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# Ultrasonography of the Carotid and Popliteal Artery to Predict Coronary Artery Disease

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*ABSTRACT*

In the present study, we determined the intima-media thickness (IMT) of the common carotid artery (CCA) and popliteal artery (PA) with ultrasonography and repeated the examinations to assess the possibility of increasing the sensitivity and specificity for predicting the presence of coronary arteriosclerosis. The subjects were 102 patients (73 men, 29 women) aged 34 to 83 years. We adopted the thicker side as representing the IMT (IMT max) for both the CCA and PA. With serial determinations, the sensitivity and specificity of ultrasonography for predicting coronary artery stenosis were 55.3% and 75%, respectively, when either the CCA-IMT max was 1.2 mm or more or the PA-IMT max was 1.0 mm or more. With parallel determinations, the corresponding sensitivity and specificity were 60.5% and 68.8%, respectively, when both the CCA-IMT max was 0.7 mm or more and the PA-IMT max was 0.9 mm or more. In conclusion, repeated examination of CCA-IMT max and PA-IMT max improves the sensitivity and specificity of CCA and PA ultrasonography for predicting coronary artery stenosis and is useful for risk stratification in patients with suspected ischemic heart disease. (Jikeikai Med J 2005 ; 52 : 39-45)

Key words : coronary artery disease, carotid artery, popliteal artery, ultrasonography, intima-media thickness, atherosclerosis

## INTRODUCTION

Coronary angiography (CAG) has been regarded as the gold standard for diagnosing coronary atherosclerosis. It has also been considered essential for assessing the presence and severity of ischemic heart disease and for evaluating the indications for revascularization procedures, such as percutaneous coronary intervention and coronary artery bypass grafting[1,2]. However, CAG is an invasive procedure with possible complications[3]. Therefore, risk stratification is important for patients with suspected ischemic heart disease, and the indication for CAG must be assessed in these patients[1]. The procedures most often performed for such risk stratification include stress electrocardiography (ECG) testing and stress myocardial scintigraphy. However, the sensitivity and specificity of the stress ECG testing are poor. Although stress myocardial scintigraphy is more sensitive and specific, it requires patient preparation and long examination times, is extremely expensive, and can be performed at a limited number of institutions. For these reasons, stress myocardial scintigraphy is rarely performed for screening purposes. Under these circumstances, some studies have shown that common carotid artery (CCA) intima-media thickness (IMT) obtained with ultrasonography in patients with arteriosclerosis is useful and is correlated with the presence of coronary atherosclerosis[4-10]. We have also demonstrated the usefulness of both CCA and

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popliteal artery (PA) ultrasonography for diagnosing coronary atherosclerosis[7,11]. However, our previous studies included subjects who had undergone coronary revascularization procedures, such as percutaneous coronary intervention and coronary artery bypass grafting, and did not focus on the diagnosis of coronary artery stenosis.

In the present study, we examined the IMT of the CCA and PA with ultrasonography performed almost simultaneously and investigated the possibility of predicting the presence of coronary atherosclerosis on the basis of IMT in subjects who had not undergone coronary revascularization.

## SUBJECTS AND METHODS

### 1. *Subjects*

The subjects were 102 consecutive patients with suspected angina pectoris who had undergone initial CAG at The Jikei University Kashiwa Hospital from September 1997 through March 2000. Patients who had undergone revascularization procedures, such as percutaneous coronary intervention and coronary artery bypass grafting, were excluded. Several subjects had previously been included in a study by Nagata et al.[11].

### 2. *CAG*

CAG was performed with the standard procedure through the femoral or the brachial artery[12]. At least three specialists with expertise in performing CAG evaluated the status of the coronary arterial circulation, according to the American Heart Association Classification[13]. According to this classification, based on the threshold for the appearance of symptoms of myocardial ischemia, stenosis of greater than 75% on CAG is considered significant. For this reason, in the present study, only coronary lesions causing severe stenosis of 75% or more, which are assumed to be potentially associated with angina pectoris, were considered.

### 3. *Determination of CCA-IMT*

One of three ultrasonologists with at least 3 years' experience performing ultrasonography at our clinical laboratories determined the CCA-IMT with an ultrasonic imaging system (EUB-565A, Hitachi Medical Corp., Tokyo) and a 7.5-MHz linear probe[7,11]. The patients were instructed to lie supine with the anterior region of the neck in the sniffing position. The IMT was determined on longitudinal sections 1 cm proximal to the carotid bifurcation[14]. The IMT was determined at both superficial and deep sites of the CCA, and the greater of the two values was used as the CCA-IMT[7]. The CCA-IMT was also determined on both the right and left sides. All values are expressed in millimeters as the mean±1 SD.

### 4. *Determination of the PA-IMT*

The PA-IMT was measured by one of three ultrasonologists with at least 3 years' experience performing ultrasonography at our clinical laboratories, using the same ultrasonic imaging system and probe. The patients were instructed to lie in the prone position, and the PA-IMT was measured in the popliteal fossa on both the right and left sides. The PA-IMT was determined at both superficial and deep sites of the PA, and the greater value of the two was used as the PA-IMT[11]. All values are expressed in millimeters as the mean±1 SD.

### 5. *Analysis*

Statistical analysis was performed with the JMP version 3.2.6 software program (SAS Institute Inc., Cary, NC, USA). Correlations between the CCA-IMT and PA-IMT on the right and left sides and the left-right differences in the CCA-IMT and PA-IMT were analyzed with the paired t-test. Differences were considered significant at $p<0.05$. Receiver operating characteristic (ROC) curves aimed at diagnosing 75% coronary artery stenosis were prepared from the greater of the right and left CCA-IMT as the representative CCA-IMT max and from greater of the right and left PA-IMT as the representative PA-IMT

max. Cutoff points were determined at which the specificity reached the maximum at a sensitivity of 90% or more and at which the sensitivity reached the maximum at a specificity of 90% or more. To evaluate the possibility of improving the accuracy of the analysis, the ROC curves for determining the above-mentioned cutoff points were also prepared with CCA-IMT max and PA-IMT max values determined at serial examinations and at parallel examinations. The likelihood ratios at which the diagnosis of 75% stenosis could be made were calculated from the CCA-IMT max and PA-IMT max.

## Results

### 1. *Subjects*

The subjects were 102 patients (median age : 60 years ; range : 34-83 years) consisting of 73 men (median age : 60 years ; range : 34-78 years) and 29 women (median age : 59 years ; range : 39-83 years ; Table 1).

### 2. *CAG*

Thirty-eight (37.3%) of the 102 patients showed 75% stenosis of the coronary arteries on CAG.

Table 1. Characteristics of patients

| | | |
|---|---|---|
| Age | Median | range |
| total | 60 | (34～83) |
| male | 60 | (34～78) |
| female | 59 | (39～83) |
| Gender | N | (%) |
| male | 73 | (71.2) |
| female | 29 | (28.4) |
| Risk Factor | N | (%) |
| Current smoking | 46 | (45.1) |
| Hypertension | 41 | (40.2) |
| Hyperlipidemia | 64 | (62.7) |
| Diabetes | 24 | (24.5) |
| Obesity | 23 | (22.6) |
| FH | 7 | ( 6.9) |

Obesity was defined as body mass index (body weight/height$^{2)}$ of 26 or more; FH, familial history of ischemic heart disease

### 3. *CCA-IMT*

The left CCA-IMT (0.85±0.22 mm ; range, 0.5-1.5 mm) was significantly greater than the right CCA-IMT (0.82±0.22 mm ; range, 0.5-1.5 mm ; $p<0.05$). The right and left CCA-IMT values were weakly correlated ($r=0.67$ ; $p<0.001$). The CCA-IMT max was 0.90±0.24 mm (range, 0.6-1.5 mm). The ROC curves drawn with the CCA-IMT max for predicting the presence of 75% coronary artery stenosis are shown in Fig. 1 ; the sensitivity for predicting coronary artery stenosis was 94.7% and the specificity was 14.1% when the cutoff value was 0.7 mm or more. The sensitivity was 31.6% and the specificity was 90.6% when the cutoff value was 1.2 mm or more.

### 4. *PA-IMT*

The right PA-IMT (0.80±0.16 mm ; range, 0.5-1.2 mm) and left PA-IMT (0.80±0.13 ; range 0.6-1.2 mm) did not differ significantly. The right and left PA-IMT values were weakly correlated ($r=0.54$ ; $p<0.001$). The PA-IMT max was 0.85±0.15 mm (range, 0.6-1.2 mm). The ROC curves drawn with PA-IMT max for predicting the presence of 75% stenosis are shown in Fig. 1 ; the sensitivity for

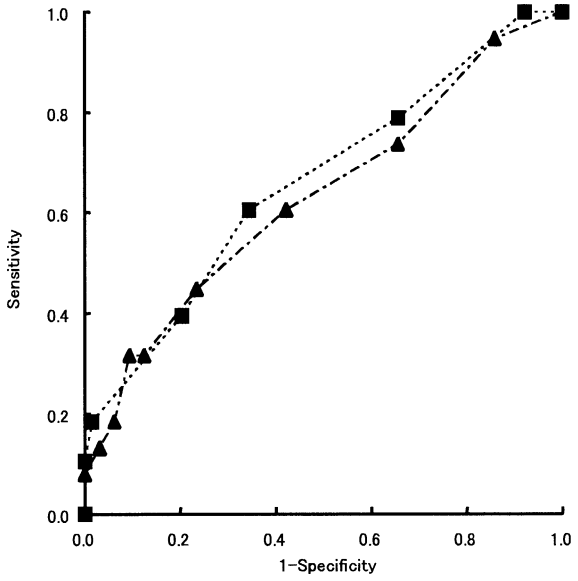


Fig. 1. ROC curves of CCA-IMT max (closed triangle) and PA-IMT max (closed square) for diagnosing coronary artery stenosis.

predicting 75% coronary artery stenosis was 100% and the specificity was 7.8% when the cutoff value was 0.7 mm or more. The sensitivity was 18.4% and the specificity was 98.4% when the cutoff value was 1.2 mm or more.

*5. Relation between CCA-IMT max and PA-IMT max*

The CCA-IMT max and PA-IMT max were weakly correlated ($r=0.35$ ; $p<0.001$). The CCA-IMT max was significantly greater than the PA-IMT max ($p<0.05$).

*6. Improving the accuracy of predicting 75% stenosis*

ROC curves for predicting 75% stenosis with CCA-IMT max alone, PA-IMT max alone, and either PA-IMT max or CCA-IMT max at a cutoff value of 1.2 mm or more were calculated (Fig. 2a). At this cutoff value of CCA-IMT max and PA-IMT max, the sensitivity for predicting stenosis was 36.8% and the specificity was 90.6%. ROC curves for predicting 75% coronary artery stenosis with CCA-IMT max alone, PA-IMT max alone, and both the PA-IMT max and CCA-IMT max at a cutoff value of 0.7 mm or more were also calculated (Fig. 2b). At this cutoff value the sensitivity for predicting 75% stenosis improved to 94.7% and the specificity improved to 21.9%.

*7. Likelihood ratio*

The likelihood ratios for diagnosing 75% stenosis from the CCA-IMT max and PA-IMT max values are shown in Table 2. In regard to the diagnosis of 75% coronary stenosis on the basis of CCA-IMT max and PA-IMT max, there was no fixed tendency towards a likelihood ratio for the CCA-IMT max. In contrast, relatively favorable results were obtained for the PA-IMT max. The likelihood ratio was 0.0 at a PA-IMT max of 0.6 mm and 5.1 at a PA-IMT max of 1.1 mm, showing a possible increase in specificity at the latter value.

## DISCUSSION

Some reports have suggested that determining the CCA-IMT and PA-IMT with ultrasonography may be useful for predicting coronary artery

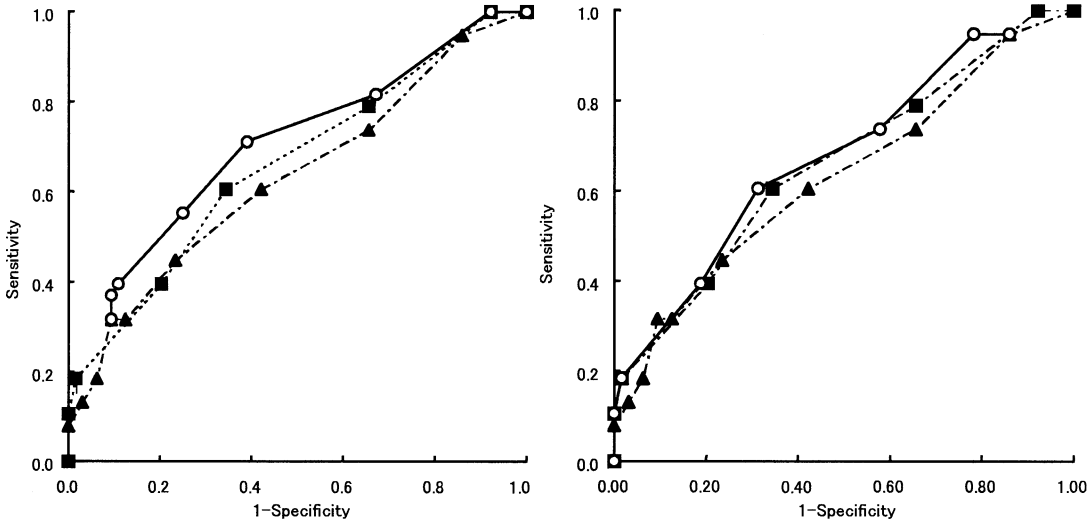


Fig. 2a. (left) : ROC curves of CCA-IMT max alone (closed triangle), PA-IMT max alone (closed square), and PA-IMT max or CCA-IMT max at a cutoff value of 1.2 mm or more (open circle) for diagnosing coronary artery stenosis of 75% or more.

Fig. 2b. (right) : ROC curves of CCA-IMT max alone (closed triangle), PA-IMT max alone (closed square), and PA-IMT max when CCA-IMT max was 0.7 mm or more (open circle) for making diagnosis of 75% or more stenosis coronary artery.

Table 2. Likelihood ratio for making the diagnosis of 75% stenosis positive at CAG using by CCA-IMT max and PA-IMT max.

| | CCA-IMT max | | | PA-IMT max | | |
|---|---|---|---|---|---|---|
| Value (mm) | total (N) | positive in CAG (N) | LR | total (N) | positive in CAG (N) | LR |
| 0.6 | 11 | 2 | 0.37 | 5 | 0 | 0.00 |
| 0.7 | 21 | 8 | 1.04 | 25 | 8 | 0.79 |
| 0.8 | 20 | 5 | 0.56 | 27 | 7 | 0.59 |
| 0.9 | 18 | 6 | 0.84 | 17 | 8 | 1.50 |
| 1.0 | 12 | 5 | 1.20 | 20 | 8 | 1.12 |
| 1.1 | 2 | 0 | 0.00 | 4 | 3 | 5.06 |
| 1.2 | 7 | 5 | 4.21 | 4 | 4 | ∞ |
| 1.3 | 4 | 2 | 1.68 | - | - | - |
| 1.4 | 4 | 2 | 1.68 | - | - | - |
| 1.5 | 3 | 3 | ∞ | - | - | - |

CAG, coronary angiography; CCA-IMT max, thicker one of right or left side of intima media thickness of common carotid artery; LR, likelihood ratio; PA-IMT max, thicker one of right or left side of intima media thickness of popliteal artery.

lesions[4-11]. In the present study, we determined the CCA-IMT and PA-IMT almost simultaneously and investigated whether they are correlated. We also determined the CCA-IMT and PA-IMT sequentially to assess the possibility of increasing the sensitivity and specificity of these determinations for predicting the presence of coronary arteriosclerotic lesions.

### 1. *CCA and PA ultrasonography*

We found that the left CCA-IMT was significantly ($p<0.05$) greater than the right CCA-IMT; in contrast, the right and left the PA-IMT values did not differ ($p=0.58$). Several earlier studies have also found that the left CCA-IMT was significantly greater than the right CCA-IMT[15,16].

The correlation between the right and left sides was weak for both the CCA-IMT ($r=0.67$) and the PA-IMT ($r=0.54$). Therefore, in the present study, the greater of the values for the two sides was adopted as the representative CCA-IMT max and the PA-IMT max. Although the CCA-IMT max was significantly ($p<0.05$) greater than the PA-IMT max, the correlation between the two values was weak ($r=0.35$). These results suggest the CCA-IMT max and PA-IMT max are independent factors. The weak correlation between the CCA-IMT and PA-IMT might be attributed to differences between the carotid and femoral arteries[6,17-19].

### 2. *Improvement in accuracy by serial and parallel examinations*

Because the CCA-IMT max and PA-IMT max can be considered independent factors, we investigated whether combining them could improve the accuracy of predicting 75% coronary artery stenosis. The sensitivity was increased by serial determinations, and the specificity was increased by parallel determinations. With serial examinations, the sensitivity was 39.5% and the specificity was 89.1% when the CCA-IMT max was 1.2 mm or more or the PA-IMT max was 1.1 mm or more. When the CCA-IMT max was 1.2 mm or more or the PA-IMT max was 1.0 mm or more, the sensitivity increased to 55.3% but the specificity decreased to 75%. With parallel examinations, the accuracy of prediction improved, with a sensitivity of 60.5% and a specificity of 68.8% when the CCA-IMT max was 0.7 mm or more and the PA-IMT max was 0.9 mm or more.

Stress ECG testing has been considered diagnostically valuable because of its high specificity. However, stress ECG testing is generally less sensitive than other diagnostic imaging procedures, such as stress myocardial scintigraphy[20,21]. A meta-analysis of 147 studies of patients who underwent both CAG and stress ECG testing[22] found that the mean sensitivity of stress ECG testing was 68% (range, 23%-100%) and the mean specificity was 77% (range, 17%-100%). An analysis limited to results of 58 tests focusing on diagnosis in patients without a history of myocardial infarction found a mean sensitivity of 67% and a mean specificity of 72%. A study designed to minimize the bias of close examination in 814 male subjects revealed a sensitivity of 45% and a specificity of 85%[23]. The results of the present study suggest that simultaneous CCA and PA ultrasonography is useful for predicting coronary arteriosclerotic lesions, because its specificity is similar to that of stress ECG testing, although its sensitivity is slightly lower.

Thus, the presence of coronary artery lesions can

be predicted with high specificity on the basis of CCA-IMT and PA-IMT. In the present study, the predictive value of PA-IMT for the diagnosis of coronary artery stenosis was almost equal to that of CCA-IMT, maybe slightly better, and the combined use of PA-IMT and CCA-IMT increased sensitivity while maintaining high specificity.

Stress ECG testing and stress myocardial scintigraphy are used as screening procedures for risk stratification in patients with ischemic heart disease. Both procedures have contraindications, because they require exercise tolerance and are difficult to perform if patients are in poor physical condition[24]. Because the evaluation in stress ECG testing is based on ECG changes, evaluating some stress ECG findings relative to resting ECG findings can be difficult[25]. However, ultrasonography can be performed in patients who are not candidates for exercise testing, including those with little or no exercise tolerance. Furthermore, evaluation with ultrasonography is based on clearly defined criteria. Thus, CCA and PA ultrasonography are noninvasive examinations that can be performed safely and easily. For this reason, predicting critical coronary artery lesions on the basis of CCA-IMT and PA-IMT may be useful for risk stratification in patients with ischemic heart disease who have poor exercise tolerance and are not candidates for exercise testing.

## CONCLUSION

Although the CCA-IMT max and PA-IMT max are of similar value for evaluating the coronary arteries, the two are weakly correlated. However, simultaneous examination of the CCA-IMT max and PA-IMT max improves the sensitivity and specificity and is useful for risk stratification in patients with suspected ischemic heart disease.

## REFERENCES

1. Gibbons RJ, Chatterjee K, Daley J, Douglas JS, Fihn SD, Gardin JM, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina : a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). J Am Coll Cardiol 1999 ; 33 : 2092-197.
2. Smith SC Jr, Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines)-executive summary : a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). J Am Coll Cardiol 2001 ; 37 : 2215-39.
3. Scanlon PJ, Faxon DP, Audet AM, Carabello B, Dehmer GJ, Eagle KA, et al. ACC/AHA guidelines for coronary angiography : a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol 1999 ; 33 : 1756-824.
4. Crouse JR 3rd, Craven TE, Hagaman AP, Bond MG.. Association of coronary disease with segment-specific intimal-medial thickening of the extracranial carotid artery. Circulation 1995 ; 92 : 1141-7.
5. Hulthe J, Wikstrand J, Emanuelsson H, Wiklund O, de Feyter PJ, Wendelhag I. Atherosclerotic changes in the carotid artery bulb as measured by B-mode ultrasound are associated with the extent of coronary atherosclerosis. Stroke 1997 ; 28 : 1189-94.
6. Lekakis JP, Papamichael CM, Cimponeriu AT, Stamatelopoulos KS, Papaioannou TG, Kanakakis J, et al. Atherosclerotic changes of extracoronary arteries are associated with the extent of coronary atherosclerosis. Am J Cardiol 2000 ; 85 : 949-52.
7. Kusaka M, Carotid artery ultrasonography and pulse wave velocity as predictiors of coronary artery disease. Jikeikai Med J 1997 ; 44 : 161-72.
8. Geroulakos G, O'Gorman DJ, Kalodiki E, Sheridan DJ, Nicolaides AN. The carotid intima-media thickness as a marker of the presence of severe symptomatic coronary artery disease. Eur Heart J 1994 ; 15 : 781-5.
9. Khoury Z, Schwartz R, Gottlieb S, Chenzbraun A, Stern S, Keren A. Relation of coronary artery disease to atherosclerotic disease in the aorta, carotid, and femoral arteries evaluated by ultrasound. Am J Cardiol 1997 ; 80 : 1429-33.
10. Nowak J, Nilsson T, Sylven C, Jogestrand T. Potential of carotid ultrasonography in the diagnosis of coronary artery disease : a comparison with exercise test and variance ECG. Stroke 1998 ; 29 : 439-46.
11. Nagata M, Furutani N, Ohyama N. Usefulness of popliteal artery ultrasonography for diagnosing coronary artery disease. Jikeikai Med J 2000 ; 47 : 31-40.
12. Nobuyoshi M. Procedure. Coronary angiography and intervention (in Japanese). Tokyo : Igakushoin ; 1992.

p. 90–161.
13. Austen WG, Edwards JE, Frye RL, Gensini GG, Gott VL, Griffith LS, et al. A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. Circulation 1975 ; 51(4 Suppl) : 5–40.
14. O'Leary DH, Polak JF, Wolfson SK Jr, Bond MG, Bommer W, Sheth S, et al. Use of sonography to evaluate carotid atherosclerosis in the elderly. The Cardiovascular Health Study. CHS Collaborative Research Group. Stroke 1991 ; 22 : 1155–63.
15. Allan PL, Mowbray PI, Lee AJ, Fowkes FG. Relationship between carotid intima–media thickness and symptomatic and asymptomatic peripheral arterial disease. The Edinburgh Artery Study. Stroke 1997 ; 28 : 348–53.
16. Rosfors S, Hallerstam S, Jensen–Urstad K, Zetterling M, Carlstrom C. Relationship between intima–media thickness in the common carotid artery and atherosclerosis in the carotid bifurcation. Stroke 1998 ; 29 : 1378–82.
17. Smedby O. Geometrical risk factors for atherosclerosis in the femoral artery : a longitudinal angiographic study. Ann Biomed Eng 1998 ; 26 : 391–7.
18. Salonen JT, Salonen R. Ultrasound B–mode imaging in observational studies of atherosclerotic progression. Circulation 1993 ; 87(suppl II) : II–56 –II –65.
19. Stelle ML, Mircoli L, Magnoni AA, Giannattasio C, Ferrari AU, Mancia G. Differential alterations of common carotid and femoral artery distensibility in 12–week–old spontaneously hypertensive rats. J Hypertens 1997 ; 15 : 1665–9.
20. Ritchie JL, Bateman TM, Bonow RO, Crawford MH, Gibbons RJ, Hall RJ, et al. Guidelines for clinical use of cardiac radionuclide imaging. Report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Committee on Radionuclide Imaging), developed in collaboration with the American Society of Nuclear Cardiology. J Am Coll Cardiol 1995 ; 25 : 521–47.
21. Cheitlin MD, Alpert JS, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, et al. ACC/AHA Guidelines for the Clinical Application of Echocardiography. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Application of Echocardiography). Developed in colloboration with the American Society of Echocardiography. Circulation 1997 ; 95 : 1686–744.
22. Gianrossi R, Detrano R, Mulvihill D, Lehmann K, Dubach P, Colombo A, et al. Exercise–induced ST depression in the diagnosis of coronary artery disease : a meta–analysis. Circulation 1989 ; 80 : 87–98.
23. Froelicher VF, Lehmann KG, Thomas R, Goldman S, Morrison D, Edson R, et al. The electrocardiographic exercise test in a population with reduced workup bias : diagnostic performance, computerized interpretation, and multivariable prediction. Veterans Affairs Cooperative Study in Health Services # 016 (QUEXTA) Study Group. Quantitative Exercise Testing and Angiography. Ann Intern Med 1998 ; 128(12 Pt 1) : 965–74.
24. Fletcher GF, Balady G, Froelicher VF, Hartley LH, Haskell WL, Pollock ML. Exercise standards. A statement for healthcare professionals from the American Heart Association. Writing Group. Circulation 1995 ; 91 : 580–615.
25. Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, et al. ACC/AHA Guidelines for Exercise Testing. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). J Am Coll Cardiol 1997 ; 30 : 260–311.