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ORIGINAL ARTICLE

Important parameters in the detection of left main trunk disease using stress myocardial perfusion imaging

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Summary
Objectives: We sought noninvasively to diagnose left main trunk (LMT) disease using myocardial perfusion imaging (MPI).
Methods: Five hundred and eight patients with suspected coronary artery disease (CAD) underwent both stress MPI and coronary angiography. The extent and severity of perfusion abnormalities were assessed using a 20-segment model. In addition, perfusion defects in both left anterior descending and left circumflex arterial territories were defined as a left main (LM) pattern defect, and those in 3-coronary arterial territories as a 3-vessel pattern defect.
Results: In 42 patients with LMT disease, a summed stress score (19.4 ± 10.0 vs. 13.5 ± 10.0; $p < 0.0001$) and a summed rest score (12.1 ± 9.7 vs. 7.0 ± 7.8; $p = 0.002$) were greater than in 466 patients without LMT disease, while a summed difference score was similar (7.3 ± 7.7 vs. 6.5 ± 6.1; $p =$ NS). The prevalence of an LM-pattern defect was low in both groups (12% vs. 8%; $p =$ NS). However, a 3-vessel pattern defect (33% vs. 7%; $p < 0.0001$), lung uptake of radiotracers (38% vs. 11%; $p < 0.0001$), and transient ischemic dilation (31% vs. 13%; $p = 0.003$) were more frequently observed in patients with LMT disease than in those without. Logistic regression analysis showed that a 3-vessel pattern defect (OR = 3.5, 95% CI = 1.4—8.8; $p = 0.007$), lung uptake of radiotracers (OR = 2.5, 95% CI = 1.1—5.7; $p = 0.03$), and previous myocardial infarction (MI) (OR = 2.4, 95% CI = 1.0—5.7; $p = 0.05$) were the most important parameters to

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detect LMT disease. After excluding 163 patients with previous MI, a repeat analysis revealed that lung uptake of radiotracers (OR = 8.2, 95% CI = 2.3—29.2; $p = 0.001$) and an LM-pattern defect (OR = 6.3, 95% CI = 1.4—27.2; $p < 0.02$) were independent predictors for LMT disease.
Conclusion: In the identification of LMT disease, lung uptake of radiotracers was a single best parameter, which was independent of the presence or absence of previous MI.

Introduction

The diagnostic and prognostic value of stress myocardial perfusion imaging (MPI) is firmly established in clinical practice [1—3]. Among the diagnostic purposes of MPI for patients with suspected coronary artery disease (CAD), the identification of a significant stenosis in the left main trunk (LMT) is of utmost importance because patients in this subset are regarded as one of the highest risk groups [4—6]. Theoretically, myocardial perfusion abnormalities both in the left anterior descending and in the left circumflex arterial territories indicate a significant stenosis in the LMT [7]. Using planar thallium imaging, however, previous reports observed that the detection of LMT disease based only on this scintigraphic defect pattern has limited diagnostic accuracy [8,9], although few reports attempted to separately diagnose LMT disease from known or suspected CAD by the use of single-photon emission computed tomography (SPECT) [10—12]. The purpose of this study, therefore, was to evaluate the diagnostic utility of SPECT MPI in the detection of patients with LMT disease.

Methods

Study patients

We retrospectively evaluated 508 consecutive patients with known or suspected CAD, who underwent both stress MPI and coronary angiography. Clinical grounds for suspected or unknown CAD were based on clinical symptoms, coronary risk profiles, electrocardiographic findings, or past medical history. They were aged 65 ± 11 years; 392 were men and 116 women. No patient with acute myocardial infarction (MI), unstable angina, or those with history of coronary bypass grafting was included. Written informed consent was obtained from all patients.

Coronary risk factors included in the assessment were hypertension, hypercholesterolemia, diabetes mellitus, and cigarette smoking. Hypertension was defined as a history of systolic blood pressure $\geq$140 mmHg or a diastolic blood pressure $\geq$90 mmHg or documented hypertension on at least two occasions in outpatient clinics. Hypercholesterolemia was defined as the fasting serum total cholesterol of $\geq$220 mg/dl [13]. Diabetes mellitus was diagnosed using a criteria proposed by the Japanese Diabetic Society [14]. In addition, previous MI was defined either as having a history of MI requiring hospital admission, or as unrecognized MI fulfilled by both abnormal Q waves on electrocardiogram and left ventricular segmental wall motion abnormality on echocardiogram.

Stress myocardial perfusion imaging

In 122 patients, stress MPI with ^{99m}Tc-sestamibi was performed using a 1-day protocol [15]. Symptom-limited multi-step exercise using a bicycle ergometer was undertaken in 64 patients [16]. ^{99m}Tc-sestamibi (259 MBq) was administered when submaximal heart rate, chest pain, ST-segment depression of $\geq$0.1 mV, or leg fatigue developed, and the exercise was then continued for 1 min at the same level. Image acquisition was commenced 30 min after the last exercise session. In the remaining 58 patients, adenosine triphosphate disodium (ATP) (0.16 mg/(kg min)) was administered intravenously for 6 min [17,18], and 3 min later ^{99m}Tc-sestamibi (777 MBq) was given intravenously. Image acquisition was started 30 min later.

Using ^{201}Tl (111 MBq), myocardial SPECT was performed in 386 patients; in 109 patients, SPECT was performed during exercise, and the remaining 277 patients underwent ATP-loading myocardial SPECT. The time interval between the injection of ^{201}Tl and the start of image acquisition was approximately 15 min. The protocols to stress these patients were similar to the previous methods [16,19]. Delayed images were acquired 4 h later.

Data were acquired with a 2- or 3-detector gamma camera (Prism 2000XP or Prism 3000XP, Picker, Cleveland, OH, USA) for 180° or 360° arcs.

For both radiotracers, a low-energy high-resolution parallel multi-hole collimator was used. The acquisition time for each projection was 30 s. SPECT images were reconstructed from the data by a data processor (Odyssey VP, Picker) combined with a Butterworth filter (order 8; cut-off frequency 0.25 for ^{99m}Tc-sestamibi and 0.2 for ^{201}Tl) and a ramp filter.

According to a previously reported method [20,21], each SPECT image was divided into 20 segments, with segments 1—3, 7—9, 13—14, and 19—20 corresponding to the area perfused by the left anterior descending coronary artery; segments 4, 10, and 15—16 corresponding to the areas perfused by the right coronary artery; and segments 5—6, 11—12, and 17—18 corresponding to the areas perfused by the left circumflex coronary artery. The accumulation of radiotracers in the myocardium was visually evaluated by two cardiologists using a 5-grade scale: 0 (normal), 1 (slight reduction of uptake), 2 (moderate reduction of uptake), 3 (severe reduction of uptake), or 4 (absence of radioactive uptake). The total scores for all the segments on the initial images and delayed images were designated the summed stress score and the summed rest score , respectively. The summed difference score was defined as the summed stress score minus the summed rest score [18,21].

In addition, perfusion defects in both left anterior descending and left circumflex arterial territories were defined as a left main (LM) pattern defect, and those in 3-coronary arterial territories as a 3-vessel pattern defect. As nonperfusion parameters, transient ischemic dilation, and lung uptake of radiotracers were visually assessed as described previously [20,22]. In brief, a patient was considered to show transient ischemic dilation when the largest short-axis diameter on the initial SPECT images was apparently larger than on the delayed images by consensus of two experienced observers [23]. Using a 30 s acquisition frame of the anterior projection, lung uptake of radiotracers (^{201}Tl or ^{99m}Tc-sestamibi) was considered to be increased when the mediastinum appeared as a photon-deficient region in contrast to the medial borders of the lungs; the medial lung borders were clearly delineated in the initial image, and pulmonary activity decreased substantially relative to myocardial activity on the delayed image [22]. According to aforementioned image interpretation, disagreements were resolved by consensus. A typical case is shown in Fig. 1.

Coronary angiography

Multi-direction coronary angiography was performed by the use of Judkins' method in all the patients within 3 months of stress myocardial perfusion imaging. The degree of coronary artery stenosis was measured using a caliper according to the American Heart Association criteria [24]. Significant stenosis was deemed as present when >50% actual diameter narrowing was noted. Significant CAD was defined if a significant stenosis was present in the LMT or one of the three major coronary arteries.

Statistical analysis

Results are expressed as mean ± 1 S.D. A Student's *t*-test was generally used to compare the means of

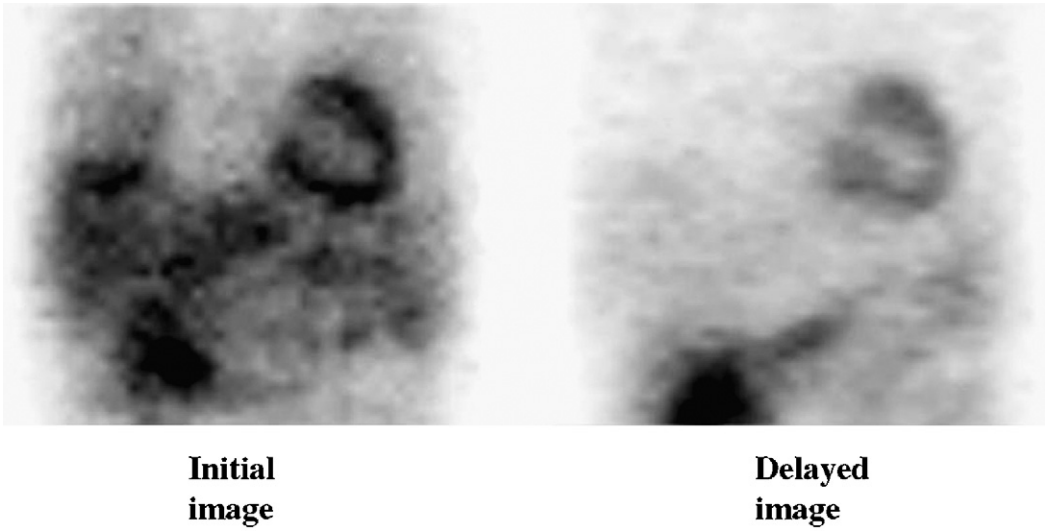

Figure 1 An example of increased lung uptake of ^{201}Tl. Lung uptake was significantly elevated in the initial image and diminished in the delayed image.

Table 1 Comparison of clinical characteristics between patients with LMT disease and those without LMT disease

	Patients with LMT disease ($n = 42$)	Patients without LMT disease ($n = 466$)	p-Value
Age (years)	69 ± 8	65 ± 11	0.015
Gender (men/women)	37/5	355/111	NS
Coronary risk factors			
Hypertension	33 (78%)	354 (76%)	NS
Hypercholesterolemia	26 (62%)	240 (52%)	NS
Diabetes mellitus	18 (43%)	156 (33%)	NS
Smoking	10 (24%)	167 (36%)	NS
History of myocardial infarction	27 (64%)	136 (29%)	<0.0001
Myocardial perfusion tracers			NS
^{201}Tl	32 (76%)	354 (76%)	
^{99m}Tc-sestamibi	10 (24%)	112 (24%)	
Stress protocol			NS
Exercise	14 (33%)	59 (34%)	
ATP	28 (67%)	307 (66%)	

ATP, adenosine triphosphate; LMT, left main trunk.

the continuous variables, and categorical variables were analyzed using a chi-square test. In the continuous variables, equity of variance of the two groups was tested by Levene's test. If the variances of the two groups were assumed to be equal a Student's t-test was used, but if not Welch's t-test was applied. To determine the cut-off values of summed scores for LMT disease, a receiver-operating characteristic curve analysis was performed. Univariate analysis was conducted with the logistic regression method and stepwise multivariate analysis was conducted with the multiple logistic regression method. Factors that showed a p-value of <0.05 in the univariate analysis were selected for multivariate analysis. Linear discriminant analysis (with stepwise variable selection with Wilks' Lambda, which is the ratio of the within-groups sum of squares to the total sum of squares) was used to assess the potential to correctly identify LMT disease. A Bayes rule with equal prior probability was used for the identification, and the results are presented as sensitivity, specificity and accuracy. A p-value of <0.05 was considered significant. The statistical computations were performed using the SPSS-PC+ computer program, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics of the patients

Forty-two patients with LMT disease were older (69 ± 8 years vs. 65 ± 11 years; $p = 0.015$) than the 466 patients without LMT disease. Previous MI (64% vs. 29%; $p < 0.0001$) was higher in patients with LMT disease than in those without, whereas that of other coronary risk factors were similar (Table 1). No significant difference was observed in the mode of stress protocol or radiotracers used between the two groups.

Table 2 Comparison of scintigraphic findings between patients with LMT disease and those without LMT disease in all patients

	Patients with LMT disease ($n = 42$)	Patients without LMT disease ($n = 466$)	p-Value
Summed stress score	19.4 ± 10.0	13.5 ± 10.0	<0.0001
Summed rest score	12.1 ± 9.7	7.0 ± 7.8	0.002
Summed difference score	7.3 ± 7.7	6.5 ± 6.1	NS
LM-pattern defect	5 (12%)	35 (8%)	NS
3-vessel pattern defect	14 (33%)	34 (7%)	<0.0001
Transient ischemic dilation	13 (31%)	59 (13%)	0.003
Lung uptake of radiotracers	16 (38%)	53 (11%)	<0.0001

LMT, left main trunk.

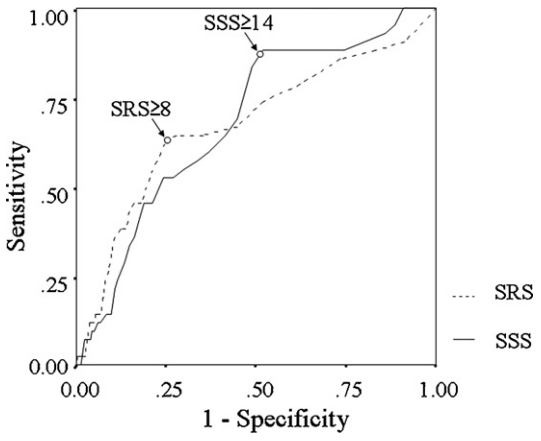

Figure 2 Receiver-operating characteristic curves to determine the cut-off value of risk classification of defect score in all patients. We defined serious as summed stress score (SSS) ≥14, summed rest score (SRS) ≥8. The area under the curve was 0.681 for SSS, 0.672 for SRS.

Myocardial perfusion analysis

In patients with LMT disease, the summed stress score (19.4 ± 10.0 vs. 13.5 ± 10.0; $p < 0.0001$) and the summed rest score were greater (12.1 ± 9.7 vs. 7.0 ± 7.8; $p = 0.002$) than in those without LMT disease, whereas the summed difference score was similar (7.3 ± 7.7 vs. 6.5 ± 6.1; p = NS) (Table 2). The incidence of a 3-vessel pattern defect was higher (33% vs. 7%; $p < 0.0001$) in patients with LMT disease than in those without, whereas the prevalence of LM-pattern defect was similar (12% vs. 8%; p = NS). Inter-observer reproducibility for lung uptake of radiotracers was 95%. The occurrences of lung uptake of radiotracers were 4% (7/165) in patients with insignificant lesions, 10% (13/126) in 1-vessel CAD, 15% (14/91) in 2-vessel CAD, and 23% (19/84) in 3-vessel CAD ($p = 0.001$ for trend). This prevalence of lung uptake of radiotracers was higher in patients with LMT disease than in those without (38% vs. 11%; $p < 0.0001$) (Table 2).

Among 53 patients without LMT disease, but showing lung uptake of radiotracers, the prevalence of 3-vessel or LM-pattern defects was only 34% (18/53), of which 78% (14/18) was observed in those with 3-vessel CAD. Among 42 patients with LMT disease, 16 of those with lung uptake of radiotracers, compared with 26 of those without, had higher incidences of severe LMT stenosis (99% stenosis in 1, 90% stenosis in 4, 75% stenosis in 1, and 50% stenosis in 10% vs. 99% stenosis in 0, 90% stenosis in 2, 75% stenosis in 10, and 50% stenosis in 14; $p = 0.05$), while the number of concomitant coronary artery stenoses was similar (3-vessel in 9, 2-vessel in 2, 1-vessel in 4, and insignificant lesion in 1-vessel vs. 3-vessel in 10, 2-vessel in 9, 1-vessel in 5, and insignificant lesion in 2; p = NS).

Univariate and multivariate analysis for the detection of LMT disease in all patients

The receiver-operating characteristic curves determined the cut-off value as 14 for a summed stress score, and 8 for a summed rest score (Fig. 2).

In the univariate analysis, six parameters were found as significant predictors for detecting LMT disease: summed stress score ≥14, summed rest score ≥8, 3-vessel pattern defect, transient ischemic dilation, lung uptake of radiotracers, and previous MI (Table 3). Multiple stepwise logistic regression analysis using six significant univariate parameters showed that 3-vessel pattern defect, lung uptake of radiotracers, and previous MI were the independent predictors in detecting LMT disease with sensitivity of 52%, specificity of 84%, and accuracy of 81% (Fig. 3). The analysis using only a perfusion parameter showed sensitivity of 33%, specificity of 93%, and accuracy of 88% (Fig. 3). The likelihood ratios of positive and negative tests were 3.3 and 1.8, respectively, in the former, and 4.7 and 1.4, respectively, in the latter statistical models. The multivariate analysis was repeated after excluding 53 patients with previous inferior MI since

Table 3 Univariate and multivariate analysis for detecting LMT disease in all patients

	Univariate		Multivariate	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Summed stress score ≥14	2.6 (1.3—4.9)	0.005		
Summed rest score ≥8	4.7 (2.4—9.0)	<0.0001		
LM-pattern defect	1.7 (0.6—4.5)	0.316		
3-vessel pattern defect	6.4 (3.1—13.2)	<0.0001	3.5 (1.4—8.8)	0.007
Transient ischemic dilation	3.1 (1.5—6.3)	0.002		
Lung uptake of radiotracers	4.8 (2.4—9.5)	<0.0001	2.5 (1.1—5.7)	0.03
Previous myocardial infarction	4.4 (2.3—8.5)	<0.0001	2.4 (1.0—5.7)	0.05

CI, confidence interval; LMT, left main trunk; OR, odds ratio.

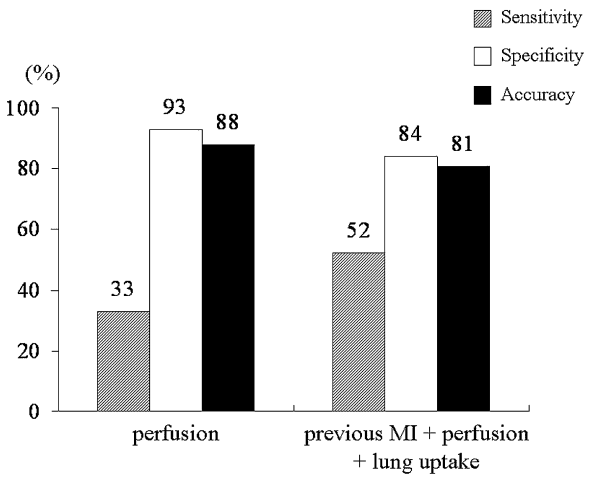

Figure 3 Diagnostic value of perfusion (3-vessel pattern defect) analysis and the combination of perfusion, previous myocardial infarction, and lung uptake parameters in the detection of left main trunk disease in all patients.

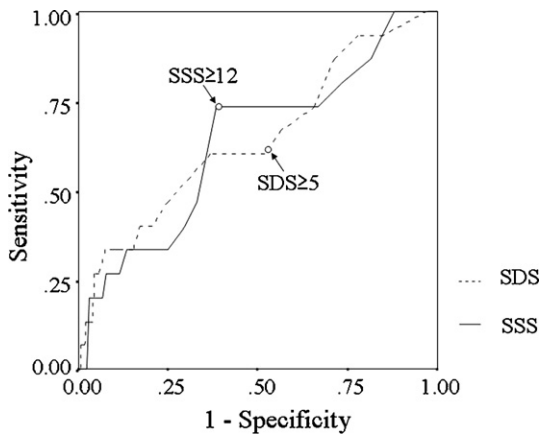

Figure 4 Receiver-operating characteristic curves to determine the cut-off value of risk classification of defect score in patients without previous myocardial infarction. We defined serious as summed stress score (SSS) ≥12, summed difference score (SDS) ≥5. The area under the curve was 0.636 for SSS, 0.643 for SDS.

the presence of inferior MI obscures an LM-pattern defect [25]. This showed that the combination of a 3-vessel pattern defect, lung uptake of radiotracers and previous MI was most important to detect LMT disease with similar diagnostic performance (53% sensitivity, 83% specificity, and 81% accuracy; $p < 0.0001$).

Univariate and multivariate analysis for the detection of LMT disease in patients without previous MI

After excluding 163 patients with previous MI, the receiver-operating characteristic curve analysis was repeated and determined the cut-off value as 12 for a summed stress score and 5 for a summed difference score (Fig. 4).

In the univariate analysis, five parameters were significant predictors for detecting LMT disease: summed stress score ≥12, LM-pattern defect, 3-vessel pattern defect, transient ischemic dilation, and lung uptake of radiotracers (Table 4). Multiple stepwise logistic regression including five significant parameters revealed that the combination of an LM-pattern defect and lung uptake of radiotracers were the most important predictors for detecting LMT disease with sensitivity of 67% and specificity of 85% (global chi-square, 34.2) (Table 4 and Fig. 5). By contrast, the analysis showed that the sensitivity and specificity in the detection of LMT disease were 27% and 93% (global chi-square, 7.3), respectively, with an LM-pattern defect only (Fig. 5). The likelihood ratios of positive and negative tests were 4.5 and 2.6, respectively, in the former, and 3.9 and 1.3, respectively, in the latter statistical models.

The detection of LMT disease according to ^{201}Tl or ^{99m}Tc-sestamibi SPECT

Since different radiotracers or stress methods were used in this study, we attempted to per-

Table 4 Univariate and multivariate analysis for detecting LMT disease in patients without previous myocardial infarction

	Univariate		Multivariate	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Summed stress score ≥12	4.1 (1.3—13.2)	0.017		
Summed difference score ≥5	1.6 (0.5—4.8)	0.409		
LM-pattern defect	4.6 (1.4—15.7)	0.014	6.3 (1.4—27.2)	0.014
3-vessel pattern defect	7.1 (2.1—24.9)	0.002		
Transient ischemic dilation	4.8 (1.6—15.0)	0.007		
Lung uptake of radiotracers	10.2 (3.4—30.4)	<0.0001	8.2 (2.3—29.2)	0.001

CI, confidence interval; LMT, left main trunk; OR, odds ratio.

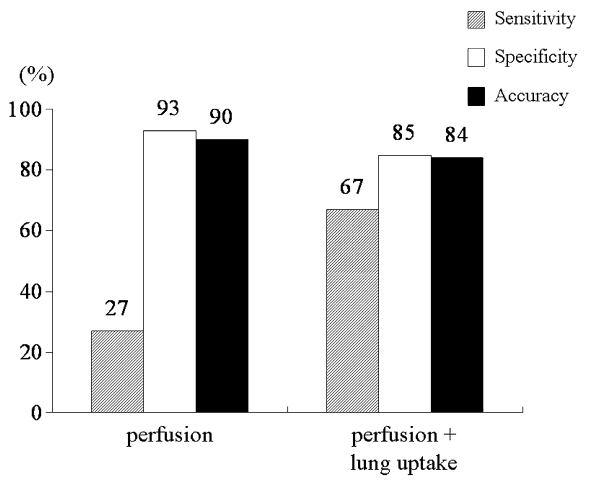

Figure 5 Diagnostic value of perfusion (left main-pattern defect) analysis and the combination of perfusion and lung uptake parameters in the detection of left main trunk disease in patients without previous myocardial infarction.

form subgroup analysis for individual protocols. In 109 patients who underwent exercise ^{201}Tl SPECT, the multivariate discriminant analysis showed 60% sensitivity, 95% specificity, and 92% accuracy ($p < 0.0001$) with the combination of lung uptake of ^{201}Tl and the pattern of perfusion abnormalities (3-vessel pattern defect in patients with previous MI and LM-pattern defect in patients without previous MI). In 277 patients who were examined by ATP ^{201}Tl SPECT, the discriminant analysis revealed 64% sensitivity, 77% specificity, and 76% accuracy ($p < 0.0001$) with the combination of lung uptake of ^{201}Tl and the

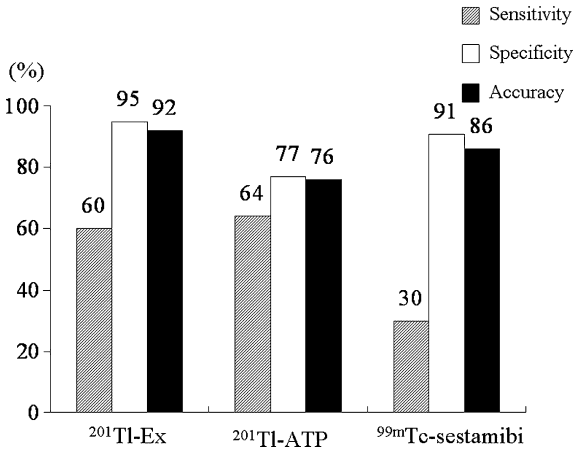

Figure 6 Diagnostic value of the combination of perfusion (3-vessel pattern defect in patients with previous myocardial infarction and left main-pattern defect in patients without previous myocardial infarction) and lung uptake parameters analysis in the detection of left main trunk disease in patients who underwent exercise ^{201}Tl SPECT, ATP ^{201}Tl SPECT, and ^{99m}Tc-sestamibi SPECT.

pattern of perfusion abnormalities. In 122 patients who underwent ^{99m}Tc-sestamibi SPECT, the multivariate analysis using the same variables showed 30% sensitivity, 91% specificity, and 86% accuracy ($p < 0.04$) (Fig. 6). Further analysis according to the stress methods could not be made because of a small number of patients with LMT disease in each subset.

Discussion

Noninvasive detection of high-risk patients among those who are suspected of having CAD by the use of MPI is very important in clinical practice since prognosis of these high-risk patients is usually improved by coronary revascularization [6,26]. Above all, the identification of a significant stenosis in the LMT, one of the highest risk subsets, is considerably important [4—6]. Moreover, the recent advancement of coronary intervention, including drug-eluting stents, has provoked controversy over the treatment for LMT disease, either by coronary artery bypass grafting or by percutaneous coronary intervention [27—31]. Consensus on this issue is to reveal full information regarding the limitations and strengths of each therapy to a given patient with LMT disease [32]. Therefore, oculostenotic dilatation of a stenosis in the LMT is problematic [33]. Rather, to take a possibility of LMT disease into consideration before diagnostic catheterization enables a fully informed therapeutic approach to these patients. To this end, noninvasive detection of LMT disease using MPI has significant clinical relevance.

In this study consisting of 508 patients with suspected CAD, the combination of a 3-vessel pattern defect, lung uptake of radiotracers (^{201}Tl or ^{99m}Tc-sestamibi) on MPI, and previous MI was most important in the detection of LMT disease with 52% sensitivity and 84% specificity. In contrast to this multivariate approach, an LM-pattern defect detected only 5 among 42 patients (12%) with LMT disease. Thus, 88% of the patients with LMT disease would have been missed if one relied only on this well-known scintigraphic parameter. A significant stenosis of the LMT is usually associated with multi-vessel CAD, and coexisting previous MI is not uncommon [10]. The presence of previous MI obscures the development of an LM-pattern defect in patients with LMT disease [25]. To exclude a potential confounding effect of previous MI, repeat analysis was performed in 345 patients without MI. In this group of patients, the combination of lung uptake of radiotracers and the LM-pattern defect on MPI best detected patients with LMT disease with

67% sensitivity and 85% specificity. Although the LM-pattern defect appeared significant in the detection of LMT disease in patients without previous MI, the majority of patients would have still been missed with this single marker. Instead, lung uptake of radiotracers was a more important parameter for identifying LMT disease, which was independent of the presence or absence of previous MI. Although lung uptake of radiotracers was also observed in patients without LMT disease, misdiagnosis was avoided in most patients by combining the pattern of perfusion abnormalities with lung uptake of radiotracers. Thus, in the interpretation of MPI for the better detection of LMT disease, the investigator should focus not only on myocardial perfusion pattern, but also on lung uptake of radiotracers, regardless of the study protocol, or of the tracers used.

Using stress MPI, several studies tried noninvasively to identify LMT disease [7—11]. Low sensitivities (13—24%) of an LM-pattern defect were reported with planner thallium imaging [7—9] while myocardial SPECT also suffered low sensitivities of this scintigraphic pattern (7—21%) [12,34]. In our study, the sensitivity of an LMT-defect pattern was 12% in patients with previous MI and 27% in those without previous MI. The key to better detect this high-risk subset is the maximum utilization of clinical markers of ischemia during stress such as chest pain, hypotension, or ST-segment depression [10,25]. In this study, however, the assessment of clinical markers for ischemia was difficult to unanimously obtain due to different study protocols applied in individual patients. In addition, ST-segment depression is seldom observed during ATP loading, which is contradictory to dipyridamole or adenosine [25,35]. Therefore, noninvasive markers used in our study were restricted to patient profile and imaging parameters. In a similar study protocol to ours, Berman et al. reported that the addition of nonperfusion data such as abnormal lung uptake and transient ischemic dilation on the high risk of abnormality by perfusion helped better detect the majority of patients (83%) with LMT disease among 1864 patients evaluated [34]. By contrast, using exercise thallium SPECT in 834 patients with suspected CAD, Iskandrian et al. found that a multi-vessel pattern defect, exercise heart rate, and ST-segment depression were the independent parameters for diagnosing LM or 3-vessel CAD, although nonperfusion data such as lung uptake of thallium were significantly associated with this high-risk subset by the univariate analysis [10]. It seems, therefore, that the diagnostic value of nonperfusion data and clinical markers of ischemia varies by the inclusion or exclusion of patients who underwent pharmacologic stress MPI. Nevertheless, clinical reality that fragile patients with advancing age are markedly increasing today indicates that MPI restricted only to exercise stress will lose its generality.

Abnormal lung uptake of ^{201}Tl is correlated with extensive CAD and/or stress-induced left ventricular dysfunction, and is regarded as a marker for poor prognosis [22,23,36—39]. Similarly, lung uptake of ^{99m}Tc-based myocardial perfusion tracers is also considered as a marker for severe CAD with poor prognosis [40—42]. Among these studies, coronary angiogram revealed a significant correlation between multi-vessel CAD and abnormal lung uptake of ^{201}Tl or ^{99m}Tc-sestamibi [22,23,40,41]. In a small study including <100 patients, LMT disease was an independent predictor of abnormal lung uptake of ^{99m}Tc-sestamibi [40]. With a larger number of patients consisting >500, this study repeatedly demonstrated the diagnostic value of abnormal lung uptake of radiotracers (^{201}Tl or ^{99m}Tc-sestamibi) to detect LMT disease. Although a lower sensitivity using lung uptake of ^{99m}Tc-sestamibi, in comparison to ^{201}Tl, was observed in our study, a high specificity of 91% was notable. Berman et al. also found a low sensitivity (20%) of lung uptake in the detection of LMT disease due partly to their study protocol of rest ^{201}Tl/post-stress ^{99m}Tc-sestamibi, which relied on ^{99m}Tc-sestamibi for the assessment of lung uptake. By contrast, ^{201}Tl SPECT was applied to most patients in our study and resulted in higher sensitivities of 60—64%. However, the occurrence of lung uptake of radiotracers may depend upon the grade of LMT narrowing and the presence of concomitant coronary arterial stenoses. If the severity of LMT stenosis is mild in a given patient, scintigraphic detection of LMT disease will be hampered, as was observed in our study. In addition, our approach to assess lung uptake of ^{201}Tl or ^{99m}Tc-sestamibi was based on visual analysis with inter-observer reproducibility of 95%, but might have a limitation in the detection of this important finding. If one would apply computer-based quantitative assessment for lung uptake of radiotracers, the diagnostic accuracy of this nonperfusion marker for LMT disease might have increased [37,40]. Although the primary purpose of this study was to identify important diagnostic parameters for LMT disease, this study demonstrated the lung uptake of radiotracers as being the best single nonperfusion marker regardless of the radioisotopes used. A prospective study using computer-based assessment for lung uptake of myocardial perfusion tracers (^{201}Tl or ^{99m}Tc-sestamibi) for this purpose is necessary.

Conclusion

In the detection of LMT disease, lung uptake of radiotracers, combined with a 3-vessel pattern defect in patients with previous MI and an LM-pattern defect in patients without MI, yielded the best diagnostic accuracy. Thus, in the interpretation of MPI for the better detection of LMT disease, the investigator should focus not only on myocardial perfusion pattern, but also on lung uptake of radiotracers, regardless of study protocol or tracers used.

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