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The usefulness of dipyridamole thallium-201 single photon emission computed tomography for predicting perioperative cardiac events in patients undergoing non-cardiac vascular surgery

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The aim of this study was to evaluate the usefulness of dipyridamole Tl-201 myocardium single photon emission computed tomography (^{201}Tl-SPECT) for predicting perioperative cardiac events in patients with arteriosclerosis obliterans (ASO) and abdominal aortic aneurysm (AAA) undergoing non-cardiac vascular surgery. ***Methods:*** Preoperative dipyridamole ^{201}Tl-SPECT imaging in association with clinical risk assessment was performed in 224 consecutive patients (97 ASO and 127 AAA). ***Results:*** The patients were classified into three groups, including low-risk (n = 173, 77%), intermediate-risk (n = 39, 18%), and high-risk (n = 12, 5%) groups according to the clinical risk stratification. The prevalence of reversible Tl-201 defect was significantly higher in the high-risk group than that in the low-risk group (83% vs. 14%, $p < 0.001$). In 180 patients who underwent vascular surgery, 9 patients (5.0%) had perioperative cardiac events, including heart failure (n = 1), unstable angina (n = 2), and other cardiac events such as arrhythmias (n = 6). The clinical variables including the clinical risk stratification did not significantly correlate with the perioperative cardiac events. In contrast, the reversible defect on ^{201}Tl-SPECT was the only variable to predict perioperative cardiac events by a stepwise logistic regression analysis (odds ratio 7.0, 95% confidence interval 1.7–28.0, $p = 0.007$). It was also a significant predictor of perioperative cardiac events in a subgroup of low risk patients (odds ratio 11.6, 95% confidence interval 2.3–57.4, $p = 0.004$). The sensitivity and specificity of the reversible defect for predicting perioperative cardiac events were 55.6% and 84.8% in all operated patients, and 57.1% and 89.7% in low risk patients, respectively. ***Conclusions:*** The preoperative dipyridamole ^{201}Tl-SPECT was useful for predicting perioperative cardiac events in patients with vascular diseases, even in patients identified as having a low risk based on the clinical risk assessment.

Key words: dipyridamole, Tl-201, SPECT, perioperative cardiac event, vascular diseases

INTRODUCTION

CORONARY ARTERY DISEASE demonstrates a high prevalence in patients with significant atherosclerotic vascular disease, such as arteriosclerosis obliterans (ASO) or abdominal aortic aneurysm (AAA), and it may cause cardiac ischemic events which are one of the most frequent and serious complications known to occur during the perioperative period of vascular reconstruction surgery.[1–3] For this reason, a preoperative cardiac risk evaluation is very important for the management of patients undergoing major vascular surgery in order to reduce the likelihood of adverse perioperative cardiac events.

Exercise ^{201}Tl scintigraphy is an effective and accurate method for detecting coronary artery disease, but its applicability is limited to patients who are able to

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complete an adequate exercise test.[4,5] On the other hand, dipyridamole ^{201}Tl scintigraphy is considered to be an equally useful diagnostic method, and it is also easy to perform in patients who are unable to exercise.[6–10] There have been many reports on the usefulness of dipyridamole ^{201}Tl scintigraphy for predicting perioperative cardiac events in patients with atherosclerotic vascular disease undergoing non-cardiac vascular surgery,[11–16] but it has not yet been clarified as to whether it is useful for predicting perioperative major cardiac events when used in unselected consecutive patients with AAA and ASO.[17,18] In addition, the usefulness of dipyridamole ^{201}Tl scintigraphy for predicting cardiac events in clinical risk stratified patients has not yet be confirmed. In contrast, ^{201}Tl scintigraphy has only been shown to be useful in identifying high risk patients among selected subgroups of patients with an intermediate clinical risk.[12]

The aim of this present study is to evaluate the usefulness of dipyridamole ^{201}Tl-SPECT for predicting perioperative cardiac events in consecutive patients with AAA and ASO stratified by a clinical risk assessment.

MATERIALS AND METHODS

Patient population

The study subjects consisted of 224 consecutive patients (age: 70.6 ± 7.6 years old; 199 men and 25 women) including 97 patients with ASO and 127 patients with AAA indicated for vascular surgery between January 1994 and June 1998.

Clinical risk assessment

The clinical variables were assessed by reviewing the preoperative medical records. They included age, sex, comorbid cardiac diseases (angina pectoris, myocardial infarction, valvular heart disease, congestive heart failure and arrhythmia), cardiac functional status, diabetes mellitus, hypertension, hyperlipidemia, smoking, Goldman's[19] and Detsky's[20] cardiac risk index (modified Goldman's cardiac risk index). The cardiac functional status was categorized into three classes: good, poor and unclear. A "good cardiac functional status" indicates a patient who can walk up a flight of stairs carrying a bag of groceries or perform an equivalent activity without cardiac symptoms. "Poor" indicates a patient who has marked limitations in his/her ordinary physical activities due to cardiac symptoms. "Unclear" indicates that the cardiac functional status cannot be stratified clearly as either good or poor because of their limited ordinary physical activity due to peripheral vascular disease. The patients were divided into three subgroups: low-, intermediate-, and high-risk groups according to the variables described above and as described previously by Mangano and Goldman.[21] "Low risk" indicates a patient who has no known coronary artery disease, a good cardiac functional status, and a low cardiac risk index (class I–II on the Goldman's or Detsky's cardiac risk index), or who has stable coronary artery disease but with a good cardiac functional status, or who has a poor non-cardiac functional status but without any known coronary artery disease, or with an unclear cardiac functional status and with no or few (≤ 2) risk factors (including age over 70, diabetes mellitus, congestive heart failure, important atrial or ventricular arrhythmia, and known vascular disease or aortic, abdominal or thoracic surgery). "Intermediate risk" indicates a patient who has coronary artery disease and an unclear cardiac functional status, or who has a poor non-cardiac functional status but without any known coronary artery disease, or with an unclear cardiac functional status and with more than three risk factors, or who has suspected coronary artery disease with an unclear cardiac functional status. "High risk" indicates a patient who has coronary artery disease and a poor cardiac functional status, or who has coronary artery disease and a high cardiac risk index (class III–IV on the Goldman's or Detsky's cardiac risk index).

Dipyridamole ^{201}Tl SPECT

All patients underwent dipyridamole ^{201}Tl-SPECT at the Nuclear Medicine section of Kyushu University Hospital before vascular surgery. Dipyridamole was infused intravenously at a rate of 0.14 mg/kg body weight/min for 4 minutes while monitoring blood pressure and a 12-lead ECG. Three minutes later, 111 MBq (3 mCi) of ^{201}Tl was injected intravenously as a bolus. No additional stress or change in position was performed. SPECT imaging was performed with a triple-head digital gamma camera (Toshiba GCA-9300A/HG, Japan) equipped with a low-energy, high-resolution collimator on a 70 ± 20% keV energy window and a 64 × 64 matrix size by means of 120-degree rotation per head for 15 minutes. The early and delayed image acquisitions were started at 7 minutes and 4 hours after ^{201}Tl injection, respectively. Transverse sections were reconstructed with a ramp filter by the filtered back projection method and were displayed in 3 standard cardiac planes including short, horizontal long, and vertical long axis. The regional ^{201}Tl uptakes in the early and delayed scan were also displayed on a Bull's eye map.

The SPECT images were reviewed by means of visual qualitative analysis and a consensus was obtained from three experienced observers of nuclear medicine (KY, MS, and MN) who were not informed of the patient's clinical data. The ^{201}Tl-SPECT findings were classified as negative if no perfusion defect was observed in the early and delayed image, and as having a persistent defect if the initial perfusion defect was unchanged in the delayed image, or as having a reversible defect if the initial perfusion defect recovered completely or partially on the delayed image.

Perioperative cardiac events

The perioperative cardiac events were assessed by reviewing the medical records during the period of vascular surgeries and until 7 days after operation, by one of the investigators (TC or HT) without knowledge of either the clinical risk evaluation or the dipyridamole ^{201}Tl-SPECT results. They included cardiac death (sudden death and death due to myocardial infarction or congestive heart failure), non-fatal myocardial infarction (diagnosed by an increase in cardiac enzymes and the development of either new Q waves or persistent ST-T wave changes), congestive heart failure (requiring symptoms or signs of pulmonary edema including evidence of chest radiography and development of signs of new left or right ventricular failure), unstable angina (requiring ≥ 2 episodes of ischemic electrocardiographic changes with cardiac symptoms or signs and with a subsequent resolution), and cardiac arrhythmia including atrial fibrillation (Af), multiple premature ventricular contraction (PVC), and ventricular tachycardia (VT) which require antiarrhythmic drugs. Major cardiac events were defined as cardiac death, non-fatal myocardial infarction, unstable angina, and congestive heart failure.

Statistical analysis

All continuous variables are shown as the mean ± SD. The univariate relationship between the clinical and dipyridamole ^{201}Tl-SPECT results and the perioperative cardiac events was assessed by Student's t-test or Mann-Whitney's U-test for continuous variables, and by the chi-square test with Yates' correction or Fisher's exact tests for dichotomous variables. Stepwise logistic regression models were used to identify any independent predictors of perioperative cardiac events. All statistical analyses were performed by BMDP statistical software (Release 7.1, BMDP statistical software, Inc., Los Angeles, CA) on SPARC station 20. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

Patient characteristics

Table 1 shows the characteristics of all patients. Out of 224 patients, 33 patients (15%) had previous myocardial infarction and 31 patients (14%) had a history of angina pectoris. Thirteen patients (6%) were Goldman's cardiac risk index class III, while 21 patients (9%) were Detsky's cardiac risk index class III or IV.

Clinical risk evaluation and ^{201}Tl-SPECT findings in all patients

One hundred and seventy-three patients (77%) were classified as belonging to the low-risk group, 39 patients (18%) were classified as the intermediate-risk group, and the remaining 12 patients (5%) were considered to belong to the high-risk group. One hundred and thirty-two patients (59%) were diagnosed as negative based on dipyridamole ^{201}Tl-SPECT imaging, 36 patients (16%) had persistent defects, and the remaining 56 patients (25%) had reversible defects. A reversible defect was found in 14% of the low-risk group patients, in 54% of the intermediate-risk group patients, and in 83% of the high-risk group patients (Fig. 1). The prevalence of the reversible defect in the high-risk and intermediate-risk groups was significantly higher than that in the low-risk group (83% and 54% vs. 14%; $p < 0.001$ and $p < 0.001$, respectively), but no significant difference was observed between the high-risk group and the intermediate-risk group ($p > 0.05$).

Table 1 Patient characteristics

Characteristics	No. of patients (%)
Age (years; mean ± SD)	70.6 ± 7.6
Age >70 years	124 (55%)
Male	199 (89%)
Arteriosclerosis obliterans (ASO)	97 (43%)
Abdominal aortic aneurysm (AAA)	127 (57%)
Smoking	200 (89%)
Hyperlipidemia	98 (44%)
Hypertension	161 (72%)
Diabetes mellitus	35 (16%)
Previous myocardial infarction	33 (15%)
Angina pectoris	31 (14%)
Goldman index	
I (0–5)	108 (48%)
II (6–12)	103 (46%)
III (13–25)	13 (6%)
Detsky index	
I (0–5)	161 (72%)
II (6–12)	42 (19%)
III (13–25)	18 (8%)
IV (>25)	3 (1%)

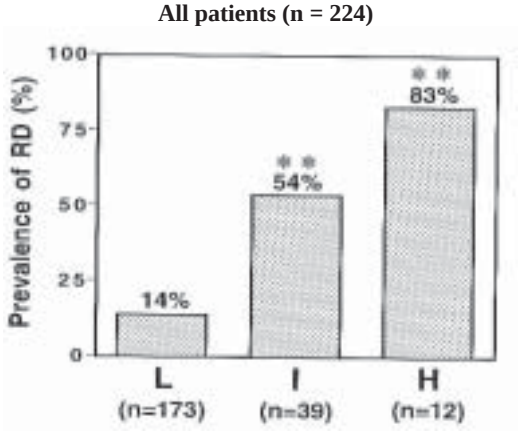

Fig. 1 The prevalence of reversible defects in all patients (n = 224). L: low-risk group, I: intermediate-risk group, H: high-risk group, RD: reversible defect, **: $p < 0.001$ vs. low-risk group.

Five patients (2.2%) out of 224 patients had dipyridamole-induced side effects including arrhythmia in 3 patients (2 PVC and 1 Af) and chest pain in 2 patients. Chest pain disappeared promptly after the intravenous administration of aminophylline.

Twenty-four patients with reversible defects (10 patients with low risk, 9 patients with intermediate risk, and 5 patients with high risk) underwent subsequent coronary angiography before vascular surgery, and significant coronary artery stenosis (defined as ≥ 75% diameter stenosis) was found in 22 patients (92%).

Characteristics of patients who had vascular surgery

One hundred and eighty patients out of 224 patients finally underwent non-cardiac vascular surgery. Vascular surgery was canceled or postponed in the remaining 44 patients (21 patients with low risk, 15 patients with intermediate risk, and 8 patients with high risk), and they comprised 12% of the low risk patients, 39% of the intermediate risk patients, and 67% of the high risk patients, respectively. The reasons why the vascular surgeries were canceled or postponed were as follows: (1) high perioperative cardiac risk (n = 14), (2) malignant diseases (n = 8), (3) slight vascular lesion (n = 7), (4) advanced age (n = 2), (5) stroke (n = 2), (6) renal failure (n = 3), (7) uncontrolled diabetes mellitus (n = 1), (8) patient refusal (n = 7).

Among the 81 patients with ASO out of 180 patients, 35 patients had aorto-iliac or aorto-femoral artery bypass graft, 46 patients had more peripheral vascular proce-

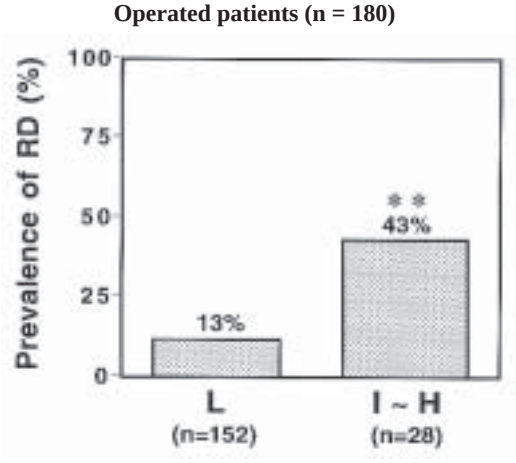

Fig. 2 The prevalence of reversible defects in all patients (n = 180) who underwent vascular surgery. L: low-risk group, I–H: intermediate and high-risk group, RD: reversible defect, **: $p < 0.001$ vs. low-risk group.

Table 2 Clinical characteristics and ^{201}Tl-SPECT findings in patients with perioperative major cardiac events

	Age/Sex	Previous CAD	Other risk factors	Goldman index	Detsky index	Clinical risk stratification	^{201}Tl-SPECT	Vascular surgery	Events
1	73/M	None	Smoking, HT	II (8)	I (5)	Low	RD bypass	Ileo-iliac	UA
2	67/M	None	Smoking, HT	I (3)	I (0)	Low	RD bypass	Aorto-femoral	UA
3	73/M	Unclear	Smoking, HT, Af	II (15)	II (10)	Intermediate	PD	AAA reconstruction	CHF

CAD: coronary artery disease, HT: hypertension, Af: atrial fibrillation, UA: unstable angina, CHF: congestive heart failure, RD: reversible defect, PD: persistent defect, AAA: abdominal artery aneurysm, ( ): cardiac risk score

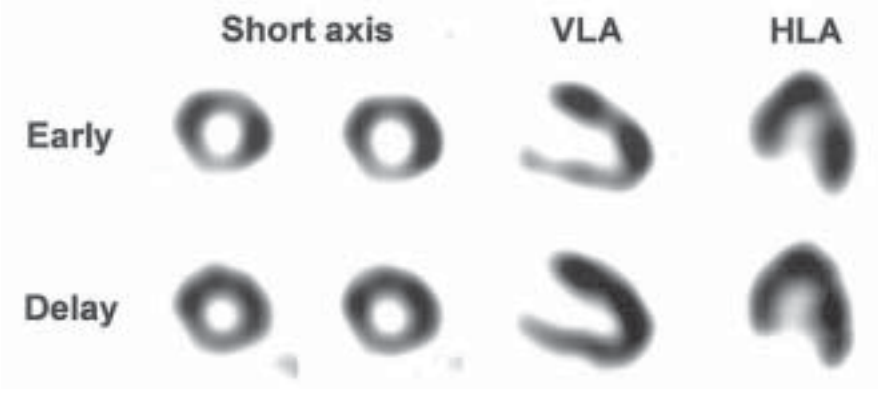

Fig. 3 A 67-year-old male patient who had an unstable angina at 7th hour after operation (case 2 in Table 2). The preoperative dipyridamole ^{201}Tl-SPECT shows some reversible perfusion defects in the anterior, antero-lateral and inferior wall. VLA: vertical long-axis, HLA: horizontal long-axis.

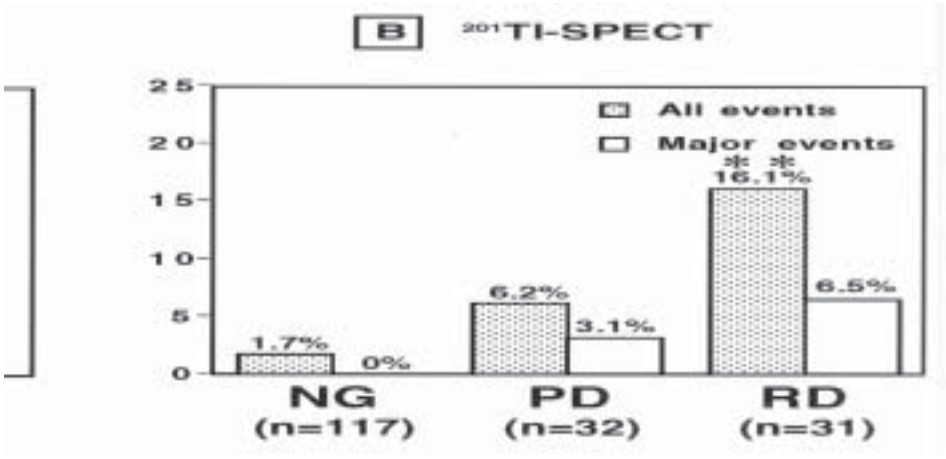

Fig. 4 The prevalence of perioperative cardiac events according to the clinical risk stratification (A) and dipyridamole ^{201}Tl-SPECT imaging (B) in 180 patients having vascular surgery. L: low-risk group, I–H: intermediate and high-risk group, NG: negative, PD: persistent defect, RD: reversible defect, **: $p < 0.01$ vs. negative.

Table 3 Relationship of preoperative clinical variables, ^{201}Tl-SPECT findings and perioperative cardiac events after vascular surgery

Variables	Cardiac events (n = 9)	No cardiac events (n = 171)	Univariate P value	Multivariate P value
Clinical variables				
Age (years; mean ± SD)	69.0 ± 6.8	70.1 ± 7.1	0.5195	
Age >70 years	4 (44%)	92 (54%)	0.8371	0.8915
Male	9 (100%)	152 (89%)	0.6004	0.1907
Arteriosclerosis obliterans (ASO)	4 (44%)	77 (45%)	0.7571	0.9561
Abdominal aortic aneurysm (AAA)	5 (56%)	94 (55%)		
Smoking	8 (89%)	154 (90%)	1.0000	0.8953
Hyperlipidemia	4 (44%)	74 (43%)	0.7825	0.7127
Hypertension	5 (56%)	121 (71%)	0.5505	0.1757
Diabetes mellitus	1 (11%)	26 (15%)	0.8858	0.5990
Previous myocardial infarction	1 (11%)	20 (12%)	0.6317	0.7017
History of angina pectoris	0 (0%)	17 (10%)	1.0000	0.0836
Goldman index (mean ± SD)	6.8 ± 4.2	6.3 ± 3.7	0.8340	
I–II class	8 (89%)	162 (95%)	0.4094	0.5303
III–IV class	1 (11%)	9 (5%)		
Detsky index (mean ± SD)	3.9 ± 3.3	5.2 ± 4.6	0.4058	
I–II class	9 (100%)	164 (96%)	1.0000	0.3158
III–IV class	0 (0%)	7 (4%)		
Intermediate~high risk	2 (22%)	26 (15%)	0.9248	0.7514
Dipyridamole ^{201}Tl-SPECT				
Persistent defect	2 (22%)	30 (18%)	0.9287	0.2019
Reversible defect	5 (56%)	26 (15%)	0.0075*	0.0071*#

Continuous variables are presented as the mean ± SD, and use Student's t-test or Mann-Whitney's U-test to compare them. The chi-square test with Yates' correction or Fisher's exact test were used as a univariate analysis to assess some dichotomous variables. A multivariate analysis is performed using the logistic regression models with each term and "reversible defect" term. #: The model with only "reversible defect" term. *: Statistically significant at $p < 0.05$.

dures including femoro-popliteal, femoro-femoral or axillo-femoral artery bypass grafts. Ninety-nine patients with AAA underwent an abdominal aortic aneurysm resection and reconstruction. Three patients had a below-the-knee amputation and six patients received a lumbar sympathectomy.

They consisted of 152 (85%) low-risk patients, 24 (13%) intermediate-risk patients, and 4 (2%) high-risk patients based on the clinical risk evaluation. Nineteen patients (13%) had reversible defects in the low-risk group, and 12 patients (43%) had it in the intermediate- and high-risk groups (Fig. 2). The prevalence of the

Table 4 Relationship of preoperative clinical variables, ^{201}Tl-SPECT findings and perioperative cardiac events after vascular surgery in low-risk group

Variables	Cardiac events (n = 7)	No cardiac events (n = 145)	Univariate P value	Multivariate P value
Clinical variables				
Age (years; mean ± SD)	69.3 ± 7.2	69.7 ± 7.3	0.7413	
Age >70 years	3 (43%)	77 (53%)	0.8865	0.6868
Male	7 (100%)	126 (87%)	0.5970	0.1753
Arteriosclerosis obliterans (ASO)	4 (57%)	67 (46%)	0.8583	0.5663
Abdominal aortic aneurysm (AAA)	3 (43%)	78 (54%)		
Smoking	6 (86%)	131 (90%)	0.5243	0.9055
Hyperlipidemia	3 (43%)	61 (42%)	0.7259	0.9118
Hypertension	4 (57%)	98 (68%)	0.8709	0.2290
Diabetes mellitus	1 (14%)	20 (14%)	1.0000	0.9655
Previous myocardial infarction	1 (14%)	11 (8%)	0.4445	0.9782
History of angina pectoris	0 (0%)	10 (7%)	1.0000	0.4910
Goldman index (mean ± SD)	5.1 ± 2.7	5.8 ± 3.1	0.5254	
I class	4 (57%)	68 (47%)	0.3673	0.9545
II class	3 (43%)	77 (53%)		
Detsky index (mean ± SD)	2.9 ± 2.7	4.3 ± 3.2	0.2563	
I class	7 (100%)	124 (86%)	0.5940	0.4910
II class	0 (0%)	21 (14%)		
Dipyridamole ^{201}Tl-SPECT				
Persistent defect	1 (14%)	20 (14%)	1.0000	0.4478
Reversible defect	4 (57%)	15 (10%)	0.0049*	0.0035*$^{\#}$

Continuous variables are presented as the mean ± SD, and use Student's t-test or Mann-Whitney's U-test to compare them. The chi-square test with Yates' correction or Fisher's exact test were used as a univariate analysis to assess any dichotomous variables. A multivariate analysis is performed using the logistic regression models with each term and "reversible defect" term.
$^{\#}$: The model with only "reversible defect" term. *: Statistically significant at $p < 0.05$.

Table 5 The predictive ability of reversible defect on dipyridamole ^{201}Tl-SPECT imaging for perioperative cardiac events

	n	Sensitivity (%)	Specificity (%)	Predictive value (%)	
				Positive	Negative
All cardiac events					
All patients	180	55.6	84.8	16.1	97.3
Low risk patients	152	57.1	89.7	21.1	97.7
Intermediate and high risk patients	28	50	57.7	8.3	93.8
Major cardiac events					
All patients	180	66.7	83.6	6.5	99.3
Low risk patients	152	100	88.7	10.5	100

reversible defect in the intermediate- and high-risk groups was significantly higher than that in the low-risk group ($p < 0.001$).

Perioperative cardiac events

Nine patients had perioperative cardiac events (5.0%), including heart failure (n = 1), unstable angina (n = 2), and others cardiac events such as Af (n = 4) and PVC (n = 2). The demographic and clinical characteristics as well as the ^{201}Tl-SPECT findings seen in 3 patients with major cardiac events are shown in Table 2, and the dipyridamole ^{201}Tl-SPECT image of case 2 is also shown in Figure 3.

Among the 9 patients with perioperative cardiac events, 7 patients (2 unstable angina, 4 Af, and 1 PVC) were in the low-risk group, and the remaining 2 patients (1 heart failure and 1 PVC) were in the intermediate- and high-risk group (Fig. 4A). Five patients (2 unstable angina, 2 Af, and 1 PVC) had reversible defects on dipyridamole ^{201}Tl-SPECT, 2 patients (1 heart failure and 1 Af) had persistent defects, while the remaining 2 patients (1 Af and 1 PVC) were negative (Fig. 4B). The prevalence of perioperative cardiac events was similar in the low and intermediate~high-risk groups (4.6% vs. 7.1%, $p > 0.05$), whereas it was significantly higher in patients with reversible defects than in those patients with negative perfusion defect (16.1% vs. 1.7%, $p < 0.01$).

To determine the predictor of perioperative cardiac events, preoperative clinical risk factors and the findings of dipyridamole ^{201}Tl-SPECT for the patients with and without cardiac events were compared by a univariate analysis. The reversible defect was the only variable that was associated with perioperative cardiac events (Table 3). Furthermore, a stepwise logistic regression analysis demonstrated that it was an independent predictor for perioperative cardiac events (odds ratio 7.0, 95% confidence interval 1.7–28.0, p = 0.007). Similar results were also found in low-risk group patients (Table 4). The reversible defect was an independent predictor associated with perioperative cardiac events even when the same analysis was performed in low-risk group patients (odds ratio 11.6, 95% confidence interval 2.3–57.4, p = 0.004).

The predictive ability of the reversible defect for perioperative cardiac events is summarized in Table 5. Both the sensitivity and the specificity for major cardiac events were high (100% and 88.7%, respectively) in the low risk patients. The negative predictive value was greater than 93% for all cardiac events and major cardiac events in all patient groups.

DISCUSSION

Coronary artery disease is prevalent among patients with significant atherosclerotic vascular disease and may be present despite the lack of any cardiac symptoms, and has been reported to occur in up to 37% of asymptomatic persons.[1] Ischemic heart disease is a major cause of morbidity and mortality in this population for both the perioperative and late periods.[1] Therefore, both the preoperative diagnosis and determination of the extent of ischemic heart disease are very important for the effective management of patients with non-cardiac vascular surgery to reduce the likelihood of adverse perioperative cardiac events. The major finding of this study is that the reversible defect of dipyridamole ^{201}Tl-SPECT is the only independent variable, which is significantly correlated with the occurrence of perioperative cardiac events in patients who underwent non-cardiac vascular surgery. In contrast, risk assessment with clinical variables was not predictive of any adverse cardiac outcomes. Our present study confirms the findings of previous reports, which showed preoperative dipyridamole ^{201}Tl scintigraphy to be an effective predictor of adverse cardiac complications in patients undergoing non-cardiac vascular surgery.[11–16]

The incidence of all cardiac events was 5.0%, and that of major cardiac events was only 1.7% in our study patients. Moreover, arrhythmias were a common perioperative cardiac event, and no perioperative cardiac death or myocardial infarction occured. These results are in clear contrast to a recent report by Leppo and Dahlberg,[22] in which the rate of death ranged from 0.6 to 3.6% for non-cardiac surgery. There are several explanations for this phenomenon. First, in most high risk patients, the surgery was either canceled or postponed based on the findings of preoperative clinical risk assessment and ^{201}Tl-SPECT imaging. Sixty-seven percent of patients with a high risk and 39% of patients with an intermediate risk had surgery either canceled or postponed, and among them 19 patients had reversible defects. Second, even patients in either the high-risk or intermediate-risk groups who underwent vascular surgery, also received more careful medical management such as intravenous nitroglycerine infusion during the perioperative period. Third, the severity of ischemic heart disease might be lower in our study population. In fact, the prevalence of previous myocardial infarction and angina pectoris was lower (15%) than that reported in previous studies (20–60%).[11–16,23–25] As a result, most study patients were classified as belonging to the low-risk group. Even in 180 patients who underwent vascular surgery, 84% of all patients were in the low-risk group. Therefore, despite the differences in the prevalence of perioperative cardiac events, our findings also confirm the results of most previous studies.[11–16,23–25]

In the present study, the sensitivity and specificity of dipyridamole ^{201}Tl-SPECT were 55.6% and 84.8% for all cardiac events, and were 66.7% and 83.6% for major cardiac events, respectively. This sensitivity is slightly lower than that found in previous studies.[11–16] The reason for this may be the lower incidence of major cardiac events. Importantly, the reversible defects identified by dipyridamole ^{201}Tl-SPECT were useful for stratifying the clinically low risk patients in our present study. In contrast, Eagle et al.[12] demonstrated that preoperative dipyridamole ^{201}Tl imaging is useful for stratifying vascular patients with an intermediate risk of coronary artery disease based on a clinical evaluation, but not in those with a low risk. Nevertheless, Hertzer et al. showed that significant coronary stenosis is present in 37% of asymptomatic patients with peripheral vascular disease.[1] In addition, Younis et al. reported that dipyridamole thallium scintigraphy is a useful noninvasive test for stratifying asymptomatic patients with coronary artery disease.[8] Therefore, a reversible defect on ^{201}Tl-SPECT could predict the occurrence of perioperative cardiac events even in low risk patients, even though the incidence of perioperative cardiac events was low (4.6% for all cardiac events and 1.3% for major cardiac events). Furthermore, only 2.2% (5/224) of patients had dipyridamole-induced side effects in our study. Iskandrian et al.[26] showed that the side effects induced by dipyridamole were mild, transient, and well tolerated and rarely require treatment, and the incidence of their occurrence was relatively lower compared to other stress test drugs such as adenosine.

Our present findings do not correlate with those of either Mangano et al. or Baron et al. since they found no association between the reversible defect and adverse cardiac outcomes,[17,18] but Mangano et al. used planar dipyridamole ^{201}Tl scintigraphy, not SPECT. Some technical limitations of planar imaging and its reliability in

detecting myocardial ischemia have already been questioned.[6] Another issue is bias in the selection of patients and difference in the intensity of postoperative diagnostic monitoring as well as factors regarding perioperative medical and surgery care.

We conclude that preoperative dipyridamole ^{201}Tl-SPECT is very useful for predicting perioperative cardiac events in patients with vascular disease before non-cardiac vascular surgery, even in patients with a low risk based on clinical risk stratification, but there are some limitations to this study. Firstly, this was a retrospective observational study. The referring physicians were not blinded to the ^{201}Tl-SPECT results, so that the performance or extent of surgical procedures and perioperative medical therapy were both potentially influenced by the ^{201}Tl-SPECT findings. In addition, a preoperative bias in the selection of patients and perioperative medical treatment might affect the occurrence of perioperative cardiac events. Secondly, the number of study patients was also relatively small.

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