertens. Res.,* **26**, 445-452.

26) Juonala, M., Magnussen, C.G., Berenson, G.S., *et al.* (2011) Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N. Engl. J. Med.*, **365**, 1876-1885.

27) Neumann, S.A., Jennings, J.R., Muldoon, M.F. and Manuck, S.B. (2005) White-coat hypertension and autonomoc nervous system dysregulation. *Am. J. Hypertens.*, **18**, 584-588.