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Determinant of Arterial Stiffness in Young Adults

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Cardiovascular disease (CVD) risk factors may be acting several decades before CVD becomes manifest. Data from young subjects may be valuable in further elucidating at this issue. We evaluated the association between baPWV (brachial-ankle pulse wave velocity) and cardiovascular risk factors in apparently healthy young adults. A total of 46 male and 91 female adolescents aged 18~25 years were studied. baPWV increased in a dose-responsive manner as the number of metabolic syndrome components. In both gender groups, baPWV was positively correlated with age. In males, waist, circumference total cholesterol, and LDL-cholesterol were positively correlated with baPWV, and in females, blood pressure (BP) was positively correlated with baPWV. Age, gender, mean BP, and Homeostasis model assessment insulin resistance (HOMA-IR) were found to be independent factors associated with baPWV levels. In conclusion, mean BP, age, gender, and HOMA-IR were associated with baPWV in young adults. This result suggests that multiple cardiovascular risk factors may be associated with an increased risk of arterial stiffness in young adults.

Key Words: baPWV, Cardiovascular risk factor, Arterial stiffness

INTRODUCTION

Cardiovascular disease (CVD) is the most important disease, leading to serious morbidity and mortality. Since the 1980s, presumably as the influence of an increasingly westernized lifestyle, the risk factors of atherosclerosis and preclinical atherosclerosis have been increasing. Increasing arterial stiffness is one of the pathological symptoms of vascular damage, and is closely associated with atherosclerotic cardiovascular diseases (Cohn, 2001).

Pulse wave velocity (PWV) is known to be an indicator of arterial stiffness and a marker of vascular damage. Recent studies have demonstrated that PWV is not only a risk marker of cardiovascular disease, but also its prognostic predictor (Tomiyama et al., 2003; Fujiwara et al., 2004; Mitchell et al., 2004). baPWV has potential as a new marker of cardiovascular risk; compared to conventional markers, it is easy to obtain and serves as an indicator of either atheroscleric cardiovascular risk or severity of atherosclerotic vascular damage. Thus, it is useful for screening the general population (Yamashina et al., 2003; Yokoyama et al., 2003).

Recent studies have shown that the validity (Yamashina et al., 2002) and reproducibility (Matsui et al., 2004) of this method are acceptable and also correlate well with aortic (Yamashina et al., 2002) or carotid-femoral PWV (Munakata et al., 2003). Pathological studies have shown that the atherosclerotic process starts during childhood (Stary, 2000) and from the late teens associations between the early stages of atherosclerotic lesions and CVD risk factors have been seen (McGill et al., 2000). This suggests that traditional CVD risk factors may be acting several decades before CVD becomes manifest. Data from young subjects may be valuable in further elucidating at this issue. The aim of this study was to describe the determinants of arterial stiffness

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in apparently healthy young adults.

MATERIALS AND METHODS

1. Participants

All participants signed an informed consent form approved by the hospital's ethical committee. School based volunteers were recruited via a public advertisement, which was written by an educational institution. A total of 46 male and 91 female apparently healthy young adults from 18~25 years of age were included. Exclusion criteria were a medical history or evidence upon physical examination of cardiovascular disease, a body weight fluctuation of more than 5 kg in the previous six months, endocrine disorders, or medication (and supplements) that could affect cardiovascular function or metabolism. We used a questionnaire to assess past and current medical illnesses of the study participants, as well as lifestyle choices such as alcohol ingestion and cigarette smoking. With respect to smoking, individuals were classified according to whether the respondent was a non-smoker, an ex-smoker, or a current smoker. And alcohol ingestion was defined as mild:≥1/2 bottle, moderate:≥1 bottle, severe ≥ 2 bottle Soju one time.

2. Methods

Anthropometric measurements were taken with the participants in light clothing and without shoes. Height to the nearest 0.1 cm and weight to the nearest 0.1 kg were measured by an automatic height-weight scale. BMI (body mass index) was calculated as the participants' weight divided by their height squared. Body fat percentages were measured with a TBF-105 body fat analyzer (Tanita Co., Tokyo, Japan). Waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. Hip circumference was measured at the widest part of the hip region, and thigh circumference was measured 10 cm proximal to the superior patella border. To reduce variation in measurements, one person measured all anthropometric parameters throughout the study. baPWV was measured using a volume-plethysmographic apparatus (PWV/ABI, Colin Co., Komaki, Japan). This device records the phonocardiogram, electrocardiogram, volume pulse form, and arterial blood pressure (BP) at both the left and right brachia and ankles. baPWV was calculated by time-phase analysis of the right brachial and volume waveforms at both ankles. The distance between the right brachium and ankle was estimated based on body height. In addition, because there was a significant correlation between the right PWV and left PWV, we used the resulting mean PWV for analysis. The coefficient of variation for interobserver reproducibility was 3.3±2.4%, while intraobserver reproducibility was 3.7 ±2.8%.

Blood samples were obtained from each participant after an 8-h overnight fast from an antecubital vein, and placed into plain vacutainer. High sensitivity C-reactive protein (hs-CRP), fasting glucose, total cholesterol, triglyceride, and HDL-cholesterol were measured by an ADVIA 1650 Chemistry system (Bayer, Tarrytown, NY, USA), and LDL-cholesterol was calculated from the Friedewald equation (Friedewald et al., 1972). Fasting insulin was measured by electrochemilumi nescence immunoassay (Roche, Indianapolis, IN, USA). Insulin resistance was estimated by the homeostatic model assessment (HOMA-IR); the calculations were as follows: HOMA-IR = (Insulin (μIU/ml) × Fasting blood glucose (mg/dl)/18) / 22.5.

According to the NCEP criteria (Executive Summary of NCEP, 2001), a participant was defined as having the metabolic syndrome if he or she fulfilled three or more of the following criteria. We applied WHO Asia-Pacific obesity criteria as a definition of abdominal obesity in this study (WHO refining obesity, 2000). Waist circumference ≥90 cm in men and ≥80 cm in women for abdominal obesity, triglyceride ≥150 mg/dl, HDL cholesterol <40 mg/dl for men and <50 mg/dl foe women, blood pressure:≥130/85 mmHg, and fasting glucose:≥110 mg/dl.

3. Statistical analysis

Data are expressed as means ± S.D. hs-CRP was logarithmically transformed prior to statistical testing to improve normality. Clinical and metabolic characteristics between genders of the study population were compared using the t-test for continuous variables. Chi-square tests were performed for proportion of smoking status and alcohol consumption. An analysis of variance (ANOVA) was performed to assess the differences in baPWV levels according to metabolic syndrome. Pearson's correlation coefficients were calculated to evaluate the relationship between baPWV and clinical variables. We used multiple linear regression analysis to the multivariates associations between baPWV as a dependent variable and CVD risk factors. Significance was

defined at the 0.05 level of confidence. All calculations were performed using the Statistical Package for Social Sciences software, version 10.0 (SPSS, Chicago, IL, USA).

RESULTS

1. Subject characteristics

The clinical characteristics of male and female young adults are shown in Table 1. Age, waist circumference, hip circumference, systolic BP, diastolic BP, fasting glucose, baPWV and cigarette smoking were significantly lower in females. However, body fat percent was significantly higher in female compared to male young adults. In contrast, there was no significant difference in BMI, WHR (waist hip ratio), fasting insulin, HOMA-IR, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, hs-CRP, and alcohol ingestion between genders.

2. Correlation between baPWV, lipids and other parameters

In both gender groups, baPWV was positively correlated with age. In males, waist circumference, total cholesterol, and LDL-cholesterol were positively correlated with baPWV, and in females, blood pressure was positively correlated with baPWV as shown in Table 2.

3. Multiple linear regression analysis to assess independent relationships between baPWV and clinical variables

Gender, age, mean blood pressure ($P<0.01$, respectively), and HOMA-IR ($P<0.05$) were found to be independent factors associated with baPWV levels after adjustments were made for potential influences of body fat percent, fasting glucose, hs-CRP, LDL-cholesterol, and smoking habit, as shown in Table 3.

4. baPWV levels according to metabolic syndrome

baPWV increased in a dose-responsive manner as the number of metabolic syndrome components as shown in Fig. 1.

DISCUSSION

In this study of young adult, we found that baPWV was associated with mean blood pressure, age, gender, and

Table 1. Clinical and metabolic characteristics of study participants

Characteristics	Male (N=46)	Female (N=91)	*P*-value
Age (years)	21.0±2.4	20.0±1.9	<0.01
Adiposity index			
BMI[a] (Kg/m^2)	22.8±2.6	21.9±3.2	0.09
Waist (cm)	77.0±6.0	69.1±6.9	<0.001
Hip (cm)	97.1±4.3	94.9±6.0	<0.05
WHR[b]	0.82±0.04	0.82±0.05	0.83
Body fat percent (%)	19.7±4.6	31.1±5.3	<0.001
Blood pressure (mmHg)			
Systolic	125.0±12.9	112.6±12.4	<0.001
Diastolic	72.7±13.2	66.9±10.1	<0.05
Mean	90.2±12.6	82.2±9.8	<0.001
Glucose tolerance index			
Fasting glucose (mg/dl)	92.3±6.9	89.7±7.0	<0.05
Fasting insulin (μIU/m)	6.8±4.2	7.1±4.1	0.99
HOMA-IR[c]	1.6±1.2	1.6±1.0	0.78
Lipid profile			
Total cholesterol (mg/dl)	163.6±25.3	167.7±25.2	0.36
Triglyceride (mg/dl)	78.3±32.5	78.6±42.9	0.97
HDL-cholesterol[d] (mg/dl)	53.6±12.5	55.4±10.6	0.39
LDL-cholesterol[e] (mg/dl)	94.3±21.3	96.7±22.2	0.55
hs-CRP[f] (mg/ml)	0.06±1.12	0.05±1.12	0.13
baPWV[g] (cm/sec)	1,261.4±144	1,101.9±110	<0.001
Smoking[h]			
None	20 (43.8)	78 (85.7)	<0.001
Ex-smoker	7 (15.2)	6 (6.6)	
Current smoker	19 (41.3)	7 (7.7)	
Alcohol[i]			
≤ Mild	12 (26.1)	36 (39.6)	0.20
Moderate	26 (56.5)	46 (50.6)	
Severe	8 (17.4)	9 (9.9)	

Data are shown as means ± the standard deviation.
P-values are calculated by t-test.
[a] Body mass index.
[b] Waist hip ratio.
[c] Homeostasis model assessment insulin resistance.
[d] High density lipoprotein cholesterol.
[e] Low density lipoprotein cholesterol.
[f] High-sensitivity C-reactive protein.
[g] Brachial-ankle pulse wave velocity.
[h] Smoking status was divided a non-smoker, an ex-smoker, or a current smoker
[i] Alcohol ingestion was defined as mild: ≥ 1/2 bottle, moderate: ≥ 1 bottle, severe ≥ 2 bottle Soju one time

Table 2. Correlations between baPWV[a] levels and various parameters

Variables	baPWV			
	Male (N=46)		Female (N=91)	
	r	*P*	*r*	*P*
Age (years)	0.347	<0.05	0.345	<0.001
Adiposity index				
BMI[b] (Kg/m^2)	0.193	0.12	0.019	0.86
Waist (cm)	0.297	<0.05	-0.05	0.64
WHR[c]	0.244	0.10	-0.025	0.81
Body fat %	0.224	0.13	0.035	0.74
Blood pressure (mmHg)				
Systolic	0.118	0.46	0.331	<0.05
Diastolic	0.070	0.65	0.410	<0.001
Mean	0.087	0.56	0.419	<0.001
Glucose tolerance index				
Fasting glucose (mg/dl)	0.057	0.71	0.068	0.52
Fasting insulin (μIU/m)	-0.213	0.16	-0.137	0.20
HOMA-IR[d]	-0.171	0.26	-0.112	0.29
Lipid profile				
Total cholesterol (mg/dl)	0.360	<0.05	0.018	0.86
Triglyceride (mg/dl)	0.022	0.89	0.089	0.40
HDL-cholesterol[e] (mg/dl)	0.017	0.91	-0.181	0.09
LDL-cholesterol[f] (mg/dl)	0.411	<0.01	0.073	0.49
Inflammatory index				
Log (hs-CRP[g]) (mg/ml)	0.142	0.35	-0.046	0.67

Coefficients (*r*) and *P*-values were calculated by the Pearson correlation model.
[a] Brachial-ankle pulse wave velocity.
[b] Body mass index.
[c] Waist-to-hip ratio.
[d] Homeostasis model assessment insulin resistance.
[e] High density lipoprotein cholesterol.
[f] Low density lipoprotein cholesterol.
[g] High-sensitivity C-reactive protein.

Table 3. Multiple regression analysis[a] to assess independent relationships between baPWV[b] and clinical variables

Variables	Parameter Estimate	SE	*P*
Gender	-114.2	38.98	<0.01
Age	16.66	5.07	<0.01
Mean BP[c]	2.70	0.96	<0.01
HOMA-IR[d]	-20.51	10.29	<0.05
LDL-cholesterol[e]	0.67	0.48	0.16
Smoking11[f]	-1.19	35.5	0.97
Smoking12[g]	-6.42	28.0	0.82
Body fat percent	-0.30	2.29	0.89
Glucose	2.10	1.54	0.18
Log (hs-CRP[h])	4.47	7.61	0.56

[a] Calculated by multiple regression model using baPWV as the dependent variable. R^2: 0.433, F-value: 9.66, P<0.001.
[b] Brachial-ankle pulse wave velocity.
[c] Mean blood pressure.
[d] Homeostasis model assessment insulin resistance
[e] Low density lipoprotein cholesterol.
[F] Non-smoker versus ex-smoker
[g] Non-smoker versus current smoker
[h] High-sensitivity C-reactive protein.

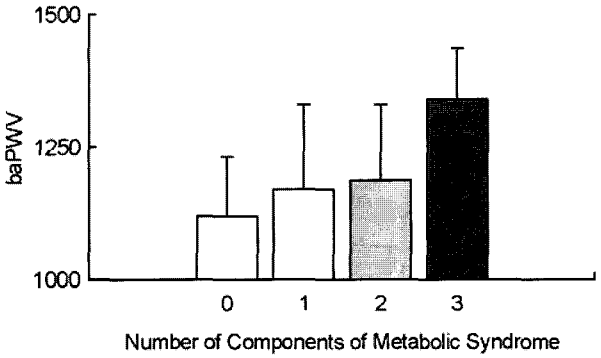

Fig. 1. baPWV (brachial-ankle pulse wave velocity) levels according to the number of components of metabolic syndrome. The respective mean baPWV levels were 1,119.8 (n=87), 1,181.9 (n=29), 1,202.6 (n=10), and 1,338.4 cm/sec (n=8) (*P* for trend <0.01).

HOM-IR. The association between PWV and blood pressure is in concordance with previous studies in university students (Shiotani et al., 2005), hypertensive adolescent (Pall et al., 2003), and adulthood (Li et al., 2004). Also, IMT (intima-media thickness) in common carotid artery was higher in hypertensive adolescents than in a healthy control group (Pall et al., 2003). Systolic blood pressure measured since childhood was a consistent and independent predict of baPWV in adult (Li et al., 2004). Those who had higher blood pressure levels in childhood had stiffer arteries 26 years later, which suggests that blood pressure even in early childhood plays a role in the process of arterial stiffening.

Using various assessment techniques, an age-dependent increase in arterial stiffness on both healthy and diseased populations has been described. We also examined the correlation between baPWV and age. This is consistent with previous investigations (Fujiwara et al., 2004; Mitchell et al., 2004). These results indicate that arteries become less elastic with age, and arterial stiffening was observed with increasing age (Oren et al., 2003). Age induces structural and functional abnormalities such as arterial wall hypertrophy and degeneration or disorganization of the medial layer. These change increase PWV because of increased arterial stiffness (Tomiyama et al., 2003).

Our finding in association between baPWV and gender and insulin resistance were also consistent with other studies. Mean IMT was higher in men than women likewise the mean PWV and the percentage with plaque were higher in men (de Bree et al., 2005). The possibility of the gender differences in arterial stiffness may be both intrinsic and influenced by sex steroids (Waddell et al., 2001). baPWV was also associated with fasting insulin and HOMA-IR values (Nakanishi et al., 2005), insulin resistance status measured cross-sectionally in adulthood by fasting glucose and insulin was also an independent determinant of arterial stiffness (Urbina et al., 2002).

In this study, in male, baPWV was significantly related to total cholesterol and LDL-cholesterol, this finding is in line recent studies (Riley et al., 1986; Liang et al., 2001; Urbina et al., 2002; Benetos et al., 2002; Tomiyama et al., 2003; Kontopoulos et al., 2003; Li et al., 2004;). These investigations reported lipid profile in adulthood was cross-sectionally associated with baPWV in young adulthood.

From this analysis in relation to the number of components of metabolic syndrome, baPWV increased in a dose-responsive manner as the number of metabolic syndrome components. This result indicate that metabolic syndrome defined as the clustering of any three or more altered components, was itself an independent predictor of stiffness. In several studies was reported that carotid arterial distensibility was associated with several variables of metabolic syndrome, as well as with clustering of variables of metabolic syndrome (van Popele et al., 2000; Scuteri et al., 2004; Nakanishi et al., 2005). The limitation of this investigation, the cross-sectional study design lacks information on the time sequence of events.

In conclusion, mean blood pressure, age, gender, and HOM-IR were associated with baPWV in young adults. It may be important to focus on multiple cardiovascular risk factors early in life. Interventions related to modifiable risk factors, such as the prevention of smoking, weight control, and encouragement of physical exercise and prudent diet, if undertaken early in life, may retard the development of atherosclerosis.

REFERENCES

Benetos A, Waeber B, Izzo J, Mitchell G, Resnick L, Asmar R, Safar M. Influence of age, risk factors, and cardiovascular and renal disease on arterial stiffness: clinical applications. Am J Hypertens. 2002. 15: 1101-1108.

Cohn JN. Arterial compliance to stratify cardiovascular risk: more precision in therapeutic decision making. Am J Hypertens. 2001. 14: 258S-263S.

de Bree A, Mennen LI, Zureik M, Ducros V, Guilland JC, Nicolas JP, Emery-Fillon N, Blacher J, Hercberg S, Galan P. Homocysteine is not associated with arterial thickness and stiffness in healthy middle-aged French volunteers. Int J Cardiol. 2005. (in press).

Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. JAMA. 2001. 285: 2486-2497.

Friedewald WT, Levy RI, Fridrikson DS. Estimation of concentrations of low density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem. 1972. 18: 499-502.

Fujiwara Y, Chaves P, Takahashi R, Amano H, Kumagai S, Fujita K, Yoshida H, Wang DG, Varadhan R, Uchida H, Shinkai S. Relationships between brachial-ankle pulse wave velocity and conventional atherosclerotic risk factors in community-dwelling people. Prev Med. 2004. 39: 1135-1142.

Kontopoulos AG, Athyros VG, Pehlivanidis AN, Demitriadis DS, Papageorgiou AA, Boudoulas H. Long-term treatment effect of atorvastatin on aortic stiffness in hypercholesterolaemic patients. Curr Med Res Opin. 2003. 19: 22-27.

Li S, Chen W, Srinivasan SR, Berenson GS. Childhood blood pressure as a predictor of arterial stiffness in young adults: the bogalusa heart study. Hypertension. 2004. 43: 541-546.

Liang YL, Shiel LM, Teede H, Kotsopoulos D, McNeil J, Cameron JD, McGrath BP. Effects of Blood Pressure, Smoking, and Their Interaction on Carotid Artery Structure and Function. Hypertension 2001. 37: 6-11.

Matsui Y, Kario K, Ishikawa J, Eguchi K, Hoshide S, Shimada K. Reproducibility of arterial stiffness indices (pulse wave velocity and augmentation index) simultaneously assessed by automated pulse wave analysis and their associated risk factors in essential hypertensive patients.Hypertens Res. 2004. 27: 851-857.

McGill HC Jr, McMahan CA, Zieske AW, Sloop GD, Walcott JV, Troxclair DA, Malcom GT, Tracy RE, Oalmann MC, Strong JP. Associations of coronary heart disease risk factors with

the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler Thromb Vasc Biol. 2000. 20: 1998-2004.

Mitchell GF, Parise H, Benjamin EJ, Larson MG, Keyes MJ, Vita JA, Vasan RS, Levy D. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. Hypertension 2004. 43: 1239 -1245.

Munakata M, Ito N, Nunokawa T, Yoshinaga K. Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. Am J Hypertens. 2003. 16: 653-657.

Nakanishi N, Shiraishi T, Wada M. Brachial-ankle pulse wave velocity and metabolic syndrome in a Japanese population: the Minoh study. Hypertens Res. 2005. 28: 125-131.

Oren A, Vos LE, Bos WJ, Safar ME, Uiterwaal CS, Gorissen WH, Grobbee DE, Bots ML. Gestational age and birth weight in relation to aortic stiffness in healthy young adults: two separate mechanisms? Am J Hypertens. 2003. 16: 76-79.

Pall D, Settakis G, Katona E, Csiba L, Kakuk G, Limburg M, Bereczki D, Fulesdi B. Debrecen Hypertension Study. Increased common carotid artery intima media thickness in adolescent hypertension: results from the Debrecen Hypertension study. Cerebrovasc Dis. 2003. 15: 167-172.

Riley WA, Freedman DS, Higgs NA, Barnes RW, Zinkgraf SA, Berenson GS. Decreased arterial elasticity associated with cardiovascular disease risk factors in the young. Bogalusa Heart Study. Arteriosclerosis. 1986. 6: 378-386.

Scuteri A, Najjar SS, Muller DC, Andres R, Hougaku H, Metter EJ, Lakatta EG. Metabolic syndrome amplifies the age-associated increases in vascular thickness and stiffness. J Am Coll Cardiol. 2004. 21: 1388-1395.

Shiotani A, Motoyama M, Matsuda T, Miyanishi T. Brachial-ankle pulse wave velocity in Japanese university students. Intern Med. 2005. 44: 696-701.

Stary HC. Lipid and macrophage accumulations in arteries of children and the development of atherosclerosis. Am J Clin Nutr. 2000. 72: 1297S-1306S.

Tomiyama H, Yamashina A, Arai T, Hirose K, Koji Y, Chikamori T, Hori S, Yamamoto Y, Doba N, Hinohara S. Influences of age and gender on results of noninvasive brachial-ankle pulse wave velocity measurement--a survey of 12517 subjects. Atherosclerosis. 2003. 166: 303-309.

Urbina EM, Brinton TJ, Elkasabany A, Berenson GS. Brachial artery distensibility and relation to cardiovascular risk factors in healthy young adults (The Bogalusa Heart Study). Am J Cardiol. 2002. 89: 946-951.

van Popele NM, Westendorp IC, Bots ML, Reneman RS, Hoeks AP, Hofman A, Grobbee DE, Witteman JC. Variables of the insulin resistance syndrome are associated with reduced arterial distensibility in healthy non-diabetic middle-aged women. Diabetologia 2000. 43: 665-672.

Waddell TK, Dart AM, Gatzka CD, Cameron JD, Kingwell BA. Women exhibit a greater age-related increase in proximal aortic stiffness than men. J Hypertens. 2001. 9: 2205-2212.

WHO, The Asia-Pacific perspective: refining obesity and its treatment, IOTF, February 2000.

Yamashina A, Tomiyama H, Arai T, Hirose K, Koji Y, Hirayama Y, Yamamoto Y, Hori S. Brachial-ankle pulse wave velocity as a marker of atherosclerotic vascular damage and cardiovascular risk. Hypertens Res. 2003. 26: 615-622.

Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, et al. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. Hypertens Res. 2002. 25: 359-364.

Yokoyama H, Hirasawa K, Aoki T, Ishiyama M, Koyama K. Brachial-ankle pulse wave velocity measured automatically by oscillometric method is elevated in diabetic patients with incipient nephropathy. Diabet Med. 2003. 20: 942-945.