Atherosclerosis 206 (2009) 168–172

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Carotid arterial elasticity is a sensitive atherosclerosis value reflecting visceral fat accumulation in obese subjects

Ai Tokita[a], Yasushi Ishigaki[a], Hisashi Okimoto[a], Hideyuki Hasegawa[c], Yoshiro Koiwa[d], Makoto Kato[e], Hisamitsu Ishihara[a], Yoshinori Hinokio[a], Hideki Katagiri[b], Hiroshi Kanai[c], Yoshitomo Oka[a,*]

[a] Division of Molecular Metabolism and Diabetes, Tohoku University Graduate School of Medicine, 2-1 Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan
[b] Division of Advanced Therapeutics for Metabolic Diseases, Tohoku University Graduate School of Medicine, Japan
[c] Department of Electrical Engineering, Tohoku University Graduate School of Engineering, Tohoku University, Sendai, Japan
[d] Oizumi Memorial Hospital, Shiroishi, Japan
[e] Panasonic Shikoku Electronics Co., Ltd., Yokohama, Japan

ARTICLE INFO

Article history:
Received 30 August 2008
Received in revised form 29 January 2009
Accepted 30 January 2009
Available online 20 February 2009

Keywords:
Elasticity
Obesity
Ultrasound
Visceral adiposity
Early stage atherosclerosis

ABSTRACT

Background: We previously reported the arterial elasticity value we measured to reflect the characteristic features of vessel walls, and to possibly be useful for detecting early stage atherosclerosis in type 2 diabetes. Obesity, especially visceral adiposity, is well known to play a crucial role in the development of metabolic disorders and atherosclerosis. To assess whether arterial elasticity value reflects the effect of obesity on atherosclerosis, we examined the associations of obesity characteristics with atherosclerosis values including arterial elasticity, carotid intima–media thickness (IMT) and pulse wave velocity (PWV).
Methods: Three atherosclerosis values were measured in 78 obese subjects (body mass index ≥30). We investigated the associations of atherosclerosis values with obesity-related parameters including abdominal fat accumulation determined by computed tomography.
Results: Arterial elasticity values were positively related to established atherosclerosis values, carotid IMT and PWV, in obese subjects. Age, systolic blood pressure and hypertension also correlated with these atherosclerosis values. Single regression analysis showed all three atherosclerosis values to correlate significantly with visceral fat area. Intriguingly, visceral fat area is an independent variable affecting arterial elasticity, but not IMT or PWV. Furthermore, multiple regression analysis revealed that arterial elasticity correlates strongly with visceral fat area.
Conclusions: Arterial elasticity value we measure is a new parameter for evaluating atherosclerosis in subjects with visceral adiposity and more sensitive than the currently established atherosclerosis values, carotid IMT and PWV. Measuring arterial elasticity has the potential to reveal minute vascular changes, and may have broad clinical applications for evaluating early stage atherosclerosis.

Obesity has increased dramatically, becoming a global epidemic in recent decades [1]. Obesity is closely associated with the development of atherosclerosis [2], via rising incidences of metabolic disorders, including diabetes, dyslipidemia, hypertension, inflammation, and the prothrombotic state [3]. Furthermore, obesity is involved in sympathetic nerve activation as well as cardiac structural and functional adaptations [4], and is reportedly an independent cardiovascular risk factor [5]. Recent studies have shown that adipocytokines, such as PAI-1, TNF-α and adiponectin, play crucial roles in the development of metabolic disorders and atherosclerosis, in various tissues including the vasculature [6]. In particular, visceral fat accumulation, rather than the body mass index (BMI) or subcutaneous fat accumulation, was shown to be strongly associated with various obesity-related disorders [7], and is thus considered to be a major risk factor for cardiovascular disease [8]. Many studies have shown that increasing body weight is closely related to the surrogate markers associated with atherosclerosis, such as carotid intima–media thickness (IMT) and pulse wave velocity (PWV). In addition, visceral adiposity is reportedly related to atherosclerosis, which is determined by carotid IMT [9–13], coronary calcification [14] and arterial stiffness [15,16]. In some reports, this relationship persisted after adjustments for multiple linear regression analysis [12–15]. While visceral fat areas were correctly measured by computed tomography (CT) scans in few studies [12,15], abdominal ultrasound was employed in many

* Corresponding author. Tel.: +81 22 717 7611; fax: +81 22 717 7611.
E-mail address: oka-y@mail.tains.tohoku.ac.jp (Y. Oka).

0021-9150/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.atherosclerosis.2009.01.046

reports [9–11,13,14,16], which is often imprecise to determine visceral fat area. It has been widely recognized that non-invasive methods of evaluating atherosclerosis have limitations, such as slow changes in carotid IMT and the influence of blood pressure on PWV. Thus, an accurate and practical means of evaluating atherosclerosis is needed.

Recently, we developed a novel non-invasive method for measuring a change in thickness of multiple layers preset in arterial wall during a single heartbeat [17,18]. Briefly, multiple points were preset from the luminal surface to the adventitia of the posterior wall along an ultrasonic beam and the displacements at these preset points were estimated by applying the phased tracking method to the received echo. A layer was defined as being between two points. A minute change in thickness of the layer was obtained by subtraction of the displacements at these two points and then, the strain of the layer was obtained by dividing the change in thickness by the original thickness set at the end diastole. By changing the depth and applying the same procedure, the strains at multiple depths in arterial wall were obtained at constant intervals, usually 80 μm. This innovative phased tracking method enables us to evaluate regional characteristics of the artery in detail; during a single heartbeat these sites either deform easily in soft regions or there is little deformation in hard regions. We integrated changes in thickness, which we describe with the term "arterial elasticity". This "arterial elasticity" measurement is a promising approach to evaluating atherosclerosis [19,20]. Therefore, we applied this method to in vivo detection of regional changes in human carotid arterial walls. In a study of subjects with type 2 diabetes, carotid arterial elasticity correlated significantly with currently established values for atherosclerosis, such as carotid artery IMT and PWV. Intriguingly, in subjects with IMT <1.1 mm, who are classified as not having atherosclerosis as defined by IMT criteria, arterial elasticity correlated with the number of risk factors, i.e. diabetes, dyslipidemia, hypertension and smoking, suggesting that arterial elasticity has potential for detecting early stage atherosclerosis. It was also suggested that measuring arterial elasticity would allow evaluation of qualitative changes in the carotid arterial wall [21].

Herein, to assess whether the effect of obesity on atherosclerosis can be evaluated using arterial elasticity, we examined the associations of obesity characteristics with atherosclerosis values including arterial elasticity, carotid IMT and PWV. We further evaluated the impact of fat distribution on atherosclerosis.

1. Methods

1.1. Study subjects

The study subjects were recruited from among patients with BMI over 30 at Tohoku University Hospital. Patients with type 1 diabetes, renal failure (serum creatinine >2.0 mg/dL), severe heart failure (NYHA functional class 2–4), atrial fibrillation and peripheral arterial disease were excluded from the study. The study protocol was approved by the Tohoku University Institutional Review Board. Informed consent was obtained from each patient.

We used the following criteria for the diagnosis of metabolic disorders. Diabetes was defined as fasting blood glucose ≥7.0 mmol/dl (126 mg/dl) and/or hemoglobin A1c ≥6.5%, based on the definition proposed by the Japan Diabetes Society, or taking antidiabetic drugs including insulin. Dyslipidemia was defined as LDL cholesterol ≥3.6 mmol/dl (140 mg/dl) and/or triglyceride ≥1.7 mmol/l (150 mg/dl), based on the definition proposed by the Japan Atherosclerosis Society in 2007, or taking lipid-lowering drugs. The subjects whose systolic blood pressure (BP) ≥140 mmHg and/or diastolic BP ≥90 mmHg (Japanese Society of Hypertension guidelines 2004) or who were taking antihypertensive drugs were defined as having hypertension. The subjects who currently smoked were classified as current smokers.

1.2. Measurement of arterial wall elasticity

Real-time measurement of regional elasticity in the far wall of common carotid artery (CCA) was achieved based on a previously described method [22] with ultrasound diagnostic equipment (prototype system by Panasonic), which was specialized for measuring regional elasticity. With this system, an ultrasound beam sequentially scanned an artery along its length at 32 positions at intervals of 200 μm with a linear type 7.5-MHz probe.

Multiple points were preset from the luminal surface to the adventitia along each beam at constant intervals of 80 μm, and the displacements at these preset points were estimated by applying the phased tracking method to the received echo. A layer was defined as being between two points, where the distance between these two points (i.e. the thickness of the layer) was set at 320 μm. As shown in Fig. 1C, minute changes in thickness of the layer were obtained by subtraction of the displacements at these two points and then, the strain of the layer was obtained by dividing the change in thickness by the original thickness (320 μm) which was set at the end diastole. By changing the depth of the layer at intervals of 80 μm and applying the same procedure, the strains at multiple depths were obtained at intervals of 80 μm.

The elasticity of each layer was obtained from the maximal strain and the pulse pressure measured at the upper arm. The maximal strain is defined by the absolute value of difference between the maximum and minimum of the measured change in thickness, as shown in Fig. 1C, and the maximal strain was determined at each location, independent of time.

Using the above procedure, the elasticity was obtained at intervals of 80 μm in the direction of depth and 200 μm along its length, as shown in Fig. 1B. Regional elasticity values of multiple sites in each layer were displayed as shown in Fig. 1A and a mean regional elasticity value (kPa) of bilateral CCA was used for analysis.

1.3. Measurement of carotid artery intima–media thickness

IMT of the carotid arteries was measured using ultrasound diagnostic equipment (EUB-450, Hitachi Medico, Tokyo, Japan) with an electrical linear transducer (center-frequency of 7.5 MHz). By B-mode ultrasound, CCA, carotid bulb, and portions of the internal and external carotid arteries on both sides were scanned with the subject in the supine position. IMT was measured at a point on the far wall of the CCA, 1 cm proximal to the bifurcation [23], from the longitudinal scan plane that showed the intima–media boundaries most clearly.

1.4. Measurement of PWV

PWV values were measured using an automatic waveform analyzer (BP-203RPE; Colin Co., Komaki, Japan) [24]. Pulse waves were recorded on the right brachial artery and both posterior tibial arteries. The average PWV was calculated by dividing the arm–ankle distance by the pulse wave transmission time between these points on both sides.

1.5. Measurement of abdominal fat area

Abdominal subcutaneous and intra-abdominal fat areas were measured by CT scans with a SOMATOM Definition (Siemens AG., Munich, Germany) at the level of the fourth lumbar vertebra. The border of the intra-abdominal cavity was outlined on the CT image and the total area of visceral fat was measured at an attenuation range of −200 and −50 Hounsfield units [25].

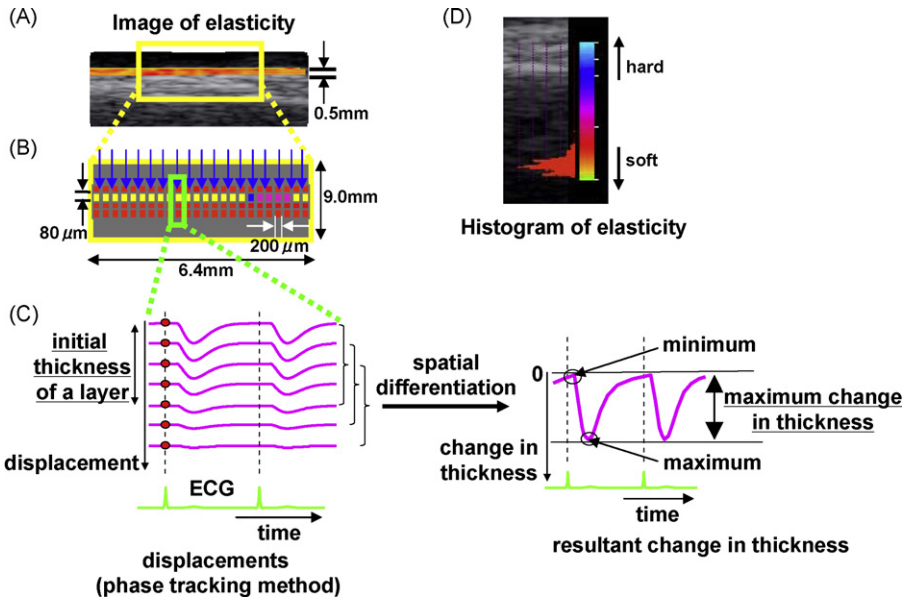

Fig. 1. Evaluation of carotid artery elasticity by phase tracking method. Arterial elasticity is displayed as a 2D cross-sectional color image, which is updated at every heartbeat (A). Multiple sites are preset from the luminal surface to the adventitia (113 depths × 32 beams per 9 mm × 6.4 mm scanned area) and elasticity in each module is measured by the phase tracking method (B). The arterial wall was divided into multiple layers with thicknesses set at 320 μm. The changes in thickness at each depth during the cardiac cycle are simultaneously obtained, and the maximum change in thickness corresponds to the elasticity in each module (C). The elasticity distribution is shown as a histogram (D).

1.6. Statistical analysis

Variables were compared using Pearson's regression analysis. Then, a multiple linear regression analysis was performed to evaluate the independent parameters that were significantly related to arterial elasticity. All data are expressed means ± S.D., and a p-value less than 0.05 was accepted as indicating statistical significance. All statistical analyses were performed using the Statistical Package for the Social Sciences version 13.0 (SPSS Japan Inc., Tokyo, Japan).

2. Results

The clinical characteristics of 78 subjects are shown in Table 1. Mean age is 41.0 ± 13.9 years, BMI 37.6 ± 7.2 (kg/m^2). Thus, the subjects were relatively young and categorized as having moderate, extreme or severe obesity according to Japanese guidelines.

To assess the clinical relevance of carotid artery elasticity in obese subjects, the arterial elasticity value was compared to atherosclerosis values obtained with currently established methods, carotid IMT and PWV. Arterial elasticity showed significant positive correlations with both carotid IMT (r = 0.422, p < 0.01) and PWV (r = 0.360, p < 0.01) in obese subjects (Fig. 2). Similar positive correlations among these three atherosclerosis values were observed in our previous results in subjects with type 2 diabetes [21]. The IMT value in this study was 0.61 ± 0.17 (range: 0.30–1.20) mm and PWV was 1396 ± 260 (range: 992–2117) cm/s, i.e. these obese subjects did not have advanced atherosclerosis, in contrast to the results in subjects with type 2 diabetes in our previous study (IMT: 0.94 ± 0.30 mm, PWV: 1703 ± 356 cm/s).

We then explored the association of carotid arterial elasticity with the clinical and demographic characteristics of these obese

Table 1
Subject characteristics.

Number	78
Age, years	41.0 ± 13.9
Gender (male), %	29.5
Body weight, kg	98.8 ± 24.2
BMI, kg/m^2	37.6 ± 7.2
Fasting blood glucose, mg/dl	121.3 ± 47.6
HbA1c, %	6.5 ± 1.8
Serum insulin μU/ml	17.8 ± 13.2
HOMA-R	4.5 ± 3.8
Systolic BP, mmHg	126.9 ± 14.4
Diastolic BP, mmHg	79.8 ± 10.7
Total cholesterol, mg/dl	208.2 ± 43.5
HDL cholesterol, mg/dl	45.8 ± 9.6
LDL cholesterol, mg/dl	132.6 ± 32.9
Triglyceride, mg/dl	184.1 ± 177.4
Uric acid, mg/dl	5.9 ± 1.5
Visceral fat area, cm^2	150.3 ± 55.7
Subcutaneous fat area, cm^2	405.7 ± 160.0
Diabetes, %	46.8
Dyslipidemia, %	60.3
Hypertension, %	48.7
Current smoker, %	28.0

Mean ± S.D.

Table 2
Associations between atherosclerosis values and subject characteristics.

Variables	r		
	Elasticity	IMT	PWV
Age	0.46**	0.44**	0.67**
Male	0.27*	0.24**	−0.086
Body weight	0.03	−0.075	−0.11
BMI	0.07	−0.06	0.045
Fasting blood glucose	0.14	0.032	0.14
HbA1c	−0.02	−0.036	0.0095
Total cholesterol	0.20	0.061	0.030
HDL cholesterol	−0.03	0.19	0.060
LDL cholesterol	0.15	0.034	−0.049
Triglyceride	−0.03	0.005	−0.040
Systolic BP	0.38**	0.27*	0.35**
Diastolic BP	0.28*	0.26*	0.047
Uric acid	0.15	0.10	−0.20
Diabetes	0.15	0.091	0.39**
Dyslipidemia	0.04	−0.11	0.037
Hypertension	0.37**	0.39**	0.51**

* p < 0.05.
** p < 0.01.

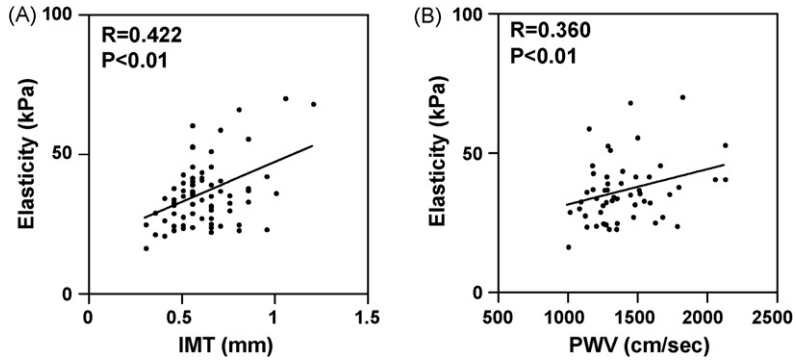

Fig. 2. Correlations of arterial elasticity with carotid IMT (A) and PWV (B) in obese subjects.

Table 3
Associations between each atherosclerosis value and fat distribution.

Variables	*r*		
	Elasticity	IMT	PWV
Visceral fat area	0.42**	0.25*	0.31*
Subcutaneous fat area	−0.066	−0.111	0.046

* $p < 0.05$.
** $p < 0.01$.

subjects. As shown in Table 2, arterial elasticity correlated with age ($r = 0.46$, $p < 0.01$), gender ($r = 0.27$, $p < 0.05$), BP, both systolic ($r = 0.38$, $p < 0.01$) and diastolic ($r = 0.28$, $p < 0.05$), and hypertension ($r = 0.37$, $p < 0.01$). Carotid IMT and PWV also showed similar associations with age, systolic BP and hypertension.

To evaluate whether fat distribution affects atherosclerosis in obese subjects, we performed a single regression analysis of atherosclerosis values with subcutaneous or visceral fat accumulation, as determined by CT scanning. Interestingly, visceral fat area correlated significantly with arterial elasticity as well as carotid IMT and PWV (Table 3), whereas subcutaneous fat area showed no apparent association with these three atherosclerosis values in the present study. Then, we performed multiple linear regression analysis with parameters related to atherosclerosis values, i.e. age, hypertension and visceral fat area (Tables 2 and 3), to search for independent variables affecting atherosclerosis values in obese subjects. As shown in Table 4, each atherosclerosis value is associated with age, indicating that age is also a strong atherosclerosis determinant in obese subjects. Intriguingly, the analysis revealed that visceral fat area is an independent variable showing a positive correlation with carotid arterial elasticity, but not carotid IMT or PWV. We next analyzed the results in a different way, to determine which of the atherosclerosis values is most strongly associated with visceral adiposity. Visceral fat area was significantly associated with both arterial elasticity and PWV, though the correlation with arterial elasticity was stronger (Table 5). These results suggest

Table 4
Multivariate adjustment for parameters related to atherosclerosis values.

Variables	Regression coefficient		
	Elasticity[a]	IMT[b]	PWV[c]
Age	0.30*	0.34**	0.52**
Visceral fat area	0.28**	0.075	−0.06
Hypertension	0.13	0.019	0.32*

[a] $R^2 = 0.32$.
[b] $R^2 = 0.25$.
[c] $R^2 = 0.47$.
* $p < 0.05$
** $p < 0.01$.

Table 5
Multivariate adjustment for parameters related to visceral fat area.

Variables	Regression coefficient	*p*
Elasticity	0.34	0.0041
IMT	0.034	0.77
PWV	0.22	0.047

$R^2 = 0.23$.

that arterial elasticity is an excellent parameter of atherosclerosis as compared with currently established atherosclerosis values and might reflect the cardiovascular risk of visceral adiposity.

3. Discussion

We measured two established atherosclerosis values, carotid IMT and PWV, in addition to "arterial elasticity", which was measured by a novel method, in this study. Similar to our previous results in subjects with type 2 diabetes [21], the arterial elasticity value was significantly associated with those of carotid IMT and PWV. These results raise the possibility of evaluating atherosclerosis in obese subjects with this novel method of measuring elasticity. The important finding of the present study is that arterial elasticity is a better measurement than either carotid IMT or PWV for evaluating the effect of visceral fat accumulation on atherosclerosis in obese subjects; the multiple linear regression analysis revealed that only carotid arterial elasticity, not carotid IMT or PWV, showed a positive correlation with visceral fat area.

In addition, our present results clearly shows that visceral adiposity rather than subcutaneous adiposity is an important factor affecting atherosclerosis in Japanese obese subjects with BMI over 30, since all three parameters for evaluating atherosclerosis, arterial elasticity, carotid IMT and PWV, were significantly associated with visceral fat area but not with subcutaneous fat area. Abdominal fat accumulation, especially visceral adiposity, is well known to play a crucial role in the development of metabolic syndrome [26], leading to atherosclerosis and ultimately cardiovascular disease [6]. Indeed, visceral adiposity determined by CT scanning was related to the incidence of coronary artery disease [8]. Furthermore, recent reports have shown several surrogate markers for atherosclerosis, such as carotid IMT [9–13] and arterial stiffness [15], to be associated with intra-abdominal fat accumulation in subjects without advanced atherosclerosis. Since obesity is increasing explosively world-wide, a practical and non-invasive method is urgently needed for early detection of atherosclerosis before serious cardiovascular events occur.

Herein, we have shown that our novel method of measuring arterial elasticity has potential for detecting early stage atherosclerosis in obese subjects. This ultrasonic method accurately tracks arterial wall movements based on both the phase and the

magnitude of demodulated signals, allowing instantaneous determination of the position of an object. With this method, it is possible to accurately detect small-amplitude velocity signals, less than a few micrometers, which are superimposed on arterial motion due to the heartbeat. Thus, the values obtained with this method reflect an important characteristic of vessel walls, i.e. arterial elasticity. We previously reported arterial elasticity to be a promising method of evaluating early stage atherosclerosis in subjects with type 2 diabetes [21]. Taken together with the present results in obese subjects, these finding indicate that measurement of arterial elasticity might be broadly applicable to evaluation of subjects with atherosclerosis-prone metabolic disorders.

This novel method also has potential for evaluating the elasticity distribution in vessel walls with high spatial resolution; the elasticity distribution is demonstrated as a histogram as shown in Fig. 1D. Properties of the histogram, such as deviation and the shape of the distribution, which were not used in this study, would provide additional information regarding qualitative changes in atherosclerosis. This possibility should be pursued in future investigations.

Several studies have examined which obesity-related values, including body weight, BMI, waist–hip ratio and abdominal fat accumulation, are closely associated with atherosclerosis values such as carotid IMT [27,28] and PWV [29]. However, comparisons among these atherosclerosis values were not conducted, i.e., which of the atherosclerosis values, IMT, PWV or elasticity, is most strongly associated with obesity-related values remains to be determined. This is the first report demonstrating arterial elasticity to have a stronger association with visceral fat area in obese subjects than the two most widely used atherosclerosis values, IMT and PWV.

The present study has several limitations. The study design was cross-sectional. Determination of whether arterial elasticity predicts cardiovascular events in the future thus awaits a prospective study. Another issue warranting further investigation is whether reducing visceral adiposity would improve arterial elasticity. Another important issue is that only approximately 30% of our study subjects were male. The difference in fat distribution by gender is well known, i.e. visceral adiposity is more frequently observed in males [30] and subcutaneous adiposity in females [25]. However, despite the female dominance in our subject group, the effect of visceral adiposity on arterial elasticity was confirmed by multiple regression analysis, implying a crucial role of visceral fat in atherosclerosis.

In conclusion, the present results indicate that arterial elasticity is a novel, sensitive parameter for evaluating atherosclerosis in obese subjects, potentially more useful than currently established atherosclerosis values. Measuring arterial elasticity hold promise of detecting minute vascular changes in early stage atherosclerosis, and may have broad clinical applications for evaluating atherosclerosis in subjects with metabolic disorders.

Acknowledgments

This work was supported by a Grant-in-Aid for Scientific Research (19591031) to Y. Ishigaki and the Global-COE Programs to Y. Oka from the Ministry of Education, Culture, Sports, Science and Technology of Japan. This work was also supported by a Grant-in-Aid for Research on Human Genome, Tissue Engineering (H17-genome-003) to Y. Oka. We thank Dr. T. Ohkubo for helpful suggestions on the statistical analysis. We also thank N. Tamura for technical support.

References

[1] Friedman JM. A war on obesity, not the obese. Science 2003;299:856–8.
[2] Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case–control study. Lancet 2005;366:1640–9.
[3] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415–28.
[4] Klein S, Burke LE, Bray GA, et al. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. Circulation 2004;110:2952–67.
[5] Poirier P, Eckel RH. Obesity and cardiovascular disease. Curr Atheroscler Rep 2002;4:448–53.
[6] Matsuzawa Y. Therapy Insight: adipocytokines in metabolic syndrome and related cardiovascular disease. Nat Clin Pract Cardiovasc Med 2006;3:35–42.
[7] Fujioka S, Matsuzawa Y, Tokunaga K, Tarui S. Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. Metabolism 1987;36:54–9.
[8] Nakamura T, Tokunaga K, Shimomura I, et al. Contribution of visceral fat accumulation to the development of coronary artery disease in non-obese men. Atherosclerosis 1994;107:239–46.
[9] Yamamoto M, Egusa G, Hara H, Yamakido M. Association of intraabdominal fat and carotid atherosclerosis in non-obese middle-aged men with normal glucose tolerance. Int J Obes Relat Metab Disord 1997;21:948–51.
[10] Kim SK, Kim HJ, Hur KY, et al. Visceral fat thickness measured by ultrasonography can estimate not only visceral obesity but also risks of cardiovascular and metabolic diseases. Am J Clin Nutr 2004;79:593–9.
[11] Liu KH, Chan YL, Chan JC, Chan WB. Association of carotid intima–media thickness with mesenteric, preperitoneal and subcutaneous fat thickness. Atherosclerosis 2005;179:299–304.
[12] Lear SA, Humphries KH, Kohli S, Frohlich JJ, Birmingham CL, Mancini GB. Visceral adipose tissue, a potential risk factor for carotid atherosclerosis: results of the Multicultural Community Health Assessment Trial (M-CHAT). Stroke 2007;38:2422–9.
[13] Kawamoto R, Ohtsuka N, Ninomiya D, Nakamura S. Association of obesity and visceral fat distribution with intima–media thickness of carotid arteries in middle-aged and older persons. Intern Med 2008;47:143–9.
[14] Snell-Bergeon JK, Hokanson JE, Kinney GL, et al. Measurement of abdominal fat by CT compared to waist circumference and BMI in explaining the presence of coronary calcium. Int J Obes Relat Metab Disord 2004;28:1594–9.
[15] Sutton-Tyrrell K, Newman A, Simonsick EM, et al. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. Hypertension 2001;38:429–33.
[16] Orr JS, Gentile CL, Davy BM, Davy KP. Large artery stiffening with weight gain in humans: role of visceral fat accumulation. Hypertension 2008;51:1519–24.
[17] Kanai H, Hasegawa H, Ichiki M, Tezuka F, Koiwa Y. Elasticity imaging of atheroma with transcutaneous ultrasound: preliminary study. Circulation 2003;107:3018–21.
[18] Hasegawa H, Kanai H, Hoshimiya N, Koiwa Y. Evaluating the regional elastic modules of a cylindeicl shell with nonuniform wall thickness. J Med Ultrason 2004;31:81–90.
[19] Kanai H, Sato M, Koiwa Y, Chubachi N. Transcutaneous measurement and spectrum analysis of heart wall vibrations. IEEE Trans Ultrason Ferroelectr Freq Control 1996;43:791–810.
[20] Kanai H, Koiwa Y, Zhang J. Real-time measurement of local myocardium motion and arterial wall thickening. IEEE Trans Ultrason Ferroelectr Freq Control 1999;46:1229–41.
[21] Okimoto H, Ishigaki Y, Koiwa Y, et al. A novel method for evaluating human carotid artery elasticity: possible detection of early stage atherosclerosis in subjects with type 2 diabetes. Atherosclerosis 2008;196:391–7.
[22] Hasegawa H, Kanai H, Hoshimiya N, Chubachi N, Koiwa Y. Accuracy evaluation in the measurement of a small change in the thickness of arterial walls and the measurement of elasticity of the human carotid artery. Jpn J Appl Phys 1998;37:3101–5.
[23] Sidhu PS, Desai SR. A simple and reproducible method for assessing intimal–medial thickness of the common carotid artery. Br J Radiol 1997;70:85–9.
[24] Munakata M, Ito N, Nunokawa T, Yoshinaga K. Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. Am J Hypertens 2003;16:653–7.
[25] Kvist H, Sjostrom L, Tylen U. Adipose tissue volume determinations in women by computed tomography: technical considerations. Int J Obes 1986;10:53–67.
[26] Bjorntorp P. Metabolic implications of body fat distribution. Diabetes Care 1991;14:1132–43.
[27] Takami R, Takeda N, Hayashi M, et al. Body fatness and fat distribution as predictors of metabolic abnormalities and early carotid atherosclerosis. Diabetes Care 2001;24:1248–52.
[28] Ingelsson E, Sullivan LM, Fox CS, et al. Burden and prognostic importance of subclinical cardiovascular disease in overweight and obese individuals. Circulation 2007;116:375–84.
[29] Yamada J, Tomiyama H, Matsumoto C, et al. Overweight body mass index classification modifies arterial stiffening associated with weight gain in healthy middle-aged Japanese men. Hypertens Res 2008;31:1087–92.
[30] Kvist H, Chowdhury B, Sjostrom L, Tylen U, Cederblad A. Adipose tissue volume determination in males by computed tomography and 40K. Int J Obes 1988;12:249–66.