

Prediction of myocardial viability in the chronic phase in patients with acute myocardial infarction using simultaneous dual-isotope imaging with ^{99m}Tc -sestamibi/ ^{123}I -BMIPP SPECT and a cadmium-zinc-telluride camera system

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Abstract

Background : To assess myocardial perfusion and fatty acid metabolism in patients with acute myocardial infarction (AMI), a cadmium-zinc-telluride (CZT) camera system was recently introduced to allow simultaneous dual-isotope single-photon emission computed tomography (SPECT) with ^{99m}Tc -sestamibi/ ^{123}I -BMIPP. The objective of this study was to determine the optimal cutoff value for %uptake of ^{99m}Tc -sestamibi/ ^{123}I -BMIPP dual SPECT in patients with AMI to predict myocardial viability in the chronic phase.

Methods : We evaluated 42 consecutive patients with AMI who underwent both dual-SPECT in the acute phase and stress myocardial SPECT using ^{99m}Tc -tracers in the chronic phase using a CZT camera. The presence of myocardial viability was defined as regional %uptake $\geq 50\%$ on ^{99m}Tc SPECT at rest in the chronic phase.

Results : The cutoff values for the prediction of viable myocardium were %uptake $\geq 47\%$ for ^{99m}Tc -sestamibi and %uptake $\geq 31\%$ for ^{123}I -BMIPP in left anterior descending (LAD) territory and %uptake $\geq 52\%$ for ^{99m}Tc -sestamibi and %uptake $\geq 48\%$ for ^{123}I -BMIPP in non-LAD territory. The respective sensitivities, specificities, and accuracies for myocardial viability prediction were 96%, 88%, and 94% for ^{99m}Tc -sestamibi and 92%, 83%, and 90% for ^{123}I -BMIPP in LAD territory and 86%, 84%, and 85% for ^{99m}Tc -sestamibi and 84%, 89%, and 85% for ^{123}I -BMIPP in non-LAD territory.

Conclusions : These results suggest that both ^{99m}Tc -sestamibi and ^{123}I -BMIPP SPECT may predict myocardial viability in the chronic phase. However, it should be noted that the optimal cutoff values for regional %uptake in the acute phase may differ for the LAD territory and non-LAD coronary territory in the prediction of myocardial viability.

Introduction

Recently, a cadmium-zinc-telluride (CZT) camera system has been introduced for the assessment of myocardial perfusion and fatty acid metabolism in patients with acute myocardial infarction (AMI) to allow simultaneous dual-isotope imaging with ^{99m}Tc -tracer/beta-methyl-p-(123I)-iodophenyl-pentadecanoic acid

(^{123}I -BMIPP), which has less radiation exposure than ^{201}Tl / ^{123}I -BMIPP dual single-photon emission computed tomography (SPECT)^{1,2)}.

Myocardial perfusion SPECT is widely used for the diagnosis of infarct areas and the evaluation of myocardial viability in patients with AMI^{3,4)}. In Japan and Europe, ^{123}I -BMIPP SPECT is also used in clinical practice in conjunction with myocardial perfusion SPECT to

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assess stunned or infarcted myocardium after percutaneous coronary intervention (PCI)^{5,6)}.

Although the presence of myocardial viability on SPECT is often defined when %uptake of the left ventricle (LV) is $\geq 50\%$ ⁷⁾, there have only been a few reports regarding cutoff values for the %uptake of ^{99m}Tc-sestamibi/¹²³I-BMIPP dual SPECT in patients with AMI for the prediction of myocardial viability in the chronic phase. In this study, we determined the optimal cutoff value of %uptake of dual SPECT in both left anterior descending (LAD) and non-LAD territories in 42 patients with AMI for the prediction of myocardial viability in the chronic phase.

Materials and Methods

Study patients

We evaluated 42 consecutive patients with AMI who underwent dual SPECT after successful primary PCI with drug-eluting stents (DES) in the acute phase and stress myocardial SPECT using ^{99m}Tc-tracers was performed in the chronic phase between October 2016 and October 2020. AMI was defined according to the universal definition of myocardial infarction⁸⁾. The PCI was performed by expert interventional cardiologists. Written informed consent for invasive coronary angiography was obtained from all participants. This study was approved by the Ethics Committee of Tokyo Medical University (T2019-0116).

^{99m}Tc-sestamibi/¹²³I-BMIPP dual SPECT

Dual SPECT was performed 9 ± 6 days after AMI following successful PCI. Initially, 370 MBq of ^{99m}Tc-sestamibi was injected. Forty minutes later, 111 MBq of ¹²³I-BMIPP was injected. Twenty minutes later, simultaneous dual SPECT was performed using a high-speed CZT camera (Discovery NM 530c; GE Healthcare, Haifa, Israel)⁹⁾. The Discovery NM 530c is equipped with a multiple-pinhole collimator and 19 stationary CZT detectors that simultaneously focus on the heart to maximize the efficiency of SPECT images. The CZT pixels are 2.46×2.46 mm in size, and each detector contains 32×32 -pixel 5-mm-thick elements. Energy windows were set at $140.5 \text{ keV} - 8.0\%$ for the lower limit and $140.5 \text{ keV} + 4.0\%$ for the upper limit for ^{99m}Tc-sestamibi and at $159 \text{ keV} - 6.0\%$ for the lower limit and $159 \text{ keV} + 10.0\%$ for the upper limit for ¹²³I-BMIPP. Image acquisition was performed with the patients in a supine position for 8 minutes and a prone position for 6 minutes. We used SPECT images in the supine position. SPECT images were reconstructed on a workstation (Xeleris; GE Healthcare) using an iterative algorithm with integrated collimator geometric modeling. A Butterworth filter (order 15; cutoff frequency, 0.28 cycles/cm) was applied to the reconstructed slices. No scatter or attenuation corrections were applied.

Stress myocardial ^{99m}Tc SPECT protocol in chronic phase

Stress myocardial SPECT with low dose (stress 185 MBq/rest 370 MBq) ^{99m}Tc-tracers (^{99m}Tc-tetrofosmin 35/^{99m}Tc-sestamibi 7) was performed 12 ± 3 months after AMI. Exercise stress was assessed in 26 patients using a symptom-limited multistep exercise with a bicycle ergometer. Sixteen patients underwent ^{99m}Tc-tracer SPECT with adenosine triphosphate (ATP) loading. The image acquisition protocol was similar for both exercise stress and ATP loading, as previously described¹⁰⁾.

Assessment of %uptake of the regional left ventricle

Regional %uptake of LV in 242 infarct regions was obtained using the QPS software (Cedars-Sinai, Los Angeles, CA, USA) with a 17-segment model¹¹⁻¹²⁾. According to a previously reported method, each QPS image was divided into 17 segments, with segments 1-2, 7-8, 13-14, and 17 (blue squares) corresponding to the areas perfused by the LAD, segments 3-4, 9-10, and 15 (pink squares) corresponding to the areas perfused by the right coronary artery (RCA), and segments 5-6, 11-12, and 16 (yellow squares) corresponding to the areas perfused by the left circumflex coronary artery (LCX)¹¹⁾ (Fig. 1). The presence of myocardial viability was defined as regional %uptake $\geq 50\%$ in stress ^{99m}Tc-tracer SPECT at rest in the chronic phase⁷⁾.

Statistical analysis

For statistical analysis, continuous values are expressed as mean \pm standard deviation. A paired t-test was used to compare the changes in %uptake of the LV for ^{99m}Tc-tracer at rest between the acute and chronic phases. A p value of <0.05 was considered statistically significant.

To predict %uptake $\geq 50\%$ in each corresponding

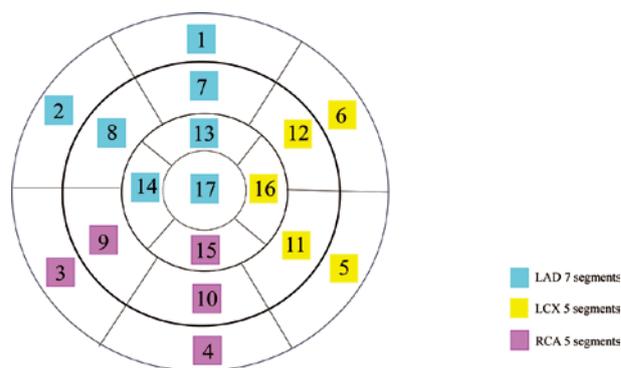


Fig. 1 QPS image with the 17-segment model of the left ventricle.

Segments 1-2, 7-8, 13-14, and 17 correspond to areas perfused by the left anterior descending coronary artery (blue square). Segments 3-4, 9-10, and 15 correspond to areas perfused by the right coronary artery (pink square). Segments 5-6, 11-12, and 16 correspond to areas perfused by the left circumflex coronary artery (yellow square)

infarct segment of the LV in the chronic phase, we performed receiver operating characteristic (ROC) curve analysis to determine the optimal cutoff values for the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP in the acute phase in LAD and non-LAD territories. Using these cutoff points, sensitivities, specificities, and accuracies for the prediction of %uptake ≥ 50% in each infarct segment of the LV in the chronic phase were obtained. Statistical computations were performed using SPSS (version 26.0; SPSS Inc., Chicago, IL, USA) and MedCalc v20.106 (MedCalc Software, Mariakerke, Belgium).

Results

Patient characteristics

Patients consisted of 38 men and 4 women with a mean age of 67 ± 11 years. ST-elevation myocardial infarction (STEMI) was observed in 33 patients, while non-STEMI was observed in the remaining 9. The infarct-related coronary artery was located most frequently in the RCA (*n* = 20, 48%), followed by the LAD (*n* = 16, 38%) and the LCX (*n* = 6, 14%). The peak serum creatine phosphokinase level (mean ± SD) was 1,946 ± 1,877 U/l. Seven patients had prior myocardial infarction with different infarct-related coronary arteries (Table 1).

Regional %uptake of dual SPECT in the LAD territory

In 112 infarct segments in the LAD territory, regional

%uptake of ^{99m}Tc-sestamibi SPECT, ¹²³I-BMIPP SPECT in the acute phase, and stress ^{99m}Tc-tracer SPECT at rest in the chronic phase were 62 ± 20%, 53 ± 23%, and 65 ± 19%, respectively. The regional %uptake of ^{99m}Tc-tracer increased significantly from the acute phase to the chronic phase (62 ± 20% vs. 65 ± 19%; *p* < 0.001).

Regional %uptake of dual SPECT in the non-LAD territory

In 130 infarct segments for non-LAD territory, regional %uptake of ^{99m}Tc-sestamibi SPECT, ¹²³I-BMIPP SPECT in the acute phase, and stress ^{99m}Tc-tracer SPECT at rest in the chronic phase were 60 ± 17%, 54 ± 18%, and 59 ± 15%, respectively. The regional %uptake of ^{99m}Tc-tracer did not change from the acute phase to the chronic phase (60 ± 17% vs. 59 ± 15%; *p* = NS).

Cutoff points for %uptake of dual SPECT and diagnostic value to predict myocardial viability in the LAD territory

In the LAD territory (16 patients, 112 segments), ROC curve analysis demonstrated that the cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP in the acute phase were ≥ 47% and ≥ 31%, respectively. The sensitivity, specificity, and accuracy in the prediction of myocardial viability were 96%, 88%, and 94% with ^{99m}Tc-sestamibi and 92%, 83%, and 90% with ¹²³I-BMIPP, respectively. There was a significant difference between the area under the ROC curve (AUC) of ^{99m}Tc-sestamibi and ¹²³I-BMIPP (0.951 vs. 0.924; *p* = 0.0372) (Fig. 2a).

Cutoff points for %uptake of dual SPECT and diagnostic value to predict myocardial viability in the non-LAD territory

In the non-LAD territory (26 patients, 130 segments), ROC curve analysis also demonstrated that the cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP in the acute phase were ≥ 52% and ≥ 48%, respectively. The sensitivity, specificity, and accuracy in the prediction of myocardial viability were 86%, 84%, and 85%, respectively, with ^{99m}Tc-sestamibi and 84%, 89%, and 85% with ¹²³I-BMIPP, respectively. There was no significant difference between the AUC of ^{99m}Tc-sestamibi and ¹²³I-BMIPP (0.919 vs. 0.926; *p* = 0.7178) (Fig. 2b).

Discussion

To the best of our knowledge, the present study is the first to determine the optimal cutoff value for the %uptake of ^{99m}Tc-sestamibi/¹²³I-BMIPP dual SPECT using a CZT system in patients with AMI to predict myocardial viability in the chronic phase. The principal findings of the present study can be summarized as follows: (1) ^{99m}Tc-sestamibi and ¹²³I-BMIPP SPECT in the acute phase had high diagnostic values for predicting the presence of myocardial viability in the chronic phase; (2) For the prediction of myocardial viability in

Table 1 Patient characteristics

Age (years)	67±11
Sex (male/female)	38/4 (90%/10%)
Risk factors	
Hypertension	27 (64%)
Diabetes mellitus	17 (40%)
Hyperlipidemia	20 (48%)
Current smoking	17 (40%)
Prior PCI	7 (17%)
Prior myocardial infarction	7 (17%)
STEMI/non-STEMI	33/9 (79%/21%)
Successful PCI	42 (100%)
Peak CPK (U/L)	1,946±1,877
<i>Infarcted related coronary artery</i>	
LAD	16 (38%)
LCX	6 (14%)
RCA	20 (48%)
Time to dual SPECT study (days)	8.5±6.7
Time to follow up stress MPI (months)	12.0±2.7

CPK, creatinine phosphokinase; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; MPI, myocardial perfusion imaging; PCI, percutaneous coronary intervention; RCA, right coronary artery; SPECT, single-photon emission computed tomography; STEMI, ST-elevation myocardial infarction.

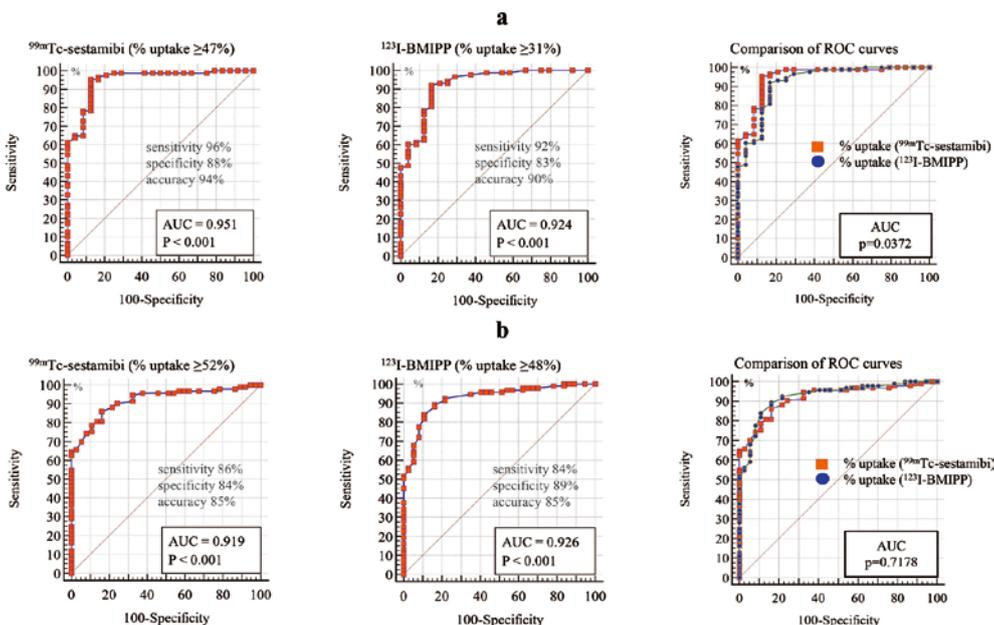


Fig. 2 a. The cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP for prediction of viable myocardium in the LAD territory (16 cases, 112 segments)
 b. The cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP for prediction of viable myocardium in the non-LAD territory (26 cases, 130 segments)

In the LAD territory, the cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP were $\geq 47\%$ and $\geq 31\%$, respectively. In the non-LAD territory, the cutoff values of the %uptake of ^{99m}Tc-sestamibi and ¹²³I-BMIPP were $\geq 52\%$ and $\geq 48\%$, respectively. There are differences of cutoff values between LAD and non-LAD territories.

¹²³I-BMIPP : beta-methyl-p-(123I)-iodophenyl-pentadecanoic acid ; LAD : left anterior descending coronary artery

the chronic phase using ^{99m}Tc-sestamibi/¹²³I-BMIPP dual SPECT in patients with AMI using a CZT camera, the optimal cutoff values of %uptake might differ between LAD and non-LAD territories.

Prediction of myocardial viability in patients with AMI using SPECT

To assess myocardial viability in patients with AMI, quantification of ^{99m}Tc-sestamibi or ¹²³I-BMIPP uptake was seldom used ; instead, visual interpretation, such as either perfusion/¹²³I-BMIPP mismatch⁵⁾⁶⁾¹³⁾ or reverse redistribution in resting perfusion scintigraphy¹⁴⁾, was employed. Ueda et al.¹³⁾ performed ^{99m}Tc-tetrofosmin/¹²³I-BMIPP dual SPECT after revascularization in AMI using a conventional Anger camera and evaluated the viability of the infarct area approximately six months later by the degree of wall motion improvement by resting ^{99m}Tc-tetrofosmin SPECT using a quantitative gated SPECT program. Myocardial viability in the chronic phase was predicted by assessing mismatched ^{99m}Tc-tetrofosmin/¹²³I-BMIPP uptake in the acute phase. A sensitivity of 90% and specificity of 72% were observed. In the present study, ^{99m}Tc-sestamibi SPECT predicted myocardial viability in the chronic phase with a sensitivity and specificity of 96% and 88% for LAD territory and 86% and 84% for non-LAD territory, respectively, with comparable diagnostic accuracy.

Quantification of tracer uptake according to coronary artery territory for predicting myocardial viability

Previously, in patients with AMI in the acute phase, few studies using quantification of either perfusion tracer or ¹²³I-BMIPP uptake at rest have been performed to predict myocardial viability in the chronic phase. To assess the viable myocardium in the chronic phase, Schneider et al¹⁵⁾ demonstrated that using an infarct location-adjusted optimal ^{99m}Tc-sestamibi threshold ($\geq 50\%$ for anterior infarcts, $\geq 35\%$ for inferior infarcts) with old myocardial infarction, the positive predictive value was 90%, the negative predictive value was 91%, and the diagnostic accuracy was 90% for the improvement of left ventricular function after successful coronary revascularization.

In the present study, for both ^{99m}Tc-sestamibi and ¹²³I-BMIPP, the optimal thresholds for predicting myocardial viability in the non-LAD territory ($\geq 52\%$ for ^{99m}Tc-sestamibi and $\geq 48\%$ for ¹²³I-BMIPP) were higher than those in the LAD territory ($\geq 47\%$ for ^{99m}Tc-sestamibi and $\geq 31\%$ for ¹²³I-BMIPP). There was a significant difference between the AUC of ^{99m}Tc-sestamibi and ¹²³I-BMIPP (0.951 vs. 0.924 ; $p = 0.0372$) in LAD territories, but there was no significant difference between the AUC of ^{99m}Tc-sestamibi and ¹²³I-BMIPP (0.919 vs. 0.926 ; $p = 0.7178$) in non-LAD territories.

The less reliable predictive value of the optimal tracer threshold in the non-LAD territory compared to that in the LAD territory was speculated to be due to the particularity of the cardiac SPECT camera (Discovery NM530c) and our SPECT protocol. Discovery NM530c was reported to be more sensitive to the presence of extracardiac activity, such as hepatic and bowel isotope activity, compared with the standard Anger camera. Consequently, reduced ^{99m}Tc tracer uptake in the inferior wall is likely to be observed⁹⁾. Nishiyama et al.¹⁶⁾ found that extracardiac activity was significantly less frequently observed in SPECT images using Discovery NM530c acquired in the prone position than in the supine position. In our study protocol, we could not use SPECT images acquired in the prone position to evaluate the inferior segments because prone-SPECT imaging at rest for stress SPECT was not performed in the chronic phase.

Limitations

This study has several limitations. First, the current study was performed retrospectively in a single institution and included a small number of patients. Therefore, we have not been able to assess wall motion improvement in the chronic phase in terms of assessing myocardial viability and a prospective approach including multiple centers and large patient groups is necessary. Second, the optimal cutoff values for %uptake of dual SPECT in predicting myocardial viability were not assessed per individual coronary territory because of the limited number of patients with AMI in the LCX territory ($n = 6$). Third, not all patients were examined by coronary angiography or coronary computed tomographic angiography in the chronic phase for assessing the coronary diameter upon stent implantation in the acute phase. Stress myocardial SPECT in the chronic phase did not show ischemic findings in the infarct territory in all patients, and the use of new-generation DES has been reported to reduce the incidence of in-stent restenosis to rates ranging from 5 to 10%¹⁷⁾. Finally, although nitrate administration is known to improve the diagnostic accuracy of ^{99m}Tc-sestamibi SPECT in detecting viable myocardium, it was not administered to the patients in this study.

Conclusion

In ^{99m}Tc-sestamibi/¹²³I-BMIPP dual SPECT using a CZT camera in patients with AMI, our findings suggest that both ^{99m}Tc-sestamibi and ¹²³I-BMIPP SPECT may be able to predict the presence of myocardial viability in the chronic phase. However, it should be noted that the optimal cutoff values for regional %uptake in the acute phase may differ for the LAD and non-LAD coronary territory in predicting myocardial viability.

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None.

Conflicts of interest

None.

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心筋梗塞急性期のテルル化亜鉛カドミウムカメラを用いた 安静 2 核種 ^{99m}Tc -sestamibi/ ^{123}I -BMIPP 同時収集 SPECT による慢性期心筋生存性の予測

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【要旨】 【はじめに】 近年、急性心筋梗塞患者の心筋血流と脂肪酸代謝の評価において、テルル化亜鉛カドミウム (CZT) カメラによる安静時 2 核種同時 ^{99m}Tc -sestamibi/ ^{123}I -BMIPP SPECT (dual SPECT) が使用可能になった。本研究の目的は急性心筋梗塞患者の慢性期心筋生存性を予測する ^{99m}Tc -sestamibi、 ^{123}I -BMIPP の 2 核種同時 SPECT の至適閾値を決めることである。

【方法】 対象は急性心筋梗塞急性期に CZT カメラで dual SPECT を施行し、慢性期に負荷 ^{99m}Tc 製剤で心筋 SPECT を施行した患者 42 例である。慢性期の安静時 ^{99m}Tc SPECT での %uptake 50% 以上を心筋生存性ありとした。

【結果】 慢性期の心筋生存性を予測する至適閾値は左前下行枝 (LAD) 領域では ^{99m}Tc -sestamibi は %uptake 47% 以上、 ^{123}I -BMIPP は %uptake 31% 以上、一方 non-LAD 領域では ^{99m}Tc -sestamibi は %uptake 52% 以上、 ^{123}I -BMIPP は %uptake 48% 以上であった。心筋生存性を予測する各々の感度、特異度、正診率は、LAD 領域では ^{99m}Tc -sestamibi は 96%、88%、94%、 ^{123}I -BMIPP は 92%、83%、90%、また non-LAD 領域では ^{99m}Tc -sestamibi は 86%、84%、85%、 ^{123}I -BMIPP は 84%、89%、85% であった。

【結論】 CZT カメラによる心筋梗塞急性期の dual SPECT は ^{99m}Tc -sestamibi だけでなく、 ^{123}I -BMIPP から慢性期の心筋生存性を予測できるが、LAD 領域と non-LAD 領域で閾値が異なることが示唆された。

〈キーワード〉 安静時 2 核種同時 ^{99m}Tc -sestamibi/ ^{123}I -BMIPP SPECT、急性心筋梗塞、心筋生存性
