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Exercise myocardial perfusion scintigraphy is useful for evaluating myocardial ischemia even in the elderly

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Pharmacologic stress testing is recommended to elderly patients as a valuable alternative to exercise testing. We examined whether exercise testing is as useful for evaluating myocardial ischemia in the elderly as in the young. The consecutive 1,508 patients who underwent exercise ^{201}Tl single-photon emission computed tomography (SPECT) were divided into six age groups: 6–29 years (n = 56), 30–44 (n = 143), 45–54 (n = 311), 55–64 (n = 498), 65–74 (n = 402), and 75–88 (n = 98). Both heart rate and rate-pressure product at peak exercise were significantly lower in patients aged 75–88 than in the other five groups. The frequency of ischemic ST depression was higher in patients aged 75–88 than in those aged 6–74, although the difference was not significant. Moreover, the frequency of ^{201}Tl transient defect was significantly higher in patients aged 75–88 than in those aged 6–74. On the other hand, the sensitivity of ischemic ST depression for ^{201}Tl transient defect was similar among the six groups, but the specificity was significantly lower in patients aged 75–88 than in those aged 6–74. In conclusion, exercise ^{201}Tl SPECT is useful for evaluating myocardial ischemia even in the elderly, but exercise electrocardiography has limitations such as lower specificity in the elderly than ^{201}Tl SPECT.

Key words: elderly, exercise testing, electrocardiography, Tl-201, SPECT

INTRODUCTION

NONINVASIVE EVALUATION is important in the diagnosis of coronary artery disease (CAD) in the elderly, who constitute an increasing percentage of patients evaluated for CAD.[1] Since a large percentage of elderly patients cannot perform adequate physical exercise because of physical impairment, exercise testing of them may result in a negative study even if they have severe CAD. Pharmacologic stress testing with dipyridamole,[2,3] adenosine[4,5] or dobutamine[6] is therefore recommended to elderly patients as a valuable alternative to exercise testing,[7–10] but it has not been assessed whether exercise testing is effective in evaluating CAD in the elderly or not.

In exercise testing, myocardial scintigraphy is more sensitive to stress-induced myocardial ischemia than electrocardiography (ECG),[11,12] and myocardial perfusion imaging has been reported to improve the sensitivity for CAD compared with ECG, regardless of the level of stress.[13] Exercise myocardial scintigraphy may therefore be more suitable for the elderly than exercise ECG because of their limited exercise capacity, but it has not been determined whether the superiority of myocardial perfusion scintigraphy over ECG in the elderly and other age groups is different.

The purposes of this study were thus to compare the frequencies of positive exercise testing in the elderly and other age group and to investigate the usefulness of exercise ECG in the elderly from the viewpoint of myocardial perfusion scintigraphy.

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SUBJECTS AND METHODS

Patients

The 1,508 consecutive patients who underwent exercise ^{201}Tl single-photon emission computed tomography

(SPECT) in our nuclear cardiology laboratory were divided into six age groups: 56 patients aged 6–29 years, 143 aged 30–44 years, 311 aged 45–54 years, 498 aged 55–64 years, 402 aged 65–74 years and 98 aged 75–88 years. Of the 1,508 patients, 417 (27.7%) previously had myocardial infarction, and 258 (17.1%) had known CAD without myocardial infarction. The frequency of myocardial infarction was not significantly different in patients aged 75–88 years from that in patients aged 6–74 years (28.3% versus 27.4%; $p = 0.86$). The exercise scintigraphy was requested for diagnostic reasons in 347 patients (23.0%) with chest pain and for evaluation of possible CAD in 177 (11.7%) with ECG abnormalities including arrhythmias and positive exercise ECG in a medical checkup. The remaining 309 patients (20.5%) with miscellaneous clinical backgrounds such as Kawasaki's disease, peripheral vascular disease, history of congestive heart failure, multiple coronary risk factors and suspected cardiomyopathy were referred to the exercise scintigraphy for evaluation of possible CAD. The percentage of female patients was not significantly different among the six groups (22.4% to 35.7%; $p = 0.13$). As a rule, we performed exercise testing for noninvasive evaluation of CAD in patients who were not restricted to bed rest. During the same period, only 63 (4.0%) of 1,571 patients who were referred to our laboratory for evaluation of CAD underwent pharmacologic stress testing because of aortic aneurysm, severe arteriosclerosis obliterans or a bedridden condition.

Exercise testing
All patients underwent symptom-limited, maximal exercise testing on an upright bicycle ergometer in a fasting state. The stress workload was 25 or 50 watts with subsequent stepwise increments of 25 watts every 2 minutes. The exercise end points included moderate-to-severe chest pain, shortness of breath, leg fatigue, hypotension, or severe arrhythmias. At peak exercise, 111–148 MBq of ^{201}Tl was injected intravenously and patients were encouraged to continue exercising for an additional 60 seconds. The ischemic depression of ST segments was defined as either horizontal or downward depression that was ≥0.1 mV below the baseline 0.08 second after the J point.

Acquisition of SPECT
Myocardial images were obtained with a large filed-of-view rotating gamma camera (ZLC 7500, Siemens Gammasonics, Inc., Des Plaines, Ill.) equipped with a high-resolution, parallel-hole collimator and interfaced with a computer (Scintipac 2400, Shimadzu Corp., Kyoto, Japan). Thirty-two projections over 180 degrees from the 45-degree right anterior oblique position to the 45-degree left posterior oblique position were acquired in a 64 × 64 matrix for 20 seconds per image. Stress imaging was begun within 10 minutes after completion of exercise, and delayed images were obtained 4 hours after the injection. No attenuation or scatter correction was used. Orthogonal images were generated by oblique-angle reconstruction producing vertical long-axis, short-axis, and horizontal long-axis slices each 6 mm thick.

Analysis of SPECT
Stress and delayed ^{201}Tl SPECTs were analyzed by previously reported methods.[12,14,15] In brief, the uptake score of ^{201}Tl in the stress and delayed images was visually determined for each of the 9 myocardial segments according to a 4-point scoring system: 3 = normal, 2 = mildly reduced, 1 = moderately reduced, and 0 = greatly reduced. A transient defect was considered present if a segment had an abnormal ^{201}Tl washout rate (< mean − 2SD of normal subjects) and its uptake score increased from the stress to the delayed image. When a patient had one or more ^{201}Tl transient defects, we considered that the patient had exercise-induced myocardial ischemia during exercise testing, but we did not consider mildly reduced uptake with minimal redistribution to be a transient defect if its distribution was not consistent with the vascular territory.

Coronary angiography (CAG)
Of the 1,508 patients, 824 (54.6%) underwent CAG within three months of exercise testing. Angiographically documented CAD was defined as a ≥75% luminal narrowing of one or more major coronary arteries or their major

Table 1 Hemodynamics before exercise and at peak exercise

	6–29 y.o.	30–44 y.o.	45–54 y.o.	55–64 y.o.	65–74 y.o.	75–88 y.o.
Before exercise						
Heart rate (beats/min)	71 ± 12	71 ± 12	69 ± 12	70 ± 13	70 ± 14	72 ± 14
Systolic BP (mmHg)	119 ± 19*	133 ± 20*	141 ± 21*	146 ± 23*	152 ± 25	154 ± 25
RPP (mmHg·beats/min)	8404 ± 1999*	9562 ± 2400*	9662 ± 2365*	10185 ± 2606*	10669 ± 2740	11063 ± 2487
At peak exercise						
Heart rate (beats/min)	158 ± 25*	153 ± 20*	145 ± 21*	137 ± 22*	130 ± 21	120 ± 24
% of age-predicted maxHR (%)	78 ± 13*	85 ± 11	85 ± 12	86 ± 14	86 ± 14	84 ± 16
Systolic BP (mmHg)	154 ± 35*	183 ± 31	190 ± 30*	186 ± 30	184 ± 29	181 ± 37
RPP (mmHg·beats/min)	24451 ± 7392*	28061 ± 6504*	27701 ± 6337*	25774 ± 6519*	24047 ± 6149*	22041 ± 6779

BP = blood pressure, RPP = rate-pressure product, maxHR = maximum heart rate; *$p < 0.05$ vs. the elderly patients aged 75–88 years.

branches. The frequency of CAG was significantly lower in those aged 75–88 years than those aged 6–74 years (40.8% versus 55.6%; $p = 0.004$).

Statistical methods
Data were expressed as mean ± SD or as proportions. Proportions were compared by means of the chi-square test or Fisher's exact test. Mean data for the two groups were compared by means of Student's t-test. When data were not normally distributed, the nonparametric Wilcoxon T test was applied. Mean data for three or more groups were compared by one-way analysis of variance followed by multiple comparison test. A value of $p < 0.05$ was used to identify statistically significant results.

RESULTS

Hemodynamics before exercise (Table 1)
Heart rate at rest was similar in all six groups ($p = 0.14$), but systolic blood pressure at rest was significantly different ($p < 0.001$), and it was significantly higher in patients aged 75–88 years than in those aged 6–29, 30–44, 45–54, and 55–64 years (all, $p < 0.05$). Similarly, the rate-pressure product at rest was significantly different among the groups ($p < 0.001$), and it was significantly higher in patients aged 75–88 years than in those aged 6–29, 30–44, 45–54 and 55–64 years (all, $p < 0.05$).

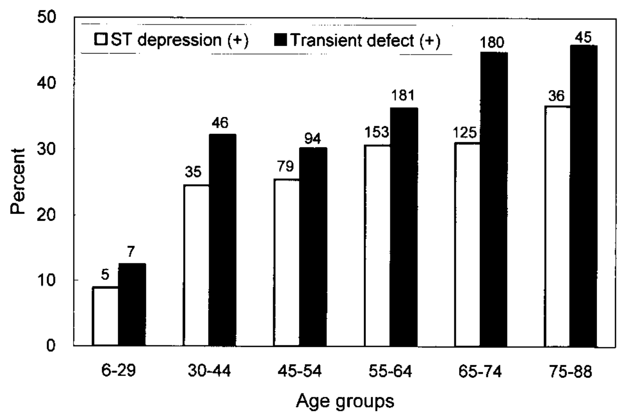

Fig. 1 Frequencies of ischemic ST depression and transient defect in patients aged 6–29, 30–44, 45–54, 55–64, 65–74, and 75–88 years. A number above each column represents the number of patients with ischemic ST depression or those with transient defect.

Hemodynamics at peak exercise (Table 1)
Heart rate at peak exercise in all six groups was significantly different ($p < 0.001$), and it was significantly lower in patients aged 75–88 than in the other five groups (all, $p < 0.05$), but the achieved percentage of age-predicted maximal heart rate was similar in patients aged 30–44, 45–54, 55–64, 65–74 and 75–88 years ($p > 0.05$), although it was significantly different among the six groups ($p = 0.002$). Systolic blood pressure at peak exercise was significantly different among the six groups ($p < 0.001$), and it was significantly higher in patients aged 75–88 than in those aged 6–29 ($p < 0.05$) but significantly lower in those aged 75–88 than in those aged 45–54. As a result, the rate-pressure product at peak exercise was significantly different in the six groups ($p < 0.001$), and it was significantly lower in those aged 75–88 than in the other five groups (all, $p < 0.05$).

Chest pain during exercise testing
The frequency of chest pain during exercise in the six groups was significantly different (3.6%, 12.6%, 9.0%, 14.5%, 16.4% and 16.3% in patients aged 6–29, 30–44, 45–54, 55–64, 65–74 and 75–88 years, respectively; $p = 0.014$), but it was not significantly different between 1,410 patients aged 6–74 years and 98 patients aged 75–88 years (13.2% versus 16.3%; $p = 0.38$).

Ischemic ST depression and transient defect
The frequency of ischemic ST depression during exercise was significantly different among the six groups ($p < 0.001$; Fig. 1). It was slightly higher in those aged 75–88 years than in those aged 6–74 years (36/98 [36.7%] versus 397/1410 [28.2%]), but the difference was not statistically significant ($p = 0.08$). On the other hand, the frequency of ^{201}Tl transient defect was significantly different among the six groups ($p < 0.001$) and was significantly higher in those aged 75–88 than in those aged 6–74 years (45/98 [45.9%] versus 508/1410 [36.0%]; $p = 0.049$; Fig. 1).

The sensitivity of ischemic ST depression for transient defect was not significantly different between patients aged 6–74 and 75–88 years (48.6% versus 50.0%; $p = 0.86$), as well as among the six groups ($p = 0.42$; Table 2). On the other hand, the specificity was significantly different between patients aged 6–74 and 75–88 years (81.0% versus 69.8%; $p = 0.045$), although it was not significantly different among the six groups ($p = 0.13$; Table 2).

Table 2 Sensitivity, specificity, positive and negative predictive value of exercise ECG for ^{201}Tl transient defect

	6–29 y.o.	30–44 y.o.	45–54 y.o.	55–64 y.o.	65–74 y.o.	75–88 y.o.
Sensitivity	28.6%	40.0%	43.0%	50.9%	52.4%	50.0%
Specificity	91.8%	81.4%	82.0%	79.2%	80.2%	69.8%
Positive predictive value	90.0%	74.5%	77.1%	74.5%	69.3%	63.8%
Negative predictive value	40.0%	51.4%	50.6%	58.2%	69.6%	58.3%

Comparison with CAG

The incidence of triple vessel disease was significantly higher in patients aged 75–88 years than in those aged 6–74 (27.5% versus 9.7%; $p < 0.001$), although that of angiographically documented CAD was not significantly different (65.0% versus 58.4%; $p = 0.41$). In 824 patients who underwent CAG, the sensitivity and specificity of transient defect for angiographically documented CAD were 67.8% and 74.7%, respectively. On the other hand, the sensitivity and specificity of ischemic ST depression for angiographically documented CAD were 44.6% and 70.6%, respectively.

DISCUSSION

In this study, the frequency of exercise-induced ^{201}Tl transient defect in patients aged ≥75 years was the highest for the six age groups, and it was significantly higher than in those aged <75, although heart rate and rate-pressure product at peak exercise were significantly lower in those aged ≥75. The frequency of ischemic ST depression in patients aged ≥75 was also the highest for the six age groups, but it was not significantly different from that in those aged <75. On the other hand, the specificity of ischemic ST depression for ^{201}Tl transient defect was significantly lower in patients aged ≥75 than in those aged <75, although the sensitivity was similar.

Since the elderly have been often supposed to be hardly able to perform physical exercise sufficient to induce myocardial ischemia, most cardiologists may expect a low positive rate of exercise testing in elderly patients compared to younger patients and may choose pharmacologic stress testing instead of exercise testing.[7,8,12,16] But it has not been reported whether the positive rate of exercise testing may be significantly lower in elderly patients than in younger patients. Contrary to expectations, this study demonstrated that the positive rate of exercise testing in elderly patients was high in exercise ECG as well as in exercise ^{201}Tl SPECT.

Several backgrounds may be involved in the high positive rate of exercise testing in the elderly. First, we must remember that old age is one of the coronary risk factors[1]; that is, the older the patients referred to cardiologists for evaluation of CAD are, the higher the prevalence of CAD is. In elderly patients, the high prevalence of CAD may result in a high positive rate of exercise testing. Similarly, the high prevalence of severe CAD in the elderly may be one of the reasons for the high positive rate. In fact, the incidence of triple vessel disease was significantly higher in patients aged 75–88 years than in those aged 6–74 among our 824 patients who underwent CAG. Second, exercise testing may be performed less often in elderly patients[17]: inactive elderly patients may have been excluded from our patient population. This bias may however be minimal in this study, because we accepted even inactive and frail elderly patients for exercise testing so far as they were not restricted to bed rest. Third, the first experience of pedaling a bicycle, which is not rare among Japanese elderly women, may have mentally stressed in some of our elderly patients and may have helped to induce myocardial ischemia.[18] On the other hand, examiners needed to push a pedal by hand to help those who had never bicycled before and had difficulty in performing the bicycle ergometer test. This assistance, which may reduce the load on the heart, may serve as a counterbalance to the mental stress. Fourth, exercise stress may occasionally induce coronary artery spasm.[19] and the incidence of coronary spasm is relatively high in Japanese.[20] Even inadequate exercise, which may be enough to cause coronary spasm, may have induced myocardial ischemia in some of our elderly patients.

Many reports have demonstrated that pharmacologic stress testing with myocardial perfusion imaging has almost the same diagnostic and prognostic abilities as exercise testing.[21–24] Compared with pharmacologic stress, however, physical exercise has the advantage of providing additional useful clinical and physiological parameters, such as total workload, maximum heart rate, exercise-induced symptoms, electrocardiographic changes and blood pressure response.[25] In daily clinical practice, therefore, the indications for pharmacologic stress testing are limited to the diagnostic evaluation of patients who are unable to do a maximal exercise stress test.[21] As mentioned above, it is also not likely that pharmacologic stress testing would be diagnostic in patients with normal coronary vessels and symptomatic coronary spasm[21]; that is, exercise testing may be more sensitive for detecting myocardial ischemia induced by coronary spasm.[19,26] Exercise testing may therefore be more favorable than pharmacologic stress testing even in frail elderly patients with physical impairments,[27] if patients are not restricted to bed rest.

The ECG of elderly patients often shows ST-T abnormalities at rest,[28,29] which may make exercise ECG less specific for diagnosing myocardial ischemia.[30,31] The low specificity of ECG for ^{201}Tl transient defect in our elderly patients may be primarily due to a high incidence of ST-T abnormalities in the elderly. In addition, the low specificity may be secondarily due to diffuse myocardial ischemia, which may be frequent in the elderly and cannot be detected by ^{201}Tl SPECT. It is therefore advisable to combine myocardial perfusion imaging with exercise testing in elderly patients, particularly with ST-T abnormalities at rest.[32]

We did not have the gold standard for myocardial ischemia or CAD. The findings of CAG were available in 824 of our 1,508 patients, but the presence of angiographically documented CAD may not necessarily implicate the inducibility of myocardial ischemia in our patients because a large percentage of them had previous myocardial infarction. In addition, anti-anginal medication was not routinely discontinued before exercise testing in our patients with known CAD, because most of them were referred to our laboratory for evaluation of effectiveness of their medication. The sensitivity of ^{201}Tl transient defect for angiographically documented CAD may therefore have been low in our patients. On the other hand, the specificity may have been low in our patients because they included patients with various clinical backgrounds such as exercise-induced coronary artery spasm and suspected cardiomyopathy.

If the purpose of this study were to investigate the diagnostic ability of exercise testing in the elderly, it would be necessary to obtain the sensitivity, specificity and predictive accuracy of exercise testing for the standard. But the purpose of this study was to investigate the clinical usefulness of exercise testing in the elderly, and the high positive rate of exercise testing in the elderly observed in this study, at least, partly demonstrated that exercise testing is useful even in the elderly. A clear demonstration can be given by comparing the prognosis of elderly patients with positive and negative exercise testing. Indeed, the prognostic significance of exercise testing has been reported in elderly patients,[33,34] but these studies selected physically active patients, who represented only some elderly patients. As the next study, we are now investigating whether exercise testing may be useful for predicting the prognosis of a large percentage of elderly patients including inactive and frail patients.

In conclusion, exercise testing, particularly with ^{201}Tl SPECT, is as useful for detecting CAD in the elderly as in the young. On the other hand, exercise ECG has limitations such as low specificity in the elderly compared with ^{201}Tl SPECT. In exercise testing of the elderly myocardial perfusion imaging may therefore be preferable to ECG.

REFERENCES

1. American Heart Association. Coronary artery disease and angina pectoris. *In* 1999 Heart and Stroke Statistical Update. Dallas, American Heart Association, pp. 10–12, 1998.
2. Albro PC, Gould KL, Westcott RJ, Hamilton GW, Ritchie JL, Williams DL. Noninvasive assessment of coronary stenoses by myocardial imaging during pharmacologic coronary vasodilation, III: clinical trial. *Am J Cardiol* 42: 751–760, 1978.
3. He ZX, Iskandrian AS, Gupta NC, Verani MS. Assessing coronary artery disease with dipyridamole technetium-99m-tetrofosmin SPECT: a multicenter trial. *J Nucl Med* 38: 44–48, 1997.
4. Verani MS, Mahmarian JJ, Hixson JB, Boyce TM, Staudacher RA. Diagnosis of coronary artery disease by controlled coronary vasodilation with adenosine and thallium-201 scintigraphy in patients unable to exercise. *Circulation* 82: 80–87, 1990.
5. Nishimura S, Mahmarian JJ, Boyce TM, Verani MS. Quantitative thallium-201 single-photon emission computed tomography during maximal pharmacologic coronary vasodilation with adenosine for assessing coronary artery disease. *J Am Coll Cardiol* 18: 736–745, 1991.
6. Hays JT, Mahmarian JJ, Cochran AJ, Verani MS. Dobutamine thallium-201 tomography for evaluating patients with suspected coronary artery disease unable to undergo exercise or vasodilator pharmacologic stress testing. *J Am Coll Cardiol* 21: 1583–1590, 1993.
7. Amanullah AM, Kiat H, Hachamovitch R, Cabico JA, Cohen I, Friedman JD, et al. Impact of myocardial perfusion single-photon emission computed tomography on referral to catheterization of the very elderly. Is there evidence of gender-related referral bias? *J Am Coll Cardiol* 28: 680–686, 1996.
8. Schulman SP, Fleg JL. Stress testing for coronary artery disease in the elderly. *Clin Geriatr Med* 12: 101–119, 1996.
9. Hirakawa K, Chikamori T, Kitaoka H, Matsumura Y, Takata J, Seo H, et al. Usefulness of dipyridamole thallium scintigraphy in the diagnosis of coronary artery disease in elderly patients. *Nippon Ronen Igakkai Zasshi* 34: 617–622, 1997.
10. Wang FP, Amanullah AM, Kiat H, Friedman JD, Berman DS. Diagnostic efficacy of stress technetium 99m-labeled sestamibi myocardial perfusion single-photon emission computed tomography in detection of coronary artery disease among patients over age 80. *J Nucl Cardiol* 2: 380–388, 1995.
11. Mahmarian JJ, Boyce TM, Goldberg RK, Cocanougher MK, Roberts R, Verani MS. Quantitative exercise thallium-201 single photon emission computed tomography for the enhanced diagnosis of ischemic heart disease. *J Am Coll Cardiol* 15: 318–329, 1990.
12. Kurata C, Tawarahara K, Sakata K, Taguchi T, Fukumoto Y, Kobayashi A, et al. Electrocardiographically and symptomatically silent myocardial ischemia during exercise testing. *Jpn Circ J* 55: 825–834, 1991.
13. Stratmann HG, Younis LT, Wittry MD, Amato M, Mrak AL, Miller DD. Effect of the stress level achieved during symptom-limited exercise technetium-99m sestamibi myocardial tomography on the detection of coronary artery disease. *Clin Cardiol* 19: 787–792, 1996.
14. 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* 119: 557–567, 1990.
15. Tawarahara K, Kurata C, Wakabayashi Y, Takeuchi K, Shouda S, Mikami T, et al. Usefulness of measurement of plasma atrial natriuretic peptide levels in exercise test in patients with coronary heart disease. *Am J Cardiol* 83: 782–785, 1999.
16. Montague TJ, Ikuta RM, Wong RY, Bay KS, Teo KK, Davies NJ. Comparison of risk and patterns of practice in patients older and younger than 70 years with acute myocardial infarction in a two-year period (1987–1989). *Am J Cardiol* 68: 843–847, 1991.
17. Yusuf S, Furberg CD. Are we biased in our approach to treating elderly patients with heart disease. *Am J Cardiol* 68: 954–956, 1991.
18. Hunziker PR, Gradel C, Muller-Brand J, Buser P, Pfisterer M. Improved myocardial ischemia detection by combined physical and mental stress testing. *Am J Cardiol* 82: 109–113, 1998.
19. Minoda K, Yasue H, Kugiyama K, Okumura K, Motomura K, Shimomura O, et al. Comparison of the distribution of

myocardial blood flow between exercise-induced and hyperventilation-induced attacks of coronary spasm: a study with thallium-201 myocardial scintigraphy. *Am Heart J* 127: 1474–1480, 1994.

20. Yasue H, Kugiyama K. Coronary spasm: clinical features and pathogenesis. *Intern Med* 36: 760–765, 1997.
21. Leppo JA. Dipyridamole-thallium imaging: the lazy man's stress test. *J Nucl Med* 30: 281–287, 1989.
22. Gupta NC, Esterbrooks DJ, Hilleman DE, Mohiuddin SM. Comparison of adenosine and exercise thallium-201 single-photon emission computed tomography (SPECT) myocardial perfusion imaging. *J Am Coll Cardiol* 19: 248-257, 1992.
23. Nishimura S, Mahmarian JJ, Boyce TM, Verani MS. Equivalence between adenosine and exercise thallium-201 myocardial tomography: a multicenter, prospective, crossover trial. *J Am Coll Cardiol* 20: 265–275, 1992.
24. Cuocolo A, Nicolai E, Soricelli A, Pace L, Nappi A, Sullo P, et al. Technetium 99m-labeled tetrofosmin myocardial tomography in patients with coronary artery disease: comparison between adenosine and dynamic exercise stress testing. *J Nucl Cardiol* 3: 194–203, 1996.
25. Wackers FJTh, Soufer R, Zaret BL. Nuclear Cardiology. *In*: Heart Disease: a textbook of cardiovascular medicine. Braunwald E (ed.), 5th ed., Philadelphia, WB Saunders, pp. 288–290, 1997.
26. Sakata K, Yoshida H, Sugino H, Iimuro M, Matsunaga Y, Ono N, et al. Assessment of quantitative exercise thallium-201 emission computed tomography in patients with vasospastic angina—value of washout rate analysis. *Jpn Circ J* 58: 379–388, 1994.
27. Thompson RF, Crist DM, Osborn LA, Atterbom HA. Treadmill exercise electrocardiography in the elderly with physical impairments. *Gerontology* 36: 112–118, 1990.
28. Rajala S, Kaltiala K, Haavisto M, Mattila K. Prevalence of ECG findings in very old people. *Eur Heart J* 5: 168–174, 1984.
29. Yasumura S, Shibata H. The effect of aging on the electrocardiographic findings in the elderly — a 10-year longitudinal study: the Koganei Study. *Arch Gerontol Geriatr* 9: 1–15, 1989.
30. Kansal S, Roitman D, Sheffield T. Stress testing with ST-segment depression at rest: an angiographic correlation. *Circulation* 54: 636–639, 1976.
31. Miranda CP, Lehmann KG, Froelicher VF. Correlation between resting ST segment depression, exercise testing, coronary angiography, and long-term prognosis. *Am Heart J* 122: 1617–1628, 1991.
32. 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: executive summary and recommendations: 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). *Circulation* 99: 2829–2848, 1999.
33. Hilton TC, Shaw LJ, Chaitman BR, Stocke KS, Goodgold HM, Miller DD. Prognostic significance of exercise thallium-201 testing in patients aged greater than or equal to 70 years with known or suspected coronary artery disease. *Am J Cardiol* 69: 45–50, 1992.
34. Ciaroni S, Delonca J, Righetti A. Early exercise testing after acute myocardial infarction in the elderly: Clinical evaluation and prognostic significance. *Am Heart J* 126: 304–311, 1993.