VIA MEDICA

ORIGINAL ARTICLE

Folia Cardiol.
2006, Vol. 13, No. 6, pp. 480–485

ISSN 1507–4145

Assessment of the intima-media thickness and pulse-wave velocity in peripheral arteries in patients with angiographically confirmed coronary artery disease

Anna Lisowska[1], Włodzimierz Jerzy Musiał[1], Anna Lewczuk[1], Piotr Lisowski[2] and Sławomir Dobrzycki[3]

[1]Department of Cardiology, Medical University, Białystok, Poland
[2]Department of Cardiosurgery, Medical University, Białystok, Poland
[3]Department of Invasive Cardiology, Medical University, Białystok, Poland

Abstract

Background: *Non-invasive methods of assessment of the vascular wall have become of significant interest in recent years. They allow better prediction of cardiovascular lesions when combined with evaluation of established cardiovascular risk factors. The aim of the study was to evaluate whether the combination of ultrasonographic assessment of intima-media thickness (IMT) and pulse-wave velocity (PWV) measurement in peripheral arteries results in an increased predictive value for the presence of atherosclerotic coronary lesions. In addition, selected established risk factors for atherosclerosis were analysed for their association with IMT and PWV.*

Methods: *Fifty patients with angiographically confirmed coronary artery disease were included in the study. In all patients ultrasonographic assessment of IMT was performed in the common carotid artery (CCA), the carotid artery bulb (CB) and the common femoral artery (CFA). Simultaneously PWV was recorded between CCA and the brachial and femoral arteries.*

Results: *A higher IMT was noted both in CB and CFA as compared to CCA. Carotid-brachial PWV was higher compared to carotid-femoral PWV. Carotid-femoral PWV correlated with IMT ($p = 0.015$) and the presence of atherosclerotic plaques ($p = 0.04$) in CB. No similar relation was found for carotid-brachial PWV. IMT in CCA, CB, and CFA was significantly higher in subjects with triple-vessel disease compared to patients with single-vessel or double-vessel disease. We also found a trend for higher PWV values in patients with multivessel disease but these differences did not reach statistical significance.*

Conclusions: *Combining ultrasonographic assessment of IMT and PWV measurements in peripheral arteries results in an increased predictive value for the presence of atherosclerotic coronary lesions. Isolated PWV measurements are less useful for non-invasive coronary risk assessment than IMT measurements.* (Folia Cardiol. 2006; 13: 480–485)

Key words: coronary artery disease, intima-media thickness, ultrasonographic assessment, pulse-wave velocity

Address for correspondence: Dr med. Anna Lisowska
Department of Cardiology, Medical Univeristy of Białystok
Skłodowskiej-Curie 24A, 15–276 Białystok, Poland
Tel.: +48 58 74 68 656, fax: +48 58 74 68 604
e-mail: anlila@poczta.onet.pl
Received: 20.05.2006 Accepted: 12.06.2006

Editorial p. 441

Introduction

Coronary artery disease (CAD) is the most common cause of death among middle-aged men and the second most common cause of death among women. It has been estimated that chronic CAD affects approximately 1 000 000 people in Poland, which amounts to 2.5% of the general population [1]. Atherosclerosis is a systemic disease affecting various arterial beds and leading to symptoms of ischaemia in the target organs. A number of methods are available to examine the arterial vessels. Although coronary angiography is the gold standard in the diagnosis of coronary lesions, it is an invasive method of limited availability and is associated with a definite risk. Thus indications for coronary angiography are strictly established [2]. There is a growing interest in non-invasive methods including ultrasonographic evaluation of the intima-media thickness (IMT), measurements of flow mediated dilatation (FMD) of the arterial vessels and pulse-wave velocity (PWV), and also in coronary calcium imaging using electron-beam computed tomography (EBCT) and magnetic resonance imaging (MRI). These modalities are particularly useful in asymptomatic patients when combined with clinical evaluation of cardiovascular risk factors. In addition, they offer an incremental prognostic value in predicting cardiovascular events [3].

The aim of this study was to evaluate whether a combination of ultrasonographic assessment of IMT and PWV measurement in the peripheral arteries results in an increased predictive value for the presence of atherosclerotic coronary lesions that might be of significant prognostic importance. In addition, we assessed selected risk factors for atherosclerosis and their effect on PWV and IMT and the correlation between the last two parameters.

Methods

We studied consecutive patients hospitalised in the Department of Cardiology of the Medical University of Białystok who had undergone coronary angiography as clinically indicated. Men aged 18–65 years were included in the study. Simultaneous ultrasonographic vascular assessment of the carotid artery and the femoral artery was performed combined with PWV measurement. We also assessed selected clinical and biochemical risk factors for atherosclerosis. Exclusion criteria included previously diagnosed diabetes, symptomatic peripheral vascular disease and severe hypertension, defined as grade III or grade IV retinopathy or left ventricular hypertrophy > 1.5 cm in echocardiography.

Table 1. Characteristics of the study group (n = 50)

Age (years)	52.6 ± 7.9
Smokers	36 (72%)
Body mass index [kg/m^2]	28.6 ± 3.5
Systolic blood pressure [mm Hg]	147.2 ± 24.1
Diastolic blood pressure [mm Hg]	94.8 ± 15.7
Total cholesterol [mg/dL]	180.8 ± 36.7
LDL cholesterol [mg/dL]	110.7 ± 31.5
HDL cholesterol [mg/dL]	37.9 ± 8.8
Triglycerides [mg/dL]	160.3 ± 58.4
Impaired glucose tolerance or diabetes in OGTT	25 (50%)
Fibrinogen [mg/dL]	413.2 ± 103.7
Platelets (× 1000/mm^3)	212.5 ± 59.7
Left ventricular ejection fraction (%)	46.2 ± 7.4

According to the above criteria 50 patients were included in the study. All the subjects had angiographically confirmed coronary lesions. Significant stenosis was defined as a > 50% decrease in arterial lumen. Depending on the number of vessels involved, CAD was classified as single, double, or triple-vessel disease. Single-vessel disease was present in 16 patients, double-vessel disease in 15 patients, and triple-vessel disease in 19 patients. Table 1 shows detailed characteristics of the study group.

Clinical and diagnostic evaluation included blood pressure measurement, baseline ECG and an exercise test, transthoracic echocardiography, coronary angiography, carotid and femoral artery ultrasound and automatic PWV measurement. A panel of biochemical parameters was measured including serum total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides and plasma fibrinogen and a platelet count and oral glucose tolerance test were conducted. Indications for coronary angiography were established on the basis of clinical and laboratory criteria using Polish Cardiac Society guidelines. Coronary angiography was performed in routine views via the transfemoral approach.

Intima-media thickness measurement

Carotid and femoral artery ultrasound was performed with a Sonos 5500 system and high-resolution 3–11 MHz linear probe using software for evaluation of the peripheral arteries in B-mode as described previously [4]. We evaluated the thickness of the IMT, the presence of atherosclerotic plaques within a vessel and Doppler blood flow variables.

The common carotid artery was evaluated within 10 mm of the bulb. The femoral artery was evaluated 10 mm proximal to the beginning of the profound femoral artery. As adequate visualisation of the walls of the internal carotid artery is difficult in some patients, this was omitted in the study. IMT was measured in the distal vessel wall, as measurement within the proximal wall is technically difficult owing to the higher density of the adventitia, resulting in increased echogenicity compared to the intima and the media. IMT was measured as the distance between the initial discrete bright line (the border between the lumen and the intima) and the second bright line (the border between the media and the adventitia) in the distal vessel wall. Two averaged IMT measurements were performed in each vascular segment. Maximal IMT values were taken into account. Atherosclerotic plaques were defined as areas with IMT > 1.3 mm. Simultaneous ECG monitoring allowed synchronisation of ultrasonographic measurements in frozen images with R waves to minimise IMT changes during the cardiac cycle. Doppler blood flow parameters were evaluated in the common carotid artery and the femoral artery using a Doppler sample placed in the middle of the arterial lumen with the angle correction at 60 degrees. The flow spectrum was recorded and the pulsation index (PI) and the resistance index (RI) were calculated using the following equations: PI = Vmax – Vmin/Vmean, and RI = Vmax – Ved/Vmax, where Vmax is maximal flow velocity, Vmin is minimal flow velocity, Vmean is mean flow velocity, and Ved is end-diastolic flow velocity.

Pulse-wave velocity measurement

PWV was measured using the Complior SP system with measurement points in the common carotid artery and the brachial artery (carotid-brachial PWV) or the femoral artery (carotid-femoral PWV). This technique involves placing one transducer on the proximal vessel and the other transducer on the distal vessel. The sampling frequency was 500 Hz. Two pulse-wave tracings were recorded simultaneously. Recording was stopped when a good quality tracing was obtained on the monitor. The time delay between the bases of the proximal (carotid) and distal (femoral or brachial) pulse waves was calculated automatically by the system software. PWV was calculated on the basis of this time delay and the distance between the two measurement points was calculated using the following equation: PWV = distance in metres/time delay of the pulse wave. Results are expressed as the mean of three measurements.

Statistical analysis

The mean values and standard deviations were calculated for continuous variables and numerical and percentage distributions for categorical variables. Pearson and Spearman correlation coefficients were calculated for normally distributed continuous variables using the Kolmogorov test and continuous variables with a skewed distribution respectively.

The statistical significance of the differences between normally distributed continuous variables and continuous variables with a skewed distribution was assessed using Student's *t* test and the Mann-Whitney test respectively. Differences between categorical variables were assessed using the χ^2 test. $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS 8.0 PL and Statistica 6.0 PL software.

All patients gave written informed consent and the study as approved by the local Ethics Committee.

Results

The results of the study are presented in Table 2. As shown, IMT in the carotid bulb and the common femoral artery was higher than in the common carotid artery. Atherosclerotic plaques were also substantially more common in these vessels. Carotid-brachial PWV was increased compared to carotid-femoral PWV.

Carotid-femoral PWV was related to age (p = = 0.005), number of cigarettes smoked (p = 0.025)

Table 2. Intima-media thickness (IMT), resistance index (RI), pulsation index (PI), pulse wave velocity (PWV) and the presence of atherosclerotic plaques in peripheral arteries.

Common carotid artery IMT [mm]	0.87 ± 0.29
Carotid artery bulb IMT [mm]	1.26 ± 0.55
Common femoral artery IMT [mm]	1.34 ± 0.57
Common carotid artery RI	0.72 ± 0.06
Common carotid artery PI	1.65 ± 0.51
Common femoral artery RI	0.97 ± 0.03
Common femoral artery PI	5.93 ± 1.84
Atherosclerotic plaques in the common carotid artery	4 (8%)
Atherosclerotic plaques in the common carotid bulb	21 (42%)
Atherosclerotic plaques in the common femoral artery	27 (54%)
Carotid-brachial PWV [m/s]	8.29 ± 1.38
Carotid-femoral PWV [m/s]	7.68 ± 1.65

and IMT in the carotid artery bulb (p = 0.015) (Fig. 1). A correlation was shown between the presence of atherosclerotic lesions in the carotid artery bulb and carotid-femoral PWV (p = 0.04) (Fig. 2). No such relation was shown for carotid-brachial PWV. In addition, there was no correlation between IMT in the common carotid artery and the common femoral artery, the presence of atherosclerotic lesions in these vessels and PWV values.

Cigarette smoking had a significant impact on both carotid-brachial PWV (p = 0.04) and carotid-femoral PWV (p = 0.01). In 25 patients with impaired glucose tolerance or diabetes carotid-femoral PWV was significantly higher compared to subjects

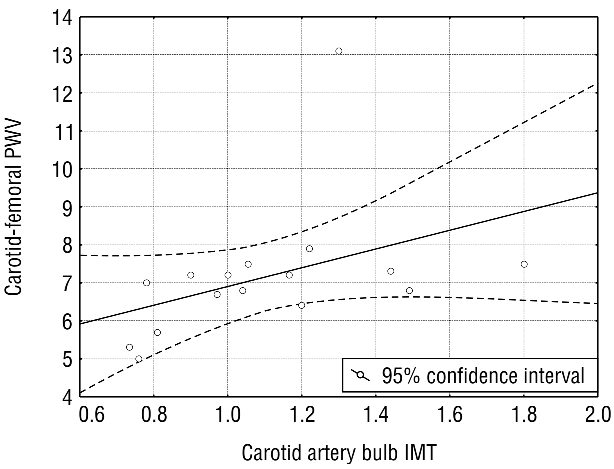

Figure 1. Correlation between carotid-femoral PWV and carotid artery bulb IMT.

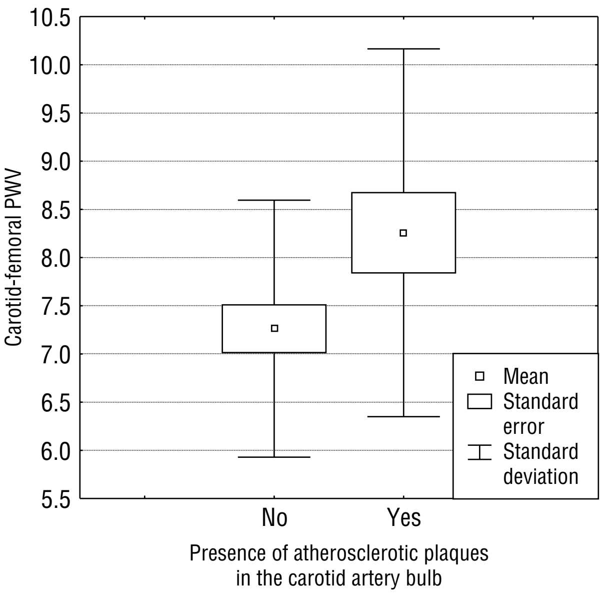

Figure 2 Correlation between carotid-femoral PWV and the presence of atherosclerotic plaques in the carotid artery bulb.

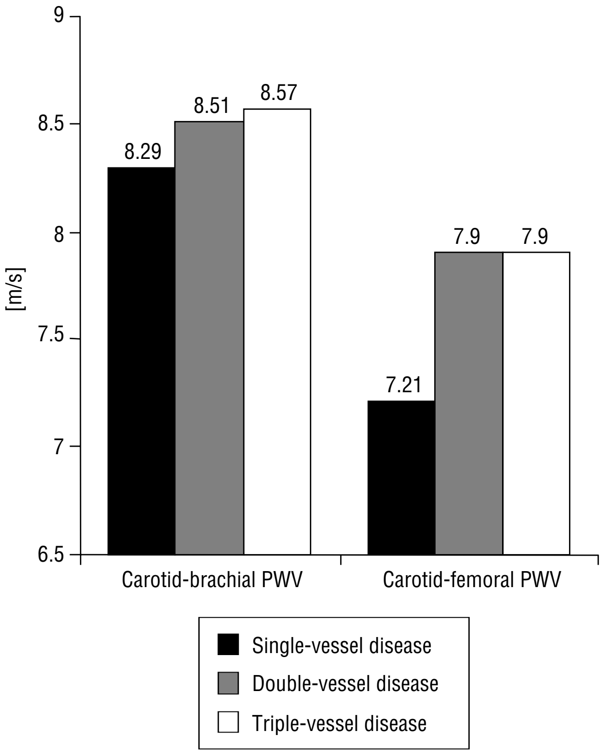

Figure 3. Correlation between carotid-brachial and carotid-femoral PWV and the extent of coronary atherosclerosis.

with normoglycaemia (8.06 *vs.* 7.07; p = 0.03). In contrast, there was no relation between total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides and PWV values.

We found a trend for higher carotid-brachial PWV and carotid-femoral PWV in subjects with double and triple-vessel disease compared to subjects with single-vessel disease, but these differences did not reach statistical significance (Fig. 3). The severity of coronary lesions was, however, significantly related to the IMT in the peripheral arteries. IMT in the common carotid artery, the carotid artery bulb, and the common femoral artery was significantly higher in subjects with triple-vessel disease compared to subjects with single and double-vessel disease (Fig. 4).

Discussion

Non-invasive measurement of PWV allows quantitative assessment of the properties of the large arteries. This method is based on a relation between PWV and the elastic and geometric properties of the vessel wall and blood density. Thus PWV is an indirect marker of vessel distensibility and stiffness. Arterial wall thickness and luminal

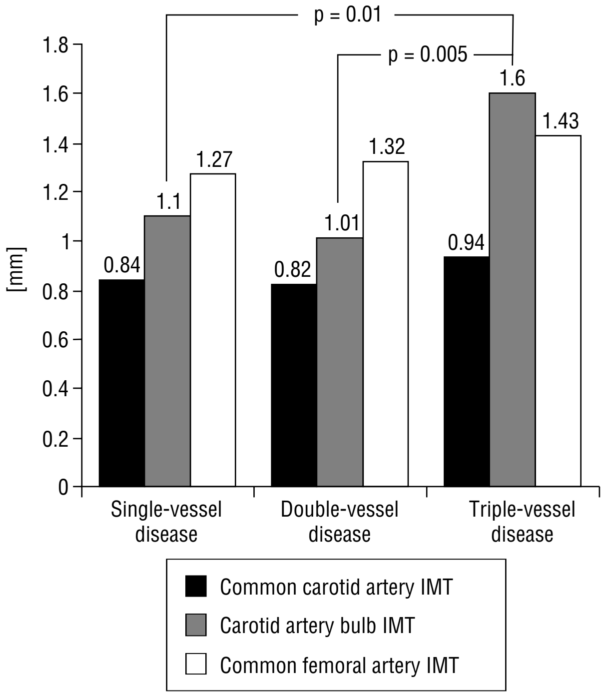

Figure 4. Correlation between common carotid artery, common carotid artery bulb and common femoral artery IMT and the extent of coronary atherosclerosis.

diameter are major factors determining the pattern of the pulse wave.

Previous studies have validated PWV measurements using the Complior device [5–7] and so we used this method in our study. Asmar et al. [5] have shown that automatic PWV measurements using this device are highly reproducible both between observers [8, 9] and in serial measurements in the same patient [8, 9].

Numerous studies have shown that large vessel stiffness increases with age [10–12]. We also found this relation in our study group but only for carotid-femoral PWV and not for carotid-brachial PWV. Cigarette smoking is another factor affecting arterial compliance [13], although this has not been confirmed in all studies [5]. In our study nearly three quarters of the subjects were smokers and cigarette smoking affected both carotid-femoral PWV and carotid-brachial PWV. Increased PWV is characteristic for subjects with hypertension [14] and PWV is affected by both systolic and diastolic blood pressure [11]. In addition, PWV is a predictor of cardiovascular events in subjects with hypertension and no coexisting cardiovascular disease, regardless of the classic risk factors [15]. Lack of a severe hypertension burden in our study group (mean systolic blood pressure 147.2 mm Hg, mean diastolic blood pressure 94.8 mm Hg) may explain why PWV was not related to blood pressure in our study.

We found no relation between lipid parameters and PWV values, which was in agreement with other authors [11, 16, 17]. In contrast, impaired glucose tolerance had a significant effect on PWV. Both our findings and those of other studies [18] show a higher PWV in subjects with impaired glucose tolerance than in healthy controls.

Studies to evaluate the relation between carotid IMT and PWV gave inconsistent results. Taniwaki et al. [19] showed a significant relation between carotid IMT and PWV in both healthy subjects and patients with type 2 diabetes. Our findings confirmed a significant correlation between carotid-femoral PWV and both IMT and the presence of atherosclerotic plaques in the carotid artery bulb. In contrast, we found no such relation for carotid-brachial PWV. We also found no correlation between IMT in the common carotid artery and the common femoral artery, the presence of atherosclerotic plaques in these vessels and PWV values. A lack of correlation between PWV values and IMT in the common carotid artery and the presence of atherosclerotic lesions in this vessel are consistent with the findings of Nishi et al. [20].

In our study a higher carotid-brachial PWV and carotid-femoral PWV were found in subjects with double and triple-vessel disease than in subjects with single-vessel disease. However, these differences did not reach statistical significance. This might have been related to an insufficient number of study subjects. Similarly, other authors have shown that PWV increases with the severity of atherosclerotic lesions [21, 22]. These observations require confirmation in larger studies.

IMT in the common carotid artery, the carotid artery bulb and the common femoral artery correlated significantly with the severity of coronary lesions and was higher in subjects with triple-vessel disease compared to subjects with single and double-vessel disease. This highlights the importance of measurements of IMT in the peripheral arteries for the prediction of coronary lesions.

The major limitation of our study was the low number of study subjects. In addition, the high percentage of smokers might have affected arterial compliance.

Conclusions

1. Combining ultrasonographic assessment of IMT and PWV measurement in peripheral arteries results in an increased predictive value

for the presence of atherosclerotic coronary lesions.
2. Isolated PWV measurements are less useful for non-invasive coronary risk assessment than are IMT measurements.

References

1. Matuszewski M, Opala G. Chirurgia tętnic wieńcowych u chorych ze zwężeniem tętnic szyjnych. In: Woś S. Choroba niedokrwienna serca — postępy w leczeniu chirurgicznym. Wydawnictwo Naukowe, "Śląsk" Katowice 2001: 254.
2. Silber S, Albertsson P, Aviles F et al. Guidelines for percutaneous coronary interventions. ESC Guidelines. Eur Heart J, 2005: 1–31.
3. Patel S, Rajaram V, Pandya S et al. Nowe nieinwazyjne markery zastępcze miażdżycy. Kardiologia po Dyplomie, 2004; 3: 22–33.
4. Lisowska A, Musiał W, Prokop J, Polaków J, Knapp M. Ultrasonograficzna ocena kompleksu błona wewnętrzna-błona środkowa tętnic obwodowych: przydatność kliniczna. Pol Przegl Kardiol, 2003; 4: 451–456.
5. Asmar R, Benetos A, Topouchian J et al. Assessment of arterial distensibility by automatic pulse wave velocity measurement. Hypertension, 1995; 26: 485–490.
6. Asmar R, Topouchian J, Pannier B et al. Pulse wave velocity as endpoint in large-scale intervention trial. The Complior study. J Hypertens, 2001; 19: 813–818.
7. Popele N, Grobbee D, Bots M et al. Association between arterial stiffness and atheromatosis. The Rotterdam Study. Stroke, 2001; 32: 454–460.
8. Bortolotto L, Blacher J, Kondo T, Takazawa K, Safar M. Assessment of vascular aging and atherosclerosis in hypertensive subjects: second derivative of photoplethysmogram versus pulse wave velocity. Am J Hypertens, 2000; 13: 165.
9. Taquet A, Binithon-Kopp C, Simon A et al. Relations of cardiovascular risk factors to aortic pulse wave velocity in asymptomatic middle-aged women. Eur J Epidemiol, 1993; 9: 298.
10. Rogers W, Hu Y, Coast D et al. Age-associated changes in regional aortic pulse wave velocity. J Am Coll Cardiol, 2001; 38: 1123–1129.
11. Nakamura U, Iwase M, Nohara S, Kanai H, Ichikawa K, Iida M. Usefulness of brachial-ankle pulse wave velocity measurement: correlation with abdominal aortic calcification. Hypertens Res, 2003; 26: 163–167.
12. Sawabe M, Takahashi R, Matsushita S et al. Aortic pulse wave velocity and the degree of atherosclerosis in the elderly: a pathological study based on 304 autopsy cases. Atherosclerosis, 2005; 179: 345–351.
13. Vlachopoulos C, Kosmopoulou F, Panagiotakos D et al. Smoking and caffeine have a synergistic detrimental effect on aortic stiffness and wave reflections. J Am Coll Cardiol, 2004; 44: 1911–1917.
14. Safar M, Levy B, Laurent S, London G. Hypertension and the arterial system: clinical and therapeutic aspects. J Hypertens, 1990; 8 (suppl. 7): S113–S119.
15. Boutoyrie P, Tropeano A, Asmar R et al. Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. Hypertension, 2002; 39: 10–15.
16. 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.
17. Kurpesa M, Rechciński T, Trzos E et al. Wpływ przewlekłego leczenia statyną na podatność tętnic w samoistnym nadciśnieniu tętniczym. Folia Cardiol, 2004; 11: 929–937.
18. Kidawa M, Rynkowska-Kidawa M, Kasprzak J, Kurpesa M, Krzemińska-Pakuła M. Dysfunkcja naczyń tętniczych u młodych pacjentów z upośledzoną tolerancją glukozy. Przegl Lek, 2002; 59: 765–769.
19. Taniwaki H, Kawagishi T, Emoto M et al. Correlation between the intima-media thickness of the carotid artery and aortic pulse-wave velocity in patients with type 2 diabetes. Diabetes Care, 1999; 22: 1851–1857.
20. Nishi Y, Koshiyama H, Honjo S, Seino Y. Poor correlation of pulse-wave velocity and intima-media thickness in diabetic subjects. Diabetes Care, 2004; 27: 2084.
21. Sakuragi S, Iwasaki J, Tokunaga N, Hiramatsu S, Ohe T. Aortic stiffness is an independent predictor of left ventricular function in patients with coronary heart disease. Cardiology, 2005; 103: 107–112.
22. Lim H, Park C, Shin S, Ahn J, Seo H, Oh D. Aortic pulse wave velocity as an independent marker of coronary artery disease. Blood Press, 2004; 13: 369–375.