

Serial dual single-photon emission computed tomography of thallium-201 and iodine-123 beta-methyl iodophenyl pentadecanoic acid scintigraphy can predict functional recovery of patients with coronary artery disease after coronary artery bypass graft surgery

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Background A mismatch between thallium-201 (²⁰¹Tl) and iodine-123 (¹²³I)-beta-methyl iodophenyl pentadecanoic acid (BMIPP) dual single-photon emission computed tomography (SPECT) reflects a dysfunctional but viable myocardium, such as stunned or hibernating myocardium, in patients with coronary artery disease (CAD). However, the cardiac function does not always improve after revascularization. The present study aimed to determine whether serial ²⁰¹Tl and ¹²³I-BMIPP dual SPECT can predict improvements in cardiac function after coronary artery bypass graft surgery (CABG) in patients with CAD.

Materials and methods The study included 98 patients with CAD requiring CABG and having a left ventricular ejection fraction (LVEF) less than 50%. The total defect score (TDS) was calculated from ²⁰¹Tl and ¹²³I-BMIPP dual-SPECT images acquired before and 3 weeks after CABG. The LVEF, left ventricular end-diastolic volume index, and end-systolic volume index were determined by means of contrast left ventriculography before and 6 months after CABG.

Results After 6 months, LVEF improved by 5% or more in 62 patients (group A) but did not improve in the remaining 36 patients (group B). Baseline TI-TDS was significantly lower (9.1 ± 4.6 vs. 14.6 ± 6.5, $P < 0.001$), and the mismatch score (BMIPP-TDS – TI-TDS) was significantly higher (6.9 ± 4.2 vs. 4.2 ± 3.9, $P = 0.002$) in group A than in group B. The extent of change in BMIPP-TDS 3 weeks after CABG

compared with that before (delta-BMIPP-TDS) was significantly greater in group A than in group B (– 5.9 ± 3.0 vs. 2.8 ± 4.3, $P < 0.001$). Stepwise multivariate analysis selected delta-BMIPP-TDS as a significant independent predictor of improvement in LVEF at 6 months after CABG (multivariate β -coefficient = – 0.718, $P < 0.001$). The degree of change in LVEF 6 months after CABG compared with that before significantly and negatively correlated with delta-BMIPP-TDS ($r = -0.631$, $P < 0.001$).

Conclusion The delta-BMIPP-TDS evaluated by serial ²⁰¹Tl and ¹²³I-BMIPP dual SPECT can predict improvements in cardiac function during the chronic phase of CAD. *Nucl Med Commun* 36:148–155 © 2015 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Revascularization for patients with coronary artery disease (CAD) aims to improve the left ventricular (LV) function [1], enhance the quality of life [2], grant freedom from anginal symptoms, and increase survival [3]. Among these factors, clinical outcomes should relate to functional improvement after coronary artery bypass graft surgery (CABG) in patients with CAD who have a viable myocardium [4]. Therefore, various imaging methods that can identify viable myocardium have been used in patients with ischemic LV dysfunction. However, cardiac function does not always improve after CABG. One reason for this is target vessels that are calcified or small in diameter, rendering them unsuitable for revascularization, as well as the length or location of lesions.

Fatty acids constitute the major fuel source for the normal myocardium under normal aerobic conditions, and iodine-123-5-(*p*-iodophenyl)-3-(*R,S*)-methylpentadecanoic acid (¹²³I-BMIPP) is clinically used as a probe to study the myocardial metabolism of fatty acids [5,6]. Regions with mismatches between ¹²³I-BMIPP uptake and perfusion imaging reportedly reflect dysfunctional but viable myocardium, such as that seen with myocardial stunning or hibernation, in which LV function will improve after revascularization [7–9]. However, changes in thallium-201 (²⁰¹Tl) and ¹²³I-BMIPP dual single-photon emission computed tomography (SPECT) findings before and after CABG have not been addressed to evaluate myocardial contractile reserve in patients with CAD.

The present study investigated whether serial ^{201}Tl and ^{123}I -BMIPP dual SPECT can predict improved cardiac function after CABG in patients with CAD.

Materials and methods

Patient population

Consecutive 181 patients with CAD and LV dysfunction who underwent isolated CABG at our institution between February 2004 and August 2006 were prospectively enrolled. All CABG surgeries were performed using standard cardiac catheterization, including coronary angiography and contrast left ventriculography (LVG). Inclusion criteria included a contrast left ventriculographic LV ejection fraction (EF) less than 50% before CABG. Exclusion criteria included having undergone a previous bypass graft or angioplasty ($n=22$ patients), having a ventricular pacemaker implanted ($n=8$), incidence of myocardial infarction within the past 8 weeks ($n=15$), and presence of severe valvular heart disease ($n=10$). After excluding these patients we analyzed data acquired from the remaining 126. Our institutional ethics review board approved the study and all patients provided written informed consent to participate.

Study protocol

Patients were assessed with ^{201}Tl and ^{123}I -BMIPP dual SPECT before and 3 weeks after CABG. All patients were reassessed using coronary angiography and contrast LVG after 6 months of follow-up. Patients with poor angiographic runoff, significant stenosis, occlusion of the bypass graft, or de-novo native coronary artery lesions at this time were excluded from the study.

^{201}Tl and ^{123}I -BMIPP dual SPECT

Dual SPECT using ^{201}Tl and ^{123}I -BMIPP was performed using a single-head gamma camera (Millennium MPR; GE Medical Systems, Waukesha, Wisconsin, USA) equipped with a low-energy, general-purpose, parallel-hole collimator. Resting patients were injected intravenously with ^{123}I -BMIPP (111 MBq) and immediately thereafter with ^{201}Tl (74 MBq). Images were started 20 min later and the camera was rotated over 180° from the 45° right anterior oblique position to the 45° left posterior oblique position in 32 views with an acquisition time of 40 s per view. Images were acquired in a 64×64 matrix using a filtered back-projection method for reconstruction. We acquired ^{201}Tl data using a symmetrical 70 keV window at 10% width (66.5–73.5 keV), and ^{123}I data using a symmetrical 159 keV window at 10% width (151.1–167 keV).

Acquired ^{201}Tl and ^{123}I -BMIPP SPECT images were divided into 17 segments on the basis of American Heart Association recommendations [10]. Regional tracer uptake was semiquantified using a scoring system in which, 0, 1, 2, 3, and 4 represented normal, mildly, moderately, significantly reduced uptake, and no uptake,

respectively, as in previously described methods [11–13]. The total defect score (TDS) for each image was calculated as the sum of all defect scores. The mismatch score was calculated using the following formula: BMIPP-TDS – Tl-TDS.

Evaluation of left ventricular function

Contrast LVG was performed (in the 30° right anterior oblique orthogonal projection) after coronary angiography before and 6 months after bypass surgery. The LVEF, LV end-diastolic volume index (EDVI), and LV end-systolic volume index (ESVI) were calculated by the area-length method as previously reported [14].

Serial changes were observed between the first and second scintigraphic parameters and left ventriculographic parameters before and after bypass surgery.

Changes between the first and second ^{201}Tl and ^{123}I -BMIPP dual-scintigraphic parameters (Tl-TDS and BMIPP-TDS) and left ventriculographic parameters (EDVI, ESVI, and LVEF) were calculated using the following formula: $\Delta(X) = [(X) \text{ value of second evaluation}] - [\text{first value of } (X)]$, where $(X) = ^{201}\text{Tl}$ and ^{123}I -BMIPP dual scintigraphic, or left ventriculographic parameters.

Statistical analysis

Data were statistically analyzed using SPSS 16.0 (SPSS Inc., Chicago, Illinois, USA), or SAS version 9.1 (SAS Institute Inc., Cary, North Carolina, USA). Numerical results are expressed as means \pm SD. Categorical data were compared between two groups using two-sided χ^2 tests, and differences between continuous variables were evaluated using an unpaired t -test. Changes from baseline were evaluated within each treatment group of patients who were assessed twice using a paired t -test and between two groups using two-way analysis of variance.

Relationships between continuous variables were assessed using linear regression analysis. Variables of interest were examined by univariate and stepwise multivariate analyses to determine the contribution of the degree of change in LVEF (delta-LVEF). Cutoff values for selecting scintigraphic parameters for predicting LVEF improvements after CABG were identified by receiver-operating characteristic analysis. In all analyses, P values less than 0.05 were deemed statistically significant.

Results

Clinical characteristics

Two patients experienced a cerebral accident, two patients died of congestive heart failure after CABG, and one died of lethal arrhythmia. Eighteen patients were excluded on the basis of follow-up coronary angiographic results at 6 months after CABG because of poor runoff of an arterial graft ($n=3$), significant stenosis of an arterial

graft ($n=4$), occluded venous grafts ($n=4$), and de-novo native coronary artery lesions ($n=7$). Five others were excluded because of incomplete follow-up data. Thus, 98 of the 126 enrolled patients (men, $n=70$; women, $n=28$; mean age, 69.6 ± 6.4 years; range, 50–81 years) completed the entire protocol.

After the 6-month follow-up, we grouped these 98 patients on the basis of at least 5% increase in left ventriculographic LVEF ($n=62$; group A) or less than 5% improvement in LVEF ($n=36$; group B). The clinical characteristics and pharmacotherapy did not significantly differ between the two groups (Table 1) except that group B used significantly more diuretics compared with group A.

Comparison of contrast left ventriculographic findings before and 6 months after CABG

Table 2 summarizes changes in EDVI, ESVI, and LVEF at 6 months after CABG. Baseline EDVI and ESVI tended to be lower and LVEF tended to be higher in group A than in group B, but the differences did not reach statistical significance.

The EDVI and ESVI at 6 months after CABG significantly decreased and increased in groups A and B, respectively, compared with baseline values. Moreover, delta-EDVI and delta-ESVI at 6 months after CABG were significantly higher in group B than in group A. The LVEF was significantly increased and decreased relative to baseline values in groups A and B, respectively, and the delta-LVEF was significantly higher in group A than in group B.

Comparison of ^{201}Tl and ^{123}I -BMIPP dual SPECT before and 3 weeks after CABG

Table 1 and Fig. 1 summarize the ^{201}Tl and ^{123}I -BMIPP dual-SPECT imaging parameters. Baseline parameters were significantly lower in the TI-TDS in group A

compared with group B, whereas BMIPP-TDS did not significantly differ between the two groups. Moreover, the mismatch score was significantly higher in group A than in group B (Table 1).

The TI-TDS and BMIPP-TDS at 3 weeks after CABG were significantly decreased relative to the baseline values in group A, but did not significantly change in group B. Moreover, delta-TI-TDS and delta-BMIPP-TDS were significantly lower in group A than in group B (Fig. 1).

Relationship between degrees of changes in LVEF and in total defect scores

The delta-LVEF significantly and negatively correlated between delta-TI-TDS ($r = -0.462$, $P < 0.001$) and delta-BMIPP-TDS ($r = -0.631$, $P < 0.001$) between baseline and 6 months (Fig. 2), with delta-BMIPP-TDS having a stronger correlation.

Evaluation of factors predicting improved cardiac function

Table 3 shows the results of univariate and multivariate analyses of factors predicting improvements in LVEF after CABG in patients with CAD. The univariate analysis selected diuretic use, baseline EDVI, baseline ESVI, baseline LVEF, baseline TI-TDS, mismatch score, delta-TI-TDS, and delta-BMIPP-TDS as predictive factors. Stepwise multivariate analysis identified baseline TI-TDS and delta-BMIPP-TDS as significant independent predictors of an improvement in LVEF at 6 months after CABG. However, the multivariate β -coefficient value for delta-BMIPP-TDS was more favorable than that for baseline TI-TDS.

Comparison of delta-BMIPP-TDS in both groups

Figure 3 shows the delta-BMIPP-TDS in both groups evaluated by the first and second BMIPP-TDS. The sensitivity, specificity, and accuracy of a delta-BMIPP-TDS cutoff of up to -3 (identified by receiver-operating characteristic analysis) to predict LVEF improvement at 6 months after CABG were 93.5% (58/62), 91.2% (33/36), and 92.9% (91/98), respectively.

Case presentation

Figure 4 shows a representative ^{201}Tl and ^{123}I -BMIPP dual SPECT before and 3 weeks after CABG in patients with CAD. This figure also shows LVG before and 6 months after CABG. Both TI-TDS and BMIPP-TDS were decreased from baseline to 3 weeks after CABG. Moreover, in this patient, LVEF was increased at a chronic phase of 6 months after CABG.

Discussion

The major finding of this study is that delta-BMIPP-TDS evaluated by serial ^{201}Tl and ^{123}I -BMIPP dual SPECT can predict improvement in cardiac function at 6 months after CABG in patients with CAD.

Table 1 Clinical characteristics of the patients

	Group A ($n=62$)	Group B ($n=36$)	P -value
Age (years)	69.3 ± 7.2	70.1 ± 4.9	0.565
Sex			0.490
Male	46 (74)	24 (67)	
Female	16 (26)	12 (33)	
Diabetes mellitus	19 (31)	14 (39)	0.507
Hypertension	47 (76)	24 (67)	0.356
Hyperlipidemia	29 (47)	16 (44)	0.837
Prior MI	40 (65)	29 (81)	0.112
More than 3 grafts	29 (47)	19 (53)	0.676
Pharmacotherapy			
ACE-I or ARB	52 (83)	26 (72)	0.198
β -Blockers	39 (62)	20 (56)	0.525
Ca antagonist	36 (58)	18 (50)	0.529
Nitrate	17 (27)	12 (19)	0.647
Diuretics	13 (21)	17 (47)	0.012
Baseline TI-TDS	9.1 ± 4.6	14.6 ± 6.5	< 0.001
Baseline BMIPP-TDS	16.1 ± 6.8	18.9 ± 9.5	0.131
Mismatch score	6.9 ± 4.2	4.2 ± 3.9	0.002

Values are represented as mean \pm SD or n (%).

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BMIPP, beta-methyl iodophenyl pentadecanoic acid; MI, myocardial infarction; TDS, total defect score; TI, thallium.

Table 2 Changes in contrast left ventriculographic parameters in both groups

	Group A (mean ± SD)			Group B (mean ± SD)		
	Baseline	6 months	Delta	Baseline	6 months	Delta
Contrast left ventriculography						
EDVI (ml/m ²)	76.8 ± 29.0	66.5 ± 22.6*	-10.3 ± 12.7	87.5 ± 33.3	93.4 ± 37.5 [†]	5.9 ± 16.7 [‡]
ESVI (ml/m ²)	46.8 ± 22.4	33.4 ± 18.0*	-13.4 ± 9.2	57.2 ± 30.7	65.7 ± 37.3 [†]	8.4 ± 13.8 [‡]
LVEF (%)	40.5 ± 6.4	52.0 ± 9.1*	11.4 ± 4.5	37.7 ± 10.3	33.8 ± 12.5*	-3.9 ± 5.5 [‡]

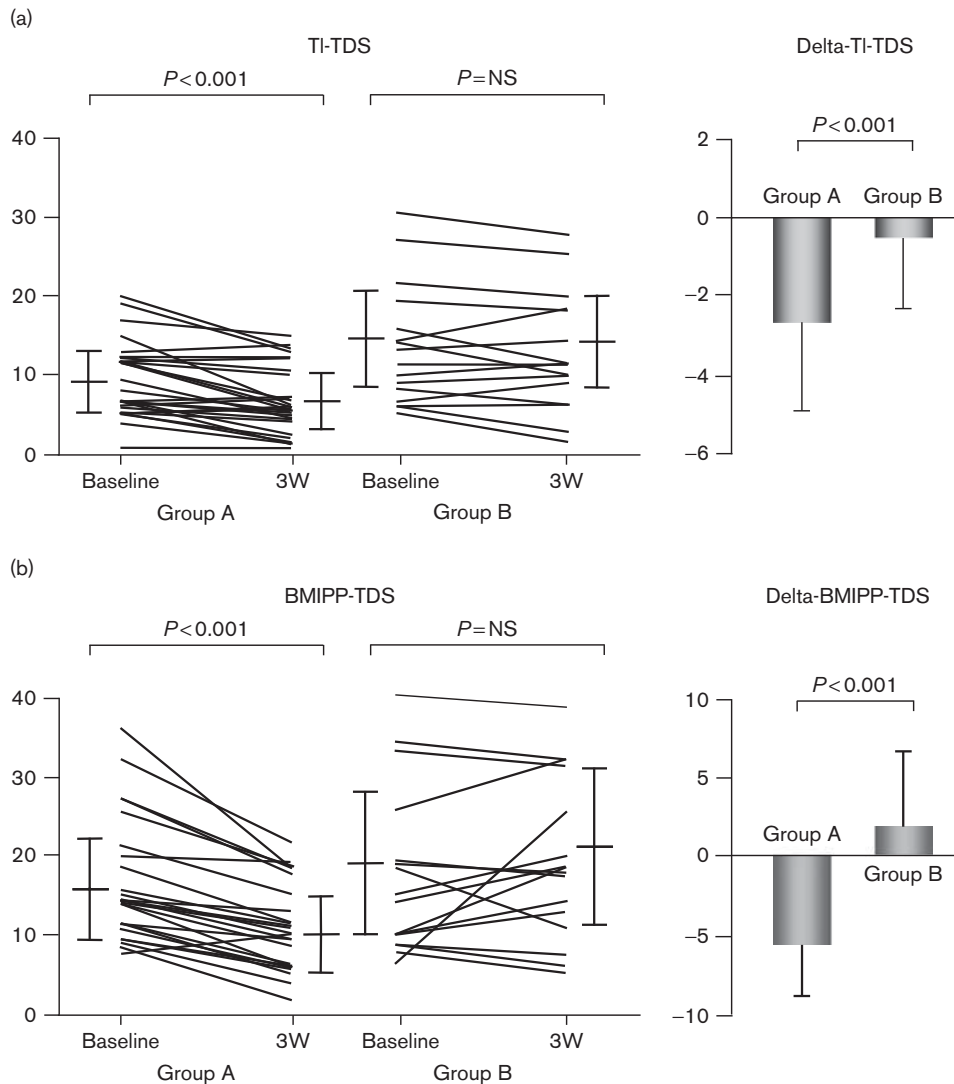
EDVI, end-diastolic volume index; ESVI, end-systolic volume index; LVEF, left ventricular ejection fraction.

**P* < 0.001.

[†]*P* < 0.05 versus baseline.

[‡]*P* < 0.001 versus group A.

Fig. 1

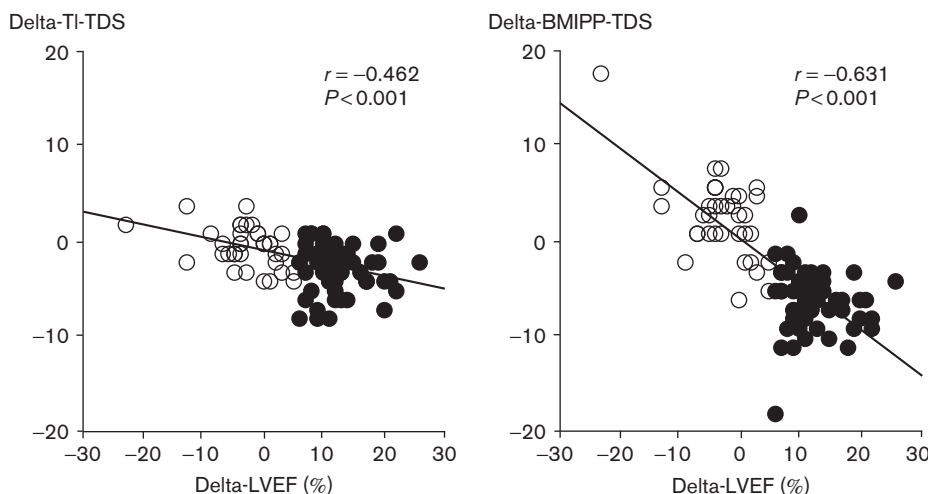


Comparison of ²⁰¹Tl and ¹²³I-BMIPP dual-scintigraphic findings for TI-TDS (a) and BMIPP-TDS (b) in the two groups. ¹²³I-BMIPP, iodine-123-beta-methyl iodophenyl pentadecanoic acid; NS, nonsignificant; TDS, total defect score; ²⁰¹Tl, thallium-201; 3W, 3 weeks after therapy.

Several studies have shown that ²⁰¹Tl imaging is useful for identifying viable myocardium in patients with CAD who had chronic ischemic LV dysfunction [15,16]. Ragosta *et al.* [16] discovered a relationship between

changes in LVEF and ²⁰¹Tl uptake before and after CABG in patients with CAD. The amount of ²⁰¹Tl uptake after CABG increased in patients with improved LVEF compared with baseline values; however, it was

Fig. 2



Correlation between the degree of changes in BMIPP-TDS at 3 weeks after bypass grafting compared with that before, and degree of changes in LVEF from baseline to after 6 months in patients with coronary artery disease. Solid circles represent group A and open circles represent group B. BMIPP, beta-methyl iodophenyl pentadecanoic acid; LVEF, left ventricular ejection fraction; TDS, total defect score; Tl, thallium.

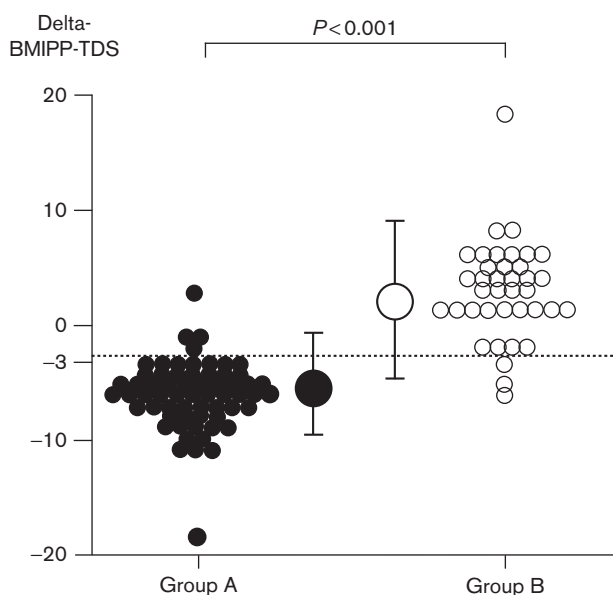
Table 3 Univariate and multivariate linear model of delta-LVEF

	Univariate		Multivariate	
	Correlation coefficient	P-value	β -coefficient	P-value
Age	-0.041	0.692		
Sex (male = 1)	0.007	0.949		
Diabetes mellitus	-0.160	0.115		
Hypertension	0.049	0.635		
Hyperlipidemia	-0.112	0.272		
Prior MI	-0.176	0.083		
More than 3 grafts	-0.059	0.561		
ACE-I or ARB	0.109	0.284		
β -Blocker	0.151	0.341		
Ca antagonist	0.079	0.440		
Nitrate	0.050	0.627		
Diuretics	-0.226	0.025		
Baseline EDVI	-0.292	0.004		
Baseline ESVI	-0.319	0.001		
Baseline LVEF	0.282	0.005		
Baseline TI-TDS	-0.447	< 0.001	-0.347	0.002
Baseline BMIPP-TDS	-0.189	0.062		
Mismatch score	0.270	0.007		
Delta-Tl-TDS	-0.462	< 0.001		
Delta-BMIPP-TDS	-0.631	< 0.001	-0.718	< 0.001

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BMIPP, beta-methyl iodophenyl pentadecanoic acid; MI, myocardial infarction; TDS, total defect score; Tl, thallium.

unchanged in patients whose LVEF did not improve [16]. We similarly found significantly increased ^{201}Tl uptake after CABG in patients with improved LVEF but not in those without. We also assessed the relationship between the degree of change in TI-TDS and the change in LVEF, but the correlation in our CAD patients was statistically weak compared with those in the study by Ragosta *et al.* [16]. Such discrepancies may be partly due to differences between the patient populations, particularly the amount of infarcted myocardium. Many of our

Fig. 3

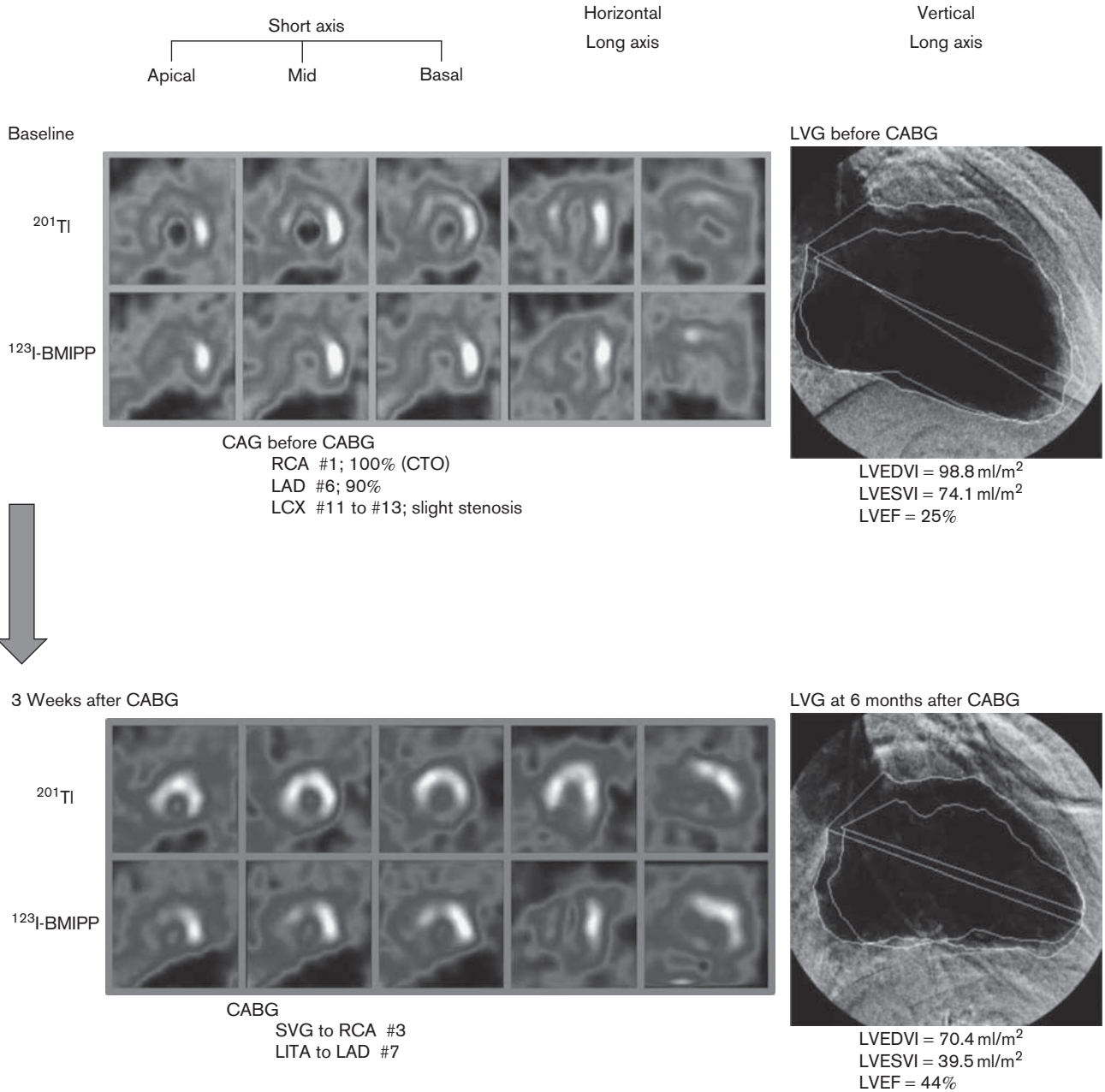


Comparison of delta-BMIPP-TDS in the two groups. Solid circles represent group A and open circles represent group B. BMIPP, beta-methyl iodophenyl pentadecanoic acid; TDS, total defect score.

patients had experienced a prior myocardial infarction and thus bypass grafting might not have significantly improved ^{201}Tl uptake because the infarcted areas had already undergone irreversible necrosis.

Long-chain fatty acids are important substrates for myocardial oxidative metabolism, as 60–80% of the ATP produced in the heart is derived from their oxidation.

Fig. 4



Representative ²⁰¹Tl and ¹²³I-BMIPP dual SPECT before and 3 weeks after CABG, and LVG before and after 6 months. CABG, coronary artery bypass graft surgery; CAG, coronary angiography; CTO, chronic total occlusion; ¹²³I-BMIPP, iodine-123-beta-methyl iodophenyl pentadecanoic acid; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LITA, left internal thoracic artery; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVI, left ventricular end-systolic volume index; LVG, left ventriculography; RCA, right coronary artery; SVG, saphenous vein graft; ²⁰¹Tl, thallium-201.

However, this process is suppressed in patients with myocardial ischemia, when lack of oxygen availability and/or mitochondrial dysfunction renders the myocardium more dependent upon glycolysis [17,18]. A methyl group branching from the fatty acid chain protects BMIPP from metabolism through beta-oxidation while retaining specific physiologic properties such as uptake

and incorporation into the triglyceride pool [19]. Myocardial ischemia is detected by ¹²³I-BMIPP as diminished oxidative fatty acid metabolism, even though abundant perfusion has been restored to the jeopardized ischemic myocardium [20,21]. This phenomenon reflects the gradual recovery of oxidative fatty acid metabolism upon the restoration of blood flow after revascularization.

Therefore, several investigators suggest that impaired myocardial ^{123}I -BMIPP uptake induced by ischemia can be reversed after revascularization in patients with CAD [22,23]. However, serial ^{123}I -BMIPP imaging has not yet been applied to the prediction of functional recovery after CABG in such patients. Here, we investigated whether serial ^{201}Tl and ^{123}I -BMIPP dual SPECT can predict improved cardiac function after CABG. We discovered that the degree of change in BMIPP-TDS (delta-BMIPP-TDS) was an independent predictor of an improvement in LVEF at 6 months after CABG and that delta-BMIPP-TDS significantly and negatively correlated with the degree of change in LVEF at 6 months after CABG when compared with that before.

In contrast, regions of mismatch between ^{123}I -BMIPP and ^{201}Tl (perfusion) images reflect dysfunctional but viable myocardium [7–9]. Therefore, systolic function should improve after revascularization in patients with CAD and scintigraphic mismatches [22,23]. Univariate analysis in the present study identified baseline mismatch scores as independent predictors of improvement in cardiac function at 6 months after CABG, but multivariate analysis did not. One explanation for this might be targets for coronary artery grafts being unsuitable because of calcifications, or having a small vessel diameter, as well as lesion length and location. Therefore, we evaluated serial ^{201}Tl and ^{123}I -BMIPP dual SPECT before and after CABG in our patients, because scintigraphic parameters should not be improved unless bypass grafting proceeded on suitable coronary arteries. We concluded that the delta-BMIPP-TDS was the most useful parameter for predicting functional recovery compared with baseline mismatch scores or perfusion defects after CABG in patients with CAD.

As the approach of comparison for cardiac perfusion and metabolism, PET is well known [24,25]. In this study, we used ^{201}Tl SPECT imaging as the perfusion tracer. However, it has been reported that ^{201}Tl follows potassium, and thus this tracer is affected by the cellular energetic status (because of its dependence on the active Na/K transport by Na/K-ATPase) [26,27]. Therefore, the mismatch score in this study might be lower than that calculated using PET. Moreover, because the complete recovery of ^{201}Tl uptake at 3 weeks after CABG might not be observed, delta-Tl-TDS might be lower than the actual status. Although the mismatch of perfusion and metabolism using PET is a widely accepted technique, PET is not available in many centers in Japan. Therefore, we used ^{123}I -BMIPP imaging and calculated delta-BMIPP-TDS, because this parameter could be expected to be more sensitive than delta-Tl-TDS. The several advantages of SPECT imaging have been raised for comparison with PET imaging: (a) it is a noninvasive measure of mitochondrial viability and recovery; (b) dual SPECT (^{201}Tl and ^{123}I -BMIPP) can be obtained in a

single scan; and (c) the half-life tracers have a longer life. For these reasons, we evaluated using ^{201}Tl and ^{123}I -BMIPP dual SPECT.

To sum up, the extent of changes in BMIPP-TDS determined by serial ^{201}Tl and ^{123}I -BMIPP dual SPECT before and 3 weeks after CABG in patients with CAD was found to be significantly greater in patients with an improved LVEF than in those without. The multivariate analysis showed that the delta-BMIPP-TDS was an independent predictor of improvement in LVEF after 6 months. Moreover, we found significant negative correlations between the delta-BMIPP-TDS and the degree of change in LVEF before and 6 months after CABG. Therefore, CAD patients with low delta-BMIPP-TDS as evaluated by serial ^{201}Tl and ^{123}I -BMIPP dual SPECT must be followed up especially carefully during medical management.

Study limitations

One limitation of the present study was the relatively small number of enrolled patients with CAD. Pharmacotherapy for CAD has considerably advanced in recent years, as clinical trials have shown favorable long-term effects of ACE inhibitors [28] and β -blockers [29] on cardiac function. However, this study did not select these therapeutic approaches as independent predictors of improved cardiac function after CABG. Accordingly, long-term effects should be evaluated in a larger cohort of patients with CAD.

In this study protocol, follow-up ^{201}Tl and ^{123}I -BMIPP dual SPECT was performed 3 weeks after CABG. Some amount of stunned myocardium after 3 weeks might be present, and may influence the ^{201}Tl imaging. In our institution, the first outpatient visit after CABG was usually scheduled at this time. For these reasons, we selected 3 weeks after CABG as the time for follow-up SPECT. Moreover, technetium-labeled imaging is known to be a more favorable radiation dosimetric technique and has more favorable imaging properties compared with ^{201}Tl imaging [30]. Furthermore, it has been reported that delayed technetium-labeled imaging reflects mitochondrial viability and detects stunned myocardium in CAD patients [31]. However, technetium-labeled imaging and ^{123}I -BMIPP are not suitable for dual SPECT because of their energy peaks. In the future, we need to evaluate follow-up SPECT data during the later period using technetium-labeled imaging.

Conclusion

In patients with CAD, delta-BMIPP-TDS evaluated with serial ^{201}Tl and ^{123}I -BMIPP dual SPECT before and at 3 weeks after CABG can predict improvements in cardiac function during the chronic phase.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- Dreyfus GD, Duboc D, Blasco A, Vigoni F, Dubois C, Brodaty D, *et al.* Myocardial viability assessment in ischemic cardiomyopathy: benefits of coronary revascularization. *Ann Thorac Surg* 1994; **57**:1402–1407, discussion 1407–1408.
- Marwick TH, Zuchowski C, Lauer MS, Secknus MA, Williams J, Lytle BW. Functional status and quality of life in patients with heart failure undergoing coronary bypass surgery after assessment of myocardial viability. *J Am Coll Cardiol* 1999; **33**:750–758.
- Haas F, Haehnel CJ, Picker W, Nekolla S, Martinoff S, Meisner H, Schwaiger M. Preoperative positron emission tomographic viability assessment and perioperative and postoperative risk in patients with advanced ischemic heart disease. *J Am Coll Cardiol* 1997; **30**:1693–1700.
- Marwick TH. The viable myocardium: epidemiology, detection, and clinical implications. *Lancet* 1998; **351**:815–819.
- Blanke H, Cohen M, Karsch KR, Fagerstrom R, Rentrop KP. Prevalence and significance of residual flow to the infarct zone during the acute phase of myocardial infarction. *J Am Coll Cardiol* 1985; **5**:827–831.
- Goodman MM, Kirsch G, Knapp FF Jr. Synthesis and evaluation of radioiodinated terminal p-iodophenyl-substituted alpha- and beta-methyl-branched fatty acids. *J Med Chem* 1984; **27**:390–397.
- Franken PR, De Geeter F, Dendale P, Demoor D, Block P, Bossuyt A. Abnormal free fatty acid uptake in subacute myocardial infarction after coronary thrombolysis: correlation with wall motion and inotropic reserve. *J Nucl Med* 1994; **35**:1758–1765.
- Ito T, Tanouchi J, Kato J, Morioka T, Nishino M, Iwai K, *et al.* Recovery of impaired left ventricular function in patients with acute myocardial infarction is predicted by the discordance in defect size on ¹²³I-BMIPP and ²⁰¹Tl SPET images. *Eur J Nucl Med* 1996; **23**:917–923.
- Hashimoto A, Nakata T, Tsuchihashi K, Tanaka S, Fujimori K, Iimura O. Postischemic functional recovery and BMIPP uptake after primary percutaneous transluminal coronary angioplasty in acute myocardial infarction. *Am J Cardiol* 1996; **77**:25–30.
- Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, *et al.* American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002; **105**:539–542.
- Kasama S, Toyama T, Hatori T, Sumino H, Kumakura H, Takayama Y, *et al.* Effects of intravenous atrial natriuretic peptide on cardiac sympathetic nerve activity and left ventricular remodeling in patients with first anterior acute myocardial infarction. *J Am Coll Cardiol* 2007; **49**:667–674.
- Kasama S, Toyama T, Hatori T, Sumino H, Kumakura H, Takayama Y, *et al.* Evaluation of cardiac sympathetic nerve activity and left ventricular remodeling in patients with dilated cardiomyopathy on the treatment containing carvedilol. *Eur Heart J* 2007; **28**:989–995.
- Kasama S, Toyama T, Iwasaki T, Sumino H, Kumakura H, Minami K, *et al.* Effects of oral nicorandil therapy on sympathetic nerve activity and cardiac events in patients with chronic heart failure: subanalysis of our previous report using propensity score matching. *Eur J Nucl Med Mol Imaging* 2014; **41**:144–154.
- Kasama S, Toyama T, Sumino H, Kumakura H, Takayama Y, Ichikawa S, *et al.* Long-term nicorandil therapy improves cardiac sympathetic nerve activity after reperfusion therapy in patients with first acute myocardial infarction. *J Nucl Med* 2007; **48**:1676–1682.
- Dilsizian V, Rocco TP, Freedman NM, Leon MB, Bonow RO. Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. *N Engl J Med* 1990; **323**:141–146.
- Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution ²⁰¹Tl imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. *Circulation* 1993; **87**:1630–1641.
- Opie LH, Owen P, Riemersma RA. Relative rates of oxidation of glucose and free fatty acids by ischaemic and non-ischaemic myocardium after coronary artery ligation in the dog. *Eur J Clin Invest* 1973; **3**:419–435.
- Schelbert HR, Henze E, Schon HR, Keen R, Hansen H, Selin C, *et al.* C-11 palmitate for the noninvasive evaluation of regional myocardial fatty acid metabolism with positron computed tomography. III. In vivo demonstration of the effects of substrate availability on myocardial metabolism. *Am Heart J* 1983; **105**:492–504.
- Knapp FF Jr, Ambrose KR, Goodman MM. New radioiodinated methyl-branched fatty acids for cardiac studies. *Eur J Nucl Med* 1986; **12**:S39–S44.
- Tamaki N, Tadamura E, Kawamoto M, Magata Y, Yonekura Y, Fujibayashi Y, *et al.* Decreased uptake of iodinated branched fatty acid analog indicates metabolic alterations in ischemic myocardium. *J Nucl Med* 1995; **36**:1974–1980.
- Nakata T, Hashimoto A, Kobayashi H, Miyamoto K, Tsuchihashi K, Miura T, Shimamoto K. Outcome significance of thallium-201 and iodine-123-BMIPP perfusion-metabolism mismatch in preinfarction angina. *J Nucl Med* 1998; **39**:1492–1499.
- Taki J, Nakajima K, Matsunari I, Bunko H, Takata S, Kawasuji M, Tonami N. Assessment of improvement of myocardial fatty acid uptake and function after revascularization using iodine-123-BMIPP. *J Nucl Med* 1997; **38**:1503–1510.
- Matsunari I, Saga T, Taki J, Akashi Y, Hirai J, Wakasugi T, *et al.* Improved myocardial fatty acid utilization after percutaneous transluminal coronary angioplasty. *J Nucl Med* 1995; **36**:1605–1607.
- Feola M, Biggi A, Chauvie S, Vado A, Leonardi G, Rolfo F, Ribichini F. Myocardial scar and insulin resistance predict cardiovascular events in severe ischaemic myocardial dysfunction: a perfusion-metabolism positron emission tomography study. *Nucl Med Commun* 2008; **29**:448–454.
- Lautamäki R, Schuleri KH, Sasano T, Javadi MS, Youssef A, Merrill J, *et al.* Integration of infarct size, tissue perfusion, and metabolism by hybrid cardiac positron emission tomography/computed tomography: evaluation in a porcine model of myocardial infarction. *Circ Cardiovasc Imaging* 2009; **2**:299–305.
- Toyama T, Hoshizaki H, Seki R, Isobe N, Adachi H, Naito S, *et al.* Evaluation of salvaged myocardium after acute myocardial infarction using single photon emission computed tomography after ²⁰¹Tl-glucose-insulin infusion. *Circ J* 2004; **68**:348–354.
- Peluffo RD, Berlin JR. Electrogenic K⁺ transport by the Na⁽⁺⁾-K⁺ pump in rat cardiac ventricular myocytes. *J Physiol* 1997; **501**:33–40.
- Abdulla J, Barlera S, Latini R, Kjoller-Hansen L, Sogaard P, Christensen E, *et al.* A systematic review: effect of angiotensin converting enzyme inhibition on left ventricular volumes and ejection fraction in patients with a myocardial infarction and in patients with left ventricular dysfunction. *Eur J Heart Fail* 2007; **9**:129–135.
- Gandhi PS, Goyal RK, Jain AR, Mallya BS, Gupta VM, Shah DS, *et al.* Beneficial effects of carvedilol as a concomitant therapy to angiotensin-converting enzyme inhibitor in patients with ischemic left ventricular systolic dysfunction. *Can J Physiol Pharmacol* 2007; **85**:193–199.
- Culver CM, Dworkin HJ. Comparison of personnel radiation dosimetry from myocardial perfusion scintigraphy: technetium-99m-sestamibi versus thallium-201. *J Nucl Med* 1993; **34**:1210–1213.
- Takeishi Y, Sukekawa H, Fujiwara S, Ikeno E, Sasaki Y, Tomoike H. Reverse redistribution of technetium-99m-sestamibi following direct PTCA in acute myocardial infarction. *J Nucl Med* 1996; **37**:1289–1294.