Usefulness of Stress Myocardial Perfusion Imaging for Evaluating Asymptomatic Patients After Coronary Stent Implantation

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Background Stent implantation in coronary angioplasty has reduced the rate of restenosis, but many patients still undergo follow-up coronary angiography (CAG). The present study was a multi-center retrospective analysis of the usefulness of stress single photon emission computed tomography (SPECT) compared with follow-up CAG in stent-implanted patients who remained asymptomatic during the follow-up period.
Methods and Results The study group of 103 patients underwent both SPECT and CAG at 4–9 months after stent implantation. Restenosis occurred in 20 (19%) of 106 vessel territories, and a reversible perfusion defect was found in 32 (30%) territories. Sensitivity, specificity, positive and negative predictive values, and accuracy of SPECT were 65%, 78%, 41%, 91%, and 76%, respectively. The accuracy was lower in territories with a prior myocardial infarction (71%), in the left circumflex artery (58%), and in cases with three-vessel disease (63%). The negative predictive value was high, but 7 false negative cases included 4 cases with prior myocardial infarction, and 2 cases with reversible defects in other vessel territories.
Conclusions Stress SPECT imaging is a useful tool for following up patients with coronary stent implantation, and follow-up CAG could be omitted in patients with negative SPECT imaging, no prior myocardial infarction, one- or two-vessel disease, and sufficient stress loading. (*Circ J* 2004; **68:** 462–466)

Key Words: Coronary angiography; Restenosis; Single photon emission computed tomography (SPECT); Stent

Restenosis after successful percutaneous transluminal coronary angioplasty (PTCA) remains an important clinical problem, and many patients undergo follow-up coronary angiography (CAG) at 3–6 months after PTCA.[1] Among the newly developed techniques for myocardial revascularization, the implantation of coronary stents has rapidly gained widespread clinical acceptance and the rate of restenosis (and also of revascularization) has been reduced compared with PTCA alone.[2–4] Therefore, follow-up CAG may be less beneficial, especially for asymptomatic patients.

The usefulness of perfusion scintigraphy in the follow-up of symptomatic and asymptomatic patients after PTCA has been defined by several studies,[5–10] and because stents are usually implanted in proximal lesions of coronary arteries, and the influence of coronary spasm at the stent site has been basically excluded, the usefulness of perfusion scintigraphy for following up patients after stent implantation is expected to increase.[11–13] However, because perfusion scintigraphy has been evaluated only qualitatively or semi-quantitatively, there are intra- and inter-observer variations.

The present study was a multi-center trial to retrospectively investigate the diagnostic value of stress single photon emission computed tomography (SPECT) in comparison with follow-up CAG in patients with stent implantation who remained asymptomatic during the follow-up period.

Methods

Patient Population

In the 5 collaborating hospitals, 114 patients underwent both stress SPECT and CAG at 4–9 months after successful stent implantation between February, 1997 and April, 2000. Eleven patients who complained of chest pain during the follow-up period were excluded from the analysis. Because stents had been implanted in 2 different vascular territories in 3 patients, 106 vascular territories in 103 patients (76 males, 27 females; 40–86 years of age) were available for evaluation. Table 1 summarizes the characteristics of the patient population. The mean interval between stent implantation and stress SPECT was 176±31 days (range, 120–266 days); 55 of 106 lesions (52 %) were related to a prior myocardial infarction (MI).

(Received January 6, 2004; revised manuscript received February 16, 2004; accepted February 20, 2004)

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Table 1 Characteristics of the Patients and Lesions

	no.
Patients	*103*
Territories	*106*
Age (years)	*65±11*
M/F	*76/27*
Diabetes mellitus	*23 (22%)*
Hypertension	*30 (29%)*
Current smoking	*22 (21%)*
Stent-implanted vessel	
LAD	*61 (58%)*
RCA	*33 (31%)*
LCX	*12 (11%)*
Diseased vessels	
1-VD	*63 (59%)*
2-VD	*35 (33%)*
3-VD	*8 (8%)*
Tube/coil stent	*61/54*
Prior MI	*55 (52%)*
Duration (days)	
Stent and SPECT	*176±31*
Stent and CAG	*190±27*
SPECT and CAG	*20±24*

LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery; 1-VD, one-vessel disease; 2-VD, two-vessel disease; 3-VD, three-vessel disease; Prior MI, prior myocardial infarction.
Data for age and duration are expressed as means±SD.

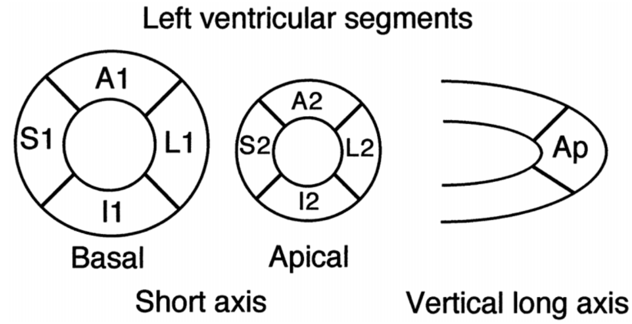

Fig 1. Nine regions of interest on 2 reconstructed short-axis slices and 1 vertical long-axis slice. A1, S1, I1, and L1: basal anterior, septal, inferior, and lateral segments; A2, S2, I2, L2: apical anterior, septal, inferior, and lateral segments; Ap: apical segments. A scan showing a reversible defect in at least one adjacent segment in the territory referable to the vessel treated by stents was considered as positive for ischemia (I1, I2 for RCA; A1, A2, S1, S2, Ap for LAD; L1, L2 for LCX).

Stent Placement

Stent types included 61 tube and 54 coiled stents (11% Palmatz-Schatz, 28% Multilink, 13% Nir, 2% Wiktor, 9% GRII, 37% GFX, 1% S670). Stents were implanted electively in 33 territories for stable angina and as emergencies in 73 territories for acute coronary syndrome (27 for unstable angina pectoris and 46 for acute MI). The mean stenosis was 94.5±7.1% before and 4.6±11.9% after stent implantation by quantitative coronary analysis.

CAG

All the patients underwent follow-up CAG 130–267 days after stent implantation (Table 1). Coronary artery stenosis was assessed by at least 2 cardiologists without knowledge of the SPECT results. Stent restenosis was defined by quantitative coronary analysis as a >50% luminal narrowing at the implantation site or at the proximal or distal edges.

Stress Scintigraphy Protocols

Of 103 patients, 96 underwent symptom-limited exercise testing using a bicycle ergometer or treadmill exercise under the standard Bruce protocol while fasting. In 7 patients who were unable to exercise, dipyridamole stress tests were performed using a 4-min infusion of 0.56 mg/kg per min dipyridamole. All tests were performed mid-morning, and cardiac medications were withheld on the morning of the day of testing. For all stress protocols, patients were continuously monitored with 12-lead electrocardiogram (ECG). Indications for stopping the exercise test were uncomfortable dyspnea or angina, serious arrhythmias, progressive reduction of systolic blood pressure, significant ST change and target heart rates. Either 1 min before the anticipated end of exercise or 3 min after the end of the dipyridamole infusion, 74 mBq ^{201}Tl (for 65 patients), 5× 37 mBq ^{99m}Tc-tetrofosmin (32 patients) or ^{99m}Tc-sestamibi (6 patients) (Nihon Mediphysic Inc and Daiichi Inc, Japan) was injected intravenously and flushed with saline, and the patient was encouraged to exercise for an additional minute. Early SPECT was performed 5–10 min after exercise and late SPECT was performed 3–4 h after early SPECT. The 15×37 mBq ^{99m}Tc-tetrofosmin or ^{99m}Tc-sestamibi was reinjected when late SPECT was performed. The SPECT images were acquired using a 2- or 3-headed SPECT system.[14] Transverse slices were reconstructed by a filtered backprojection algorithm after pre-processing of the images with Butterworth low-pass filter. Vertical long-axis, short-axis, and horizontal long-axis tomograms were reconstructed from the transverse slices.

Visual Analysis of the SPECT Images

The uptake score of perfusion imaging was visually determined for each of the total 9 myocardial segments (basal anterior, basal septum, basal inferior, basal lateral, apical anterior, apical septal, apical inferior, apical lateral walls and apex) according to a 4-point scoring system: 3=normal, 2=mildly reduced, 1=moderately reduced and 0=markedly reduced (Fig 1). We considered a scan was positive for ischemia when there was a reversible defect in at least one adjacent segment in the territory referable to the vessel treated by stents (I1, I2 for the right coronary artery, A1, A2, S1, S2, Ap for the left anterior descending artery, and L1, L2 for the left circumflex artery).[15,16] For the purposes of visual interpretation, stress and rest tomograms were evaluated by consensus of 2 observers.

Data Analysis

Data are expressed as means ± standard deviation (SD). The sensitivity of SPECT imaging was defined as the number of true-positive test results divided by the sum of the true-positive and false-negative test results. The specificity was defined as the number of true-negative test results divided by the sum of the true-negative and false-positive test results. The positive predictive value was defined as the number of true-positive test results divided by all the positive test results. The negative predictive value was defined as the number of true-negative test results divided by all the negative test results. Accuracy was defined as the number of true-positive and true-negative test results divided by the total number of tests. Categorical variables were compared among the groups of patients by chi-square analyses.

Table 2 Angiographical Restenosis and Reversible Perfusion Defect on SPECT Imaging

	Reversible perfusion defect on SPECT	
	(+)	*(–)*
Restenosis on CAG		
(+)	*13*	*7*
(–)	*19*	*67*

Table 3 Sensitivity, Specificity and Accuracy of SPECT Imaging for Evaluation of Stent Restenosis in Different Subpopulations

	no.	*Sensitivity (%)*	*Specificity (%)*	*Accuracy (%)*
All territories	*106*	*65*	*78*	*76*
Prior MI				
(–)	*51*	*70*	*83*	*80*
(+)	*55*	*60*	*73*	*71*
Stent-implanted vessel				
LAD	*61*	*64*	*80*	*77*
RCA	*33*	*86*	*77*	*79*
LCX	*12*	*0*	*70*	*58*
Diseased vessels				
1-VD	*63*	*70*	*76*	*75*
2-VD	*35*	*67*	*85*	*80*
3-VD	*8*	*0*	*71*	*63*

See Table 1 for abbreviations.

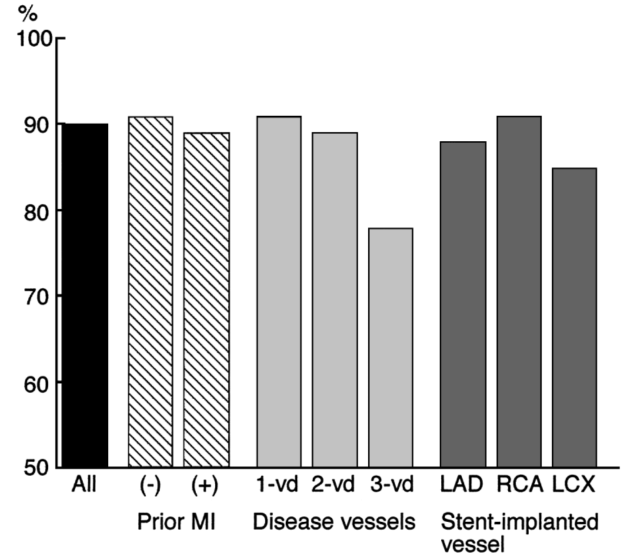

Fig 2. The negative predictive value of SPECT imaging for angiographic restenosis was defined as the number of negative cases for both SPECT and angiographical restenosis divided by all the negative SPECT results.

Results

SPECT Defect and CAG Restenosis

Table 2 shows the results of CAG and SPECT imaging in all territories. Twenty of 106 (19%) investigated coronary arteries showed >50% stenosis at the site of stent implantation in the follow-up CAG. A reversible perfusion defect was found in 32 of 106 (30%) vessel territories and angiographic restenosis was present in 13 of these territories. In contrast, restenosis was found in only 7 of 74 territories that did not show a reversible perfusion defect.

Diagnostic Performance of SPECT

The diagnostic performance of SPECT imaging for predicting angiographic restenosis is shown in Table 3. The sensitivity and specificity of SPECT imaging were 65% and 78%, respectively, the positive and negative predictive values were 41% and 91%, and the accuracy was 76%. The sensitivity, specificity and accuracy of exercise ECG testing (103 cases) were 25%, 74% and 64%, respectively.

Table 3 also shows the performance of SPECT imaging for predicting angiographic restenosis in subpopulations of vessel territories with regard to the presence of a prior MI, the number of diseased vessels, and the site of the lesion. There were no significant differences among the groups, but the accuracy tended to be lower if there was a prior MI, three-vessel disease or the lesion was in the left circumflex artery.

Prevalence of False-Negative Cases

Because the present study was designed to examine the usefulness of SPECT imaging in determining the necessity for CAG in patients who remained asymptomatic during the follow-up period after stent implantation, the causes of negative SPECT results in cases with angiographic restenoses (ie, false-negative cases) are important. Fig 2 shows the negative predictive values in all and the subpopulations of the vessel territories. The values did not differ significantly, but tended to be lower for three-vessel disease and lesions in the left circumflex artery. Table 4 summarizes the characteristics of the 7 false negative cases, which included 4 cases with a prior MI for the stent-implanted vessel, and 2 cases with reversible ischemia in other vessel territories. In 2 cases, the exercise tolerance was insufficient (<80% of target heart rate), although 1 case underwent dipyridamole infusion.

Table 4 False-Negative Cases for SPECT Imaging

Case no.	*Stent-implanted vessel*	*Diseased vessels*	*Prior MI*	*Defect in other territories*	*Exercise loading (%THR)*
1	*LAD*	*1-VD*	+	–	*107*
2	*LAD*	*1-VD*	+	–	*88*
3	*LAD*	*2-VD*	+	–	*93*
4	*LCX*	*2-VD*	+	–	*82*
5	*LCX*	*2-VD*	–	+	*62*
6	*RCA*	*3-VD*	–	+	*79**
7	*LAD*	*1-VD*	–	–	*84*

**In case 6, 4 min infusion of 0.56 mg/kg per min dipyridamole was performed in addition to exercise loading.*
%THR, percentage of target heart rate (see Table 1 for other abbreviations).

Discussion

This multi-center trial was designed to retrospectively examine the usefulness of SPECT imaging for determining the necessity of CAG in patients with stent implantation who remained asymptomatic during the follow-up period. The study population was not homogeneous in terms of the type of stress, tracer, scintigraphic modalities, and time interval between SPECT and CAG. Nevertheless, the present results indicate that SPECT imaging has a good non-invasive diagnostic performance in the follow-up evaluation of patients after coronary stent implantation.

Comparison With Previous Studies

Because restenosis is the prime limitation of PTCA, many cardiologists perform functional testing 3–6 months later, even in asymptomatic patients. Garzon and Eisenberg reviewed the diagnostic ability of exercise tolerance testing (ETT), stress nuclear imaging and stress echocardiographic imaging to detect post-PTCA restenosis in 36 previous studies and found that ETT alone was poorly diagnostic, but that the addition of nuclear imaging significantly improved the diagnosis of restenosis.[17] In their analyses, stress nuclear imaging had a sensitivity of 87% (74–100%) and a specificity of 78% (74–81%).[5–10] Three recent studies have shown similar values for sensitivity (79–95%) and specificity (73–84%) for stent restenosis.[11–13] There are several potential explanations for the finding of a high sensitivity of SPECT imaging to detect restenosis of stent-implanted vessels. First, stents tend to be placed in large vessels and frequently in the proximal segments. Therefore, in the presence of restenosis involving the stent itself, the altered flow reserve would involve a large area of myocardium and would be easily detectable by perfusion imaging. Second, recent histological and intravascular ultrasound investigations have suggested that the major determinant of late lumen loss and in-stent restenosis is neointimal tissue proliferation.[18] Because the recoil and spasm of the stent-implanted lesion could in principle be excluded, the follow-up testing can be performed at the most appropriate time interval (3–6 months) to identify patients with restenosis. Furthermore, most patients can undergo maximum exercise testing without or with minimal dosages of anti-anginal drugs.

We identified a sensitivity of 65% and a specificity of 78% for the detection of angiographic restenosis by SPECT imaging. Because the sensitivity and specificity of exercise ECG testing were 25% and 74%, SPECT imaging largely improved the diagnostic ability for detecting stent restenosis. However, the values we obtained were slightly lower than those in the other studies, for the following reasons. First, many of the previous studies had patient populations with a high prevalence of restenosis or a low prevalence of either multi-vessel disease or previous MI.[8–10] The present cases were asymptomatic with a much lower rate of restenosis (19%) than those observed in earlier studies, and included more cases of multi-vessel disease (41%) and prior MI (52%). It is noteworthy that patients with a low probability of restenosis would have a substantially high negative predictive value with SPECT imaging. Therefore, it is likely that a negative SPECT result is clinically useful in patients with a low pre-test probability of restenosis. From that viewpoint, the high negative predictive value in this study (~90%) suggests that a negative test result may be indicative of a good prognosis.[19–21] Second, some previous studies defined abnormal uptake as a positive SPECT result, whereas we used the defect reversibility criterion, which might result in a lower sensitivity of SPECT imaging to identify angiographic restenosis while retaining a high specificity.

Characteristics of False-Negative Territories

Previous studies have demonstrated lower sensitivity and specificity values in territories with a prior MI,[12,22] and the scintigraphic evaluation of stent restenosis in such cases is limited because of the pre-existing perfusion abnormalities. In the analysis by Kosa et al of SPECT imaging, the sensitivity and specificity were only 64% and 78%, respectively,[12] whereas on the present study the overall accuracy of SPECT was 71% in territories with prior MI (vs 80% in no prior MI) and the 4 territories with prior MI were false negatives. Stress-induced ischemia in other territories could also disturb the diagnostic performance of SPECT; in this study, both the negative predictive value and overall accuracy in three-vessel disease were lower than in one- or two-vessel disease. Furthermore, 2 territories were false negative because of ischemia in other territories. In these cases, however, the angiographic stenoses were between 50% and 75%. The appropriate choice of the cutoff for significant restenosis should be considered.[10,23] In addition, one territory with stent restenosis was missed, presumably because of insufficient exercise loading (62% of target heart rate). Patients who have insufficient exercise tolerance should undergo pharmacological stress for a more accurate result. Therefore, although our results indicated the usefulness of SPECT imaging as the follow-up of asymptomatic patients after coronary stent implantation, the interpretation of SPECT results should be made carefully, especially in cases of prior MI for the stent-implanted vessel, three-vessel disease, or insufficient stress loading.

In conclusion, stress SPECT imaging is a useful tool for following up patients after coronary stent implantation, and the follow-up CAG could be omitted for those with negative SPECT imaging, no prior MI in the stent-implanted vessel, one- or two-vessel disease, and sufficient stress loading. The best strategy for the follow-up of patients who have undergone coronary stent implantation in terms of accuracy, patient morbidity, and cost has yet to be determined. If our results can be confirmed in future prospective evaluations, SPECT imaging may be a useful strategy to diagnose or exclude restenosis and therefore may avoid the need for follow-up CAG in patients without or with minimal symptoms after coronary stent implantation. For this purpose, the appropriate time interval between stent implantation and stress SPECT imaging should be determined, and the influence of lesion morphology, length, and site of restenosis (eg, in-stent, proximal or distal edge of stent) on the diagnostic performance of SPECT should be examined further.

References

1. Serruys PW, Luijten HE, Beatt KJ, Geuskens R, de Feyter PJ, van den Brand M, et al. Incidence of restenosis after successful coronary angioplasty: A time-related phenomenon. *Circulation* 1988; **77:** 361–371.
2. Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease: Stent Restenosis Study Investigators. *N Engl J Med* 1994; **331:** 496–501.
3. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, et al. A comparison of balloon-expandable-stent im-

plantation with balloon angioplasty in patients with coronary artery disease: Benestent Study Group. *N Engl J Med* 1994; **331:** 489–495.
4. Sonmez K, Turan F, Gencbay M, Degertekin M, Akcay A, Duran NE. Long-term (3–5 years) clinical and angiographic follow-up results of coronary stenting in elderly patients. *Circ J* 2002; **66:** 1029–1033.
5. Hecht HS, Shaw RE, Bruce TR, Ryan C, Stertzer SH, Myler RK. Usefulness of tomographic thallium-201 imaging for detection of restenosis after percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1990; **66:** 1314–1318.
6. Hecht HS, Shaw RE, Chin HL, Ryan C, Stertzer SH, Myler RK. Silent ischemia after coronary angioplasty: Evaluation of restenosis and extent of ischemia in asymptomatic patients by tomographic thallium-201 exercise imaging and comparison with symptomatic patients. *J Am Coll Cardiol* 1991; **17:** 670–677.
7. Milan E, Zoccarato O, Terzi A, Ettori F, Leonzi O, Niccoli L, et al. Technetium-99m-sestamibi SPECT to detect restenosis after successful percutaneous coronary angioplasty. *J Nucl Med* 1996; **37:** 1300–1305.
8. Marie PY, Danchin N, Karcher G, Grentzinger A, Juilliere Y, Olivier P, et al. Usefulness of exercise SPECT-thallium to detect asymptomatic restenosis in patients who had angina before coronary angioplasty. *Am Heart J* 1993; **126:** 571–577.
9. Schroeder E, Marchandise B, De Coster P, Brichant C, Mitri K, Pieters D, et al. Detection of restenosis after coronary angioplasty for single-vessel disease: How reliable are exercise electrocardiography and scintigraphy in asymptomatic patients? *Eur Heart J* 1989; **10**(Suppl G)**:** 18–21.
10. Renkin J, Melin J, Robert A, Richelle F, Bachy JL, Col J, et al. Detection of restenosis after successful coronary angioplasty: Improved clinical decision making with use of a logistic model combining procedural and follow-up variables. *J Am Coll Cardiol* 1990; **16:** 1333–1340.
11. Milavetz JJ, Miller TD, Hodge DO, Holmes DR, Gibbons RJ. Accuracy of single-photon emission computed tomography myocardial perfusion imaging in patients with stents in native coronary arteries. *Am J Cardiol* 1998; **82:** 857–861.
12. Kosa I, Blasini R, Schneider-Eicke J, Neumann FJ, Matsunari I, Neverve J, et al. Myocardial perfusion scintigraphy to evaluate patients after coronary stent implantation. *J Nucl Med* 1998; **39:** 1307–1311.
13. Galassi AR, Foti R, Azzarelli S, Coco G, Condorelli G, Russo G, et al. Usefulness of exercise tomographic myocardial perfusion imaging for detection of restenosis after coronary stent implantation. *Am J Cardiol* 2000; **85:** 1362–1364.
14. Uehara A, Kurata C, Sugi T, Mikami T, Yamazaki K, Satoh H, et al. Peak systolic blood pressure in exercise testing is associated with scintigraphic severity of myocardial ischemia in patients with exercise-induced ST-segment depression. *Jpn Circ J* 2000; **64:** 590–594.
15. Kurata C, Sakata K, Taguchi T, Kobayashi A, Yamazaki N. Exercise-induced silent myocardial ischemia: Evaluation by thallium-201 emission computed tomography. *Am Heart J* 1990; **119:** 557–567.
16. Tawarahara K, Kurata C, Taguchi T, Kobayashi A, Yamazaki N. Exercise testing and thallium-201 emission computed tomography in patients with intraventricular conduction disturbances. *Am J Cardiol* 1992; **69:** 97–102.
17. Garzon P, Eisenberg MJ. Functional testing for the detection of restenosis after percutaneous transluminal coronary angioplasty: A meta-analysis. *Can J Cardiol* 2001; **17:** 41–48.
18. Hoffmann R, Mintz GS, Dussaillant GR, Popma JJ, Pichard AD, Satler LF, et al. Patterns and mechanisms of in-stent restenosis: A serial intravascular ultrasound study. *Circulation* 1996; **94:** 1199–1202.
19. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: A meta-analysis. *J Am Coll Cardiol* 2002; **39:** 1151–1158.
20. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Kang X, Germano G, et al. Determination of risk and its temporal variation in patients with normal stress myocardial perfusion scan. *J Am Coll Cardiol* 2003; **41:** 1329–1340.
21. Zellweger MJ, Weinbacher M, Zutter AW, Jeger RV, Mueller-Brand J, Kaiser C, et al. Long-term outcome of patients with silent versus symptomatic ischemia six months after percutaneous coronary intervention and stenting. *J Am Coll Cardiol* 2003; **42:** 33–40.
22. Wainwright RJ, Brennand-Roper DA, Maisey MN, Sowton E. Exercise thallium-201 myocardial scintigraphy in the follow-up of aortocoronary bypass graft surgery. *Br Heart J* 1980; **43:** 56–66.
23. Yanagisawa H, Chikamori T, Tanaka N, Hatano T, Morishima T, Hida S, et al. Correlation between thallium-201 myocardial perfusion defects and the functional severity of coronary artery stenosis as assessed by pressure-derived myocardial fractional flow reserve. *Circ J* 2002; **66:** 1105–1109.