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Left-ventricular dyssynchrony evaluated by TI-201 gated SPECT myocardial perfusion imaging: a comparison with Tc-99m sestamibi

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Abstract

Background and purpose—Phase analysis of gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has been validated as a reliable tool to assess left-ventricular (LV) mechanical dyssynchrony. The initial results were all confirmed from studies using technetium-99m (Tc-99m) sestamibi or tetrofosmin as the radiotracers. The purpose of this study was to evaluate the feasibility of phase analysis in thallium-201 (TI-201) gated SPECT MPI.

Materials and methods—Seventeen patients referred from a cardiology clinic for evaluation of coronary artery disease were studied. All patients underwent both TI-201 and Tc-99m sestamibi gated SPECT MPI within 1 week. An additional 34 patients with TI-201 gated SPECT and 22 patients with Tc-99m sestamibi gated SPECT, who had a low likelihood of coronary artery disease, normal LV function, and normal perfusion on MPI, were used as normal controls. LV dyssynchrony parameters, including phase standard deviation (PSD) and phase histogram bandwidth (PHB), were measured using a standard phase analysis tool and compared between TI-201 and Tc-99m sestamibi images.

Results—The LV dyssynchrony parameters correlated well ($r=0.93$ for PSD and $r=0.84$ for PHB) between TI-201 and Tc-99m sestamibi images. The dyssynchrony parameters of TI-201 were significantly larger than those of Tc-99m sestamibi (PSD: 24.5 ± 12.0 vs. 17.4 ± 9.7 , $P < 0.001$; PHB: 74.7 ± 35.5 vs. 50.6 ± 25.0 , $P < 0.001$). In comparison with normal controls, TI-201 and Tc-99m sestamibi images showed concordant results.

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Conflicts of interest

Dr Ji Chen receives royalties from the sale of Emory Cardiac Toolbox with SyncTool. For the remaining authors there are no conflicts of interest.

Conclusion—LV dyssynchrony parameters correlated well between Tl-201 and Tc-99m sestamibi images, even though the values were significantly larger for Tl-201 than for Tc-99m sestamibi. Tl-201 images showed results similar to those of Tc-99m sestamibi in the diagnosis of LV dyssynchrony.

Keywords

dyssynchrony; gated SPECT; phase analysis; thallium-201

Introduction

Phase analysis has been developed for measuring left-ventricular (LV) dyssynchrony from gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) [1]. It was shown that quantitative indices given by phase analysis, such as phase standard deviation (PSD) and phase histogram band-width (PHB), correlated well with LV dyssynchrony measured by tissue Doppler imaging [2–4]. Most importantly, these indices have been shown to predict response to cardiac resynchronization therapy in patients suffering from heart failure [5]. Recently, these indices have also been shown to be associated with increased risk for cardiac death and appropriate implantable cardiac defibrillator shocks in heart failure patients [6]. As the phase analysis technique can be applied to conventional gated SPECT MPI data with a high degree of reproducibility [7] and repeatability [8], it is rapidly becoming a standard, widespread nuclear cardiology tool in coronary artery disease (CAD), heart failure, and cardiac electrophysiology.

All of the above studies were carried out using technetium-99m (Tc-99m) sestamibi or tetrofosmin as the radiotracer. However, the majority of gated SPECT MPI studies are conducted using thallium-201 (Tl-201) in Taiwan. Although previous studies had showed that LV function parameters such as LV ejection fraction, end-systolic volume, and end-diastolic volume can be accurately measured from Tl-201 gated SPECT MPI [9–11], there is no study to show that the phase analysis technique can be applied accurately to Tl-201 gated SPECT MPI data to measure LV dyssynchrony. The purpose of this study was to assess LV dyssynchrony parameters (PSD and PHB) measured by phase analysis of resting Tl-201 gated SPECT MPI and compare the results with resting Tc-99m sestamibi gated SPECT MPI in patients with suspected or known CAD.

Materials and methods

Patient population

Seventeen consecutive patients, who had suspected or known CAD and were referred for dipyridamole–stress/rest gated Tl-201 SPECT MPI for diagnosis and/or risk stratification, were enrolled as the study group. Additional individuals, including 34 with Tl-201 SPECT and 22 with Tc-99m sestamibi SPECT, were enrolled as the normal control group. These individuals had a low likelihood of CAD, normal LV function, no heart failure symptoms, no ECG abnormalities, and normal perfusion images on MPI. The study protocol was approved by the Institutional Review Board of Show Chwan Memorial Hospital.

Gated SPECT and phase analysis

For stress/rest Tl-201 gated SPECT MPI, patients fasted for at least 4 h and were asked to abstain from caffeine-containing foods, beverages, and medications containing methylxanthine for 24 h. Dipyridamole was administered intravenously at a rate of 0.14 mg/kg/min for 4 min. 111MBq of Tl-201 was then injected 3 min after the end of the dipyridamole infusion. Stress and rest acquisitions started 5–10 min and 4 h after Tl-201 injection. A dual-head gamma camera (symbia-T2; Siemens Medical Solutions, Hoffman

Estate, Illinois, USA) equipped with a low-energy/high-resolution collimator was used. Thirty-two projections, with 50 s of data collection per projection, were obtained over a 180° arc extending from the 45° right anterior oblique to the 45° left posterior oblique position. A 20% window was centered over the 72 and 167 keV Tl-201 photopeaks. The acquisition was synchronized with ECG with an acceptance window of an *R–R* variability of 100%, and each projection was divided into 8 images/cardiac cycle. The projection images were acquired into 64×64 matrices with a 1.45 acquisition zoom. In the study group, the patients were scheduled for rest Tc-99m sestamibi gated SPECT MPI within 1 week after Tl-201 scanning.

For rest Tc-99m sestamibi scanning, patients were injected with 20 mCi of Tc-99m sestamibi. A standard resting Tc-99m gated SPECT MPI protocol (8 frames/cycle, 64 projections over 180°, 25 s per projection) was used to scan the patients at about 1 h after injection.

The perfusion images of stress and rest Tl-201 SPECT MPI were displayed in short-axis, vertical long-axis, and horizontal long-axis views. The left ventricle was divided into 20 segments and all segments were scored using a five-point scale (0=normal, 1=mildly reduced, 2=moderately reduced, 3=severely reduced, and 4=absent uptake). The summed stress score (SSS) and summed rest score (SRS) were obtained by the sum of the scores of 20 segments in stress and rest images. The summed difference score (SDS) was defined as the difference of SSS and SRS. An SSS less than 4 was considered normal [12].

The gated SPECT MPI data, for both Tl-201 and Tc-99m sestamibi, were reconstructed by filtered back projection with a Butterworth filter (order 10 and cutoff frequency 0.5 cycle/pixel). The reconstructed gated short-axis images were analyzed using an Emory Cardiac Toolbox (ECTb) equipped with SyncTool (Syntermed, Atlanta, Georgia, USA), and the parameters of LV dyssynchrony, PSD, and PHB were calculated.

Statistical analysis

Continuous variables were expressed as mean±SD and noncontinuous variables as frequency and percentage. Global dyssynchrony (PSD and PHB) were compared between rest Tl-201 and rest Tc-99m sestamibi images using a paired *t*-test and Pearson's correlation analysis. A *P* value less than 0.05 was considered significant.

Results

A total of 17 patients (age: 42–72 years; mean±SD: 62±7.2) including 14 men and three women were enrolled as the study group. The perfusion images of stress–rest Tl-201 SPECT MPI revealed normal results in seven patients. The other 10 patients were considered abnormal, with SSS, SRS, and SDS of 14.2±9.6, 6.8±6.9, and 7.4±5.2, respectively (mean ±SD).

Correlation and difference in LV dyssynchrony on using Tl-201 and Tc-99m SPECT

Among the 17 patients, 14 had normal LV function and three had heart failure. The average LV ejection fraction was 64.6±11.7% (mean±SD).

As shown in Fig. 1, the parameters of LV dyssynchrony, PSD, and PHB correlated well between resting Tl-201 SPECT and resting Tc-99m sestamibi SPECT (*r*=0.95 for PSD and *r*=0.85 for PHB). The dyssynchrony parameters of resting Tl-201 SPECT were significantly larger than those of resting Tc-99m sestamibi SPECT (PSD: 24.7±12.4 vs. 16.9±9.8, *P*<0.001; PHB: 74.5±36.5 vs. 49.7±25.4, *P*=0.002), yielding a slope of ~1.20 for both PSD and PHB.

Diagnosis of LV dyssynchrony by Tl-201 and Tc-99m SPECT

The normal limits for defining LV dyssynchrony were obtained from 34 normal individuals undergoing resting Tl-201 SPECT and from 22 normal individuals undergoing Tc-99m sestamibi SPECT. The average values of LV dyssynchrony parameters from Tl-201 SPECT were 19.0 ± 4.2 (mean $\pm$ SD) for PSD and 57.4 ± 11.5 for PHB. Using mean plus 2 SD as the cutoff values, the abnormal values for resting Tl-201 SPECT were 27.4 for PSD and 80.4 for PHB. The average values of LV dyssynchrony parameters from Tc-99m SPECT were 10.3 ± 2.5 for PSD and 33.5 ± 7.8 for PHB. Using mean plus 2SD as the cutoff values, the abnormal values for resting Tc-99m sestamibi SPECT were 15.4 for PSD and 49.2 for PHB. Compared with the normal limits, Tl-201 and Tc-99m sestamibi images showed concordant results in 16 of 17 patients (94%) with respect to the diagnosis of LV dyssynchrony with PSD (Table 1) and in 14 of 17 patients (82%) with PHB (Table 2).

Discussion

This is the first study to correlate LV dyssynchrony parameters measured by phase analysis of Tl-201 gated SPECT MPI with those of Tc-99m sestamibi. It showed that the LV dyssynchrony parameters correlated well between Tl-201 and Tc-99m sestamibi images. It is important to note that the LV dyssynchrony parameters were significantly larger when measured by Tl-201 gated SPECT MPI than by Tc-99m sestamibi. Resting Tl-201 SPECT images contained fewer counts compared with resting Tc-99m SPECT images; therefore, they had higher noises, resulting in larger dyssynchrony parameters. Although our results suggested that the LV dyssynchrony parameters were not interchangeable between Tl-201 and Tc-99m sestamibi, the diagnosis of LV dyssynchrony defined by the corresponding normal limits seemed to be similar for the two tracers. In our study, the concordance rates were 94 and 82% for PSD and PHB criteria, respectively.

Compared with Tc-99m-labeled tracers, Tl-201 has different physical characteristics – for example, attenuation and scatter. Nevertheless, the impact of attenuation or scatter on the accuracy of phase analysis has been shown to be nonsignificant in a previous study [13], wherein the LV dyssynchrony parameters calculated from gated SPECT images reconstructed without and with attenuation correction or scatter compensation were not significantly different. Tl-201 has different levels of extracardiac activities compared with Tc-99m tracers, which may introduce different interferences on adjacent myocardial regions in the reconstructed image because of filtered back projection reconstruction. In the previous study [13], the LV dyssynchrony parameters calculated from gated SPECT images reconstructed by filtered back projection and iterative reconstruction were not significantly different. Thus, the different levels of extracardiac activity between Tl-201 and Tc-99m would not significantly affect the comparison of the LV dyssynchrony parameters in this study.

Some drawbacks of Tl-201 as compared with Tc-99m tracers include longer half-life and limited injection dose with higher radiation burden to the patient. However, Tl-201 remains the most widely used tracer for MPI in many developed or developing Asian countries, including Taiwan, because it requires only a single injection for stress/rest protocols with the ability to assess myocardial viability when necessary. Other reasons that make the tracer favorable are lower cost, lower radiation burden to nuclear medicine personnel, and less physical interference of scatter from the adjacent liver and bowel. In addition, gated SPECT acquisition using Tl-201 was performed much earlier than acquisition using Tc-99m tracers after stress (5 min vs. 1 h) and has the advantage of being able to assess the early poststress function and a greater chance of detecting stress-induced functional changes [12,14,15]. Recently, we also found that stress-induced myocardial ischemia was associated with early

poststress LV mechanical dyssynchrony as assessed by phase analysis of Tl-201 gated SPECT MPI [16], which could not be demonstrated with Tc-99m sestamibi imaging [17].

The major limitation of our study is the relatively small sample size. However, our results from the prospectively enrolled, consecutive 17 patients have shown good correlations between the two tracers for both PSD and PHB, supporting the feasibility of phase analysis using Tl-201 gated SPECT images. These preliminary data should be confirmed in a larger patient population.

Conclusion

The LV dyssynchrony parameters correlated well between Tl-201 and Tc-99m sestamibi images, even though the values were significantly larger with Tl-201 than with Tc-99m sestamibi. These two kinds of images revealed similar results in the diagnosis of LV dyssynchrony. Further study may be warranted to investigate the value of Tl-201 gated SPECT MPI in the guidance of cardiac resynchronization therapy.

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Fig 1.

The correlations of left-ventricular dyssynchrony, as represented by phase standard deviation (a) and phase histogram bandwidth (b), between Tl-201 and Tc-99m MIBI SPECT MPI. MIBI, Tc-99m sestamibi; MPI, myocardial perfusion imaging; SPECT, single-photon emission computed tomography; Tc-99m, technetium-99m; Tl-201, thallium-201.

Table 1

Left-ventricular dyssynchrony defined by phase standard deviation

	MIBI normal	MIBI abnormal
Tl-201 abnormal	0	6
Tl-201 normal	10	1

MIBI, Tc-99m sestamibi; Tc-99m, technetium-99m; Tl-201, thallium-201.

Table 2

Left-ventricular dyssynchrony defined by phase histogram bandwidth (PHB)

	MIBI normal	MIBI abnormal
Tl-201 abnormal	1	4
Tl-201 normal	10	2

MIBI, Tc-99m sestamibi; Tc-99m, technetium-99m; Tl-201, thallium-201.