福岡大医紀（*Med Bull Fukuoka Univ*）：32(2), 27–31, 2005

Evaluation of Arterial Elasticity by a Pulse Contour Analysis：A One–Year Follow–Up

Kazuma TAKEUCHI[1)2)], Akira MATSUNAGA[1)], Keita NODA[1)], Munehito IDEISHI[1)], Bo ZHANG[1)], Hidenori URATA[3)], Noritsugu MORISHIGE[2)], Tadashi TASHIRO[2)] and Keijiro SAKU[1)]

[1)]*Department of Cardiology,* [2)]*Cardiovascular Surgery, Fukuoka University School of Medicine and* [3)]*First Department of Internal Medicine, Fukuoka University Chikushi Hospital, Fukuoka, Japan*

Abstract：Background：Arterial elasticity has been suggested to be either a risk factor or a marker of cardiovascular disease. A non–invasive pulse–wave contour analysis is considered to be a good modality for assessing the compliance or elasticity of the large and small arteries. The aim of this study was to determine whether the elasticity of the arteries changed within a year.

Methods：This prospective study included 57 patients with cardiovascular risk factors such as hypertension (41 patients), hyperlipidemia (37), and/or a history of smoking (5). The arterial elasticity was evaluated by a radial artery pulse wave analysis using a noninvasive sensor, a parameter estimating the algorithm and the modified Windkessel model of circulation at entry to the study and at one year after the initial evaluation. This analysis estimated the small artery elasticity index (SAEI) in a non–diseased vessel area. At entry to the study, the serum levels of lipids, lipoprotein (a), and the apolipoprotein AⅠ, AⅡ and B levels were measured.

Results：At one year after the first evaluation, the mean of SAEI in the patients had not changed significantly. No significant correlation was found between the changes in the SAEI and any of the factors that had been measured in this study.

Conclusion：The SAEI did not demonstrate any statistically significant difference at one year after the first evaluation.

Key words：Small artery elasticity, Artery compliance, Cardiovascular risk factor

Introduction

Many observational epidemiology studies and clinical trials have shown a strong association between the brachial artery sphygmomanometric pulse pressure and adverse cardiovascular events including mortality. Recent advances in noninvasive techniques to evaluate large and small artery compliance now allows us to make simple and safe assessments of both the vascular structure and compliance in humans.[1)] Several cross–sectional studies have shown that, in addition to age, other environmental and genetic factors can influence arterial stiffness.[2)–5)] Among the known cardiovascular risk factors, an increase in the blood pressure is known to be associated with increased stiffness, because hypertensives are thought to accelerate arterial aging. Among the other cardiovascular risk factors, the presence of dyslipidemia, diabetes, a high heart rate (HR), and tobacco smoking are often associated with increased stiffness, but the impact of these risk factors on the development of arterial stiffness remains unclear.

Correspondence to：Akira MATSUNAGA
Department of Cardiology, Fukuoka University School of Medicine, 7–45–1 Nanakuma, Jonan–ku, Fukuoka 814–0180, Japan
Phone：+81 (92) 801–1011 Fax：+81 (92) 865–2692 E–mail：matsunag@cis.fukuoka–u.ac.jp

In this study, the predictive factors were evaluated regarding the change in arterial elastisity based on a pulse contour analysis with a one-year follow-up study.

Methods

Patient population and Laboratory analysis

Fifty-seven patients (male/female：19/38, age：33-88；mean 62.6 years) underwent noninvasive evaluation of vascular compliance at Fukuoka University Hospital from April 2000 through February 2002. Patients who were treated at the outpatient clinic for hypertension and hyperlipidemia were entered into this study. Any patients with atrial fibrillation or flutter were excluded from this study because an adequate pulse wave analysis could not be performed. The outpatient charts were reviewed to obtain all subjects' medical histories. At the first visit, the patients were evaluated for the body mass index, and laboratory tests were taken to measure their fasting total cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein (apo) A-Ⅰ, apo A-Ⅱ, apo B and lipoprotein (a). Low density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula.

Pulse-wave analysis

Simultaneous measurements were performed with two HDI/Pulsewave CR-2000 Research Cardio Vascular Profiling Systems (Hypertension Diagnostics, Inc., Eagan, MN). The manufacturer recommends placing the blood pressure cuff on the upper arm and the sensor on the skin overlying the radial artery. We followed the manufacturer's recommendations and also placed both the cuff and the sensor on the same arm. Simultaneous measurements were made on both arms and then were averaged. The average of two measurements was used for each combination. The systolic and diastolic blood pressure and pulse waves were recorded for each subject and then were used in the analysis. The compliance parameters, large-artery elasticity index (LAEI) and small-artery elasticity index (SAEI) were calculated from the diastolic pressure decays using a third order fourth element-modified Windkessel model.[6] The percentage change of the small-artery elasticity index (ΔSAEI) and large-artery elasticity index (ΔLAEI) were calculated based on the following formulas：ΔSAEI＝(after one year SAEI－initial SAEI)/initial SAEI×100(%), ΔLAEI＝(after one year LAEI－initial LAEI)/initial LAEI×100(%).

Statistical Analysis

All parameters are given as the mean±SD. The relevant parameters were tested for normality using the Kolmogorov-Smirnov test. The parameters were compared between the groups using ANOVA. The relationship between stiffness parameters and body height was assessed using partial Spearman correlations. Possible confounders were identified first via univariate correlates (continuous variables) or ANOVA (categorical variables) and then were subsequently assessed using a multivariate regression analysis of biological variability. In addition, the overall variability was estimated using a multivariate linear regression. A value of $P<0.05$ was considered to be statistically significant.

Results

The characteristics of the fifty-seven patients were included in the study (Table 1). The mean body mass index was 23.3 kg/m^2. Hypertension was present in 40 patients (70.2%), hyperlipidemia in 37 patients (64.9%), and 5 patients (8.7%) reported to be current smokers. The antihypertensive drugs included calcium antagonists (24 patients), s-blockers (4 patients), diuretics (5 patients), angiotensin-converting enzyme inhibitors (13 patients) and angiotensin Ⅱ antagonists (15 patients), either alone or in combination. Twenty-four patients with hyperlipidemia were medically treated by the drugs, statins (n＝21) or fibrates (n＝3). None of the subjects reported any change in either their prescribed antihypertensive or antihyperlipidemic medication during the follow-up period.

The cardiac output, pulse rate, pulse pressure, systolic blood pressure (BP), diastolic BP, mean BP did not change during the one-year period (Table 2). Neither the SAEI nor LAEI changed significantly during the one-year study period. As

Table 1 Baseline characteristics of the 57 patients

Parameters	Date
Sex, male/female	19/38
Age	62.6±11.1
Body mass index (kg/m^2)	23.3±3.2
Serum total cholesterol (mg/L)	208.5±32.8
Serum HDL cholesterol (mg/L)	63.8±19.6
Serum LDL cholesterol (mg/L)	117.1±29.9
Serum triglycerides (mg/L)	137.9±75.4
Serum apo A-I (mg/L)	155.1±27.9
Serum apo A-II (mg/L)	33.0±5.9
Serum apo B (mg/L)	105.0±23.6
Lipoprotein (a) (mg/L)	23.2±26.6
Cardiovascular risk profile	
Smoking, %	5 (8.7%)
Hypertension, %	40 (70.2%)
Hyperlipidemia, %	37 (64.9%)

Values are the mean±SD.

Table 2 Vascular parameters and blood pressure at baseline and 1 year later

Haemodynamic parameters	**Baseline**	**End of follow-up**
Pulse rate (beats/min)	65.3±10.1	64.9±8.9
Systolic blood pressure (mmHg)	132.1±15.9	131.7±17.1
Diastolic blood pressure (mmHg)	75.0±11.3	74.7±10.4
Mean blood pressure (mmHg)	98.3±12.5	97.4±12.4
Cardiac index (l/min/m^2)	2.5±0.4	2.5±0.4
Systemic vascular resistance (dyn・cm・s^{-5})	2029±451	2031±484
LAEI (ml/mmHg×10)	10.6±3.5	10.3±3.8
SAEI (ml/mmHg×100)	3.4±2.1	3.0±2.0

Values are the mean±SD.

shown in Table 3, the LAEI at entry correlated with age, the systolic and mean blood pressure, and the pulse rate, whereas the SAEI was significantly correlated with the pulse pressure, systolic blood pressure, BMI, cardiac index and systemic vascular resistance. When the population was separated based on the type of anti-hyperlipidemic therapy into control and statin groups, no significant change in small artery compliance was seen (data not shown). ΔLAEI for one year was correlated with the pulse rate and LAEI at entry, but the ΔSAEI at one year did not correlate with any of the factors that were measured in this study (Table 4).

Discussion

A pulse wave analysis using a modified Windkessel model provides an independent assessment of large artery elasticity and small artery elasticity. Grey et al. reported a reduced small artery elasticity, which is a measure of endothelial dysfunction, to be significantly associated with cardiovascular events independent of age.[7] Changes in small artery elasticity may thus be due to either functional or structural alterations that are closely linked to endothelial dysfunction.[8,9] The LAEI reflects the compliance in the aorta and large arteries that distend as the arterial pressure increases with each heartbeat and contracts as it decreases. The derived SAEI has been reported to represent a lumped parameter of the smaller microcirculatory vessels that serve as an arterial wave reflection in the circulation.[10] We have previously identified a selective decrease in the SAEI in patients who have hypertension, coronary artery disease or a smoking history.[11] The primary aim of this study was to explore whether arterial stiffness changes after one year which also trying to clarify the possibility that clinical parameters, including serum lipoprotein and apolipoprotein, may play a role in increasing arterial stiffness. In this study, we found no change in the SAEI after one year, and the change observed in the small artery elasticity

Table 3 Correlation Coefficients Between the SAEI and LAEI at entry, and the baseline findings

Parameters	SAEI	LAEI
Age	−0.259	−0.431***
Sex	−0.053	0.406**
BMI	0.293***	0.038
Pulse rate	0.027	−0.412**
Pulse pressure	−0.344**	−0.378**
Systolic blood pressure	−0.354**	−0.321*
Diastolic blood pressure	−0.240	−0.097
Mean blood pressure	−0.322*	−0.254
Cardiac index	0.362**	0.356**
Systemic vascular resistance	−0.569**	0.629***
Total cholesterol	−0.078	−0.287*
LDL cholesterol	0.044	−0.235
HDL cholesterol	−0.106	−0.067
Triglycerides	−0.118	−0.073
Apo A－I	−0.197	−0.060
Apo A－Ⅱ	−0.091	−0.072
Apo B;0.251	0.251	−0.186
Log Lipoprotein (a)	−0.038	−0.106

$p<0.05$; **$p<0.01$, ***$p<0.001$.
BMI, body mass index ; LDL, low density lipoprotein ; HDL, high density lipoprotein.

Table 4 Correlation Coefficients Between the ΔSAEI and ΔLAEI, and the baseline findings

Parameters	ΔSAEI	ΔLAEI
Age	−0.071	−0.018
Sex (Male/Female)	0.189	−0.020
BMI	−0.125	−0.113
Pulse rate	−0.012	0.284*
Pulse pressure	−0.043	0.114
Systolic blood pressure	0.008	0.122
Diastolic blood pressure	0.062	0.044
Mean blood pressure	−0.065	0.071
Cardiac index	−0.011	0.025
SAEI	−0.240	−0.001
LAEI	−0.041	−0.432**
Total cholesterol	−0.075	0.220
LDL cholesterol	−0.213	0.170
HDL cholesterol	0.148	0.134
Triglycerides	0.064	−0.034
Apo A－I	0.087	0.213
Apo A－Ⅱ	0.091	−0.122
Apo B;−0.176	−0.176	0.073
Log lipoprotein (a)	−0.193	−0.124

$p<0.05$; **$p<0.01$, ***$p<0.001$.
BMI, body mass index ; LDL, low density lipoprotein ; HDL, high density lipoprotein.

(ΔSAEI) after one year was not associated with the serum lipoprotein levels, BMI or blood pressure.

Schillinger et al reported that small artery compliance was negatively correlated to Lp(a) in non－diabetic patients with atherosclerosis.[12] They ruled out any patients who received vasoactive medications such as angiotensin converting enzyme inhibitors or who had smoked within the last 12 h. In this study, the SAEI at admission did not correlate to the Lp(a) or LDL cholesterol levels. Since smokers and the patients treated with vasoactive medications were included in the present study, the correlation of the SAEI and Lp(a) might not have been identified.

Hypertension has been shown to impair arterial compliance. Shargorodsky et al reported that the treatment with angiotensin type 1 receptor antagonist in patients with hypertension increased the compliance in both the large and small arteries.[13] It was also reported that atorvastatin improves the elasticity of small arteries in patients with severe hypercholesterolemia.[14]

Although none of the subjects changed the either

their antihypertensive drugs or antihyperlipidemic medication during this study, the steady-state medications administered at the outpatient clinic might have prevented any change in artery compliance for observations as short as one year. In addition, our study confirmed the results of previous studies where a reduced degree of arterial elasticity was found to be inversely correlated with age.[2)15)]

The results of this study suggested that endothelial dysfunction as defined by a reduction in the small artery elasticity index in outpatients did not change after one year. Further clinical investigations are thus needed to confirm the relationship between risk factors and vascular compliance.

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(Received on January 28, 2005,
Accepted on March 18, 2005)