심근 기능 측정에 사용된 게이트 심근 관류 SPECT 방법의 재현성 평가: ^{201}Tl과 ^{99m}Tc-MIBI 게이트 SPECT의 비교

인하대학교병원, 핵의학과, 심장내과[1]

현인영 · 서정기[1] · 홍의수[1] · 김대혁[1] · 김성은 · 권 준[1] · 박금수[1] · 최원식 · 이우형[1]

Reproducibility of Gated Myocardial Perfusion SPECT for the Assessment of Myocardial Function: Comparison with Thallium-201 and Technetium-99m-MIBI

In Young Hyun, M.D., **Jeong Kee Seo**, M.D.,[1] **Eui Soo Hong**, M.D.,[1] **Dae Hyuk Kim**, M.D.,[1] **Sung Eun Kim**, M.D., **Jun Kwan**, M.D.,[1] **Keum Soo Park**, M.D.,[1] **Wonsick Choe**, M.D. and **Woo Hyung Lee**, M.D.[1]

Department of Nuclear Medicine and Internal Medicine,[1] Inha University College of Medicine, Incheon, Korea

Abstract

Purpose: We compared the reproducibility of ^{201}Tl and ^{99m}Tc-sestamibi (MIBI) gated SPECT measurement of myocardial function using the Germano algorithm. **Materials and Methods:** Gated SPECT acquisition was repeated in the same position in 30 patients who received ^{201}Tl and in 26 who received ^{99m}Tc-MIBI. The quantification of end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF) on ^{201}Tl and ^{99m}Tc-MIBI gated SPECT was processed independently using Cedars quantitative gated SPECT software. The reproducibility of the assessment of myocardial function on ^{201}Tl gated SPECT was compared with that of ^{99m}Tc-MIBI gated SPECT. **Results:** Correlation between the two measurements for volumes and EF was excellent by the repeated gated SPECT studies of ^{201}Tl ($r=0.928$ to 0.986; $p<0.05$) and ^{99m}Tc-MIBI ($r=0.979$ to 0.997; $p<0.05$). However, Bland Altman analysis revealed the 95% limits of agreement (2 SD) for volumes and EF were tighter by repeated ^{99m}Tc-MIBI gated SPECT (EDV: 14.1 ml, ESV: 9.4 ml and EF: 5.5%) than by repeated ^{201}Tl gated SPECT (EDV: 24.1 ml, ESV: 18.6 ml and EF: 10.3%). The root mean square (RMS) values of the coefficient of variation (CV) for volumes and EFs were smaller by repeated ^{99m}Tc-MIBI gated SPECT (EDV: 2.1 ml, ESV: 2.7 ml and EF: 2.3%) than by repeated ^{201}Tl gated SPECT (EDV: 3.2 ml, ESV: 3.5 ml and EF: 5.2%). **Conclusion:** ^{99m}Tc-MIBI provides more reproducible volumes and EF than ^{201}Tl on repeated acquisition gated SPECT. ^{99m}Tc-MIBI gated SPECT is the preferable method for the clinical monitoring of myocardial function. **(Korean J Nucl Med 2000;34:381-92)**

Key Words: Reproducibility, Gated SPECT, ^{201}Thallium, ^{99m}Tc-MIBI

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Corresponding Author: In Young, Hyun, M.D., Department of Nuclear Medicine, Inha University Hospital, 7-206 Shinheung-Dong, Jung-Gu, Incheon, 400-103, Korea,
Tel: 82-32-890-3171, Fax: 82-32-890-3164,
E-mail: iyhyun@inha.ac.kr

Introduction

Germano et al.[1] developed an automatic algorithm for ECG-gated SPECT to assess myocardial

function. It is well accepted that left ventricular cavity volume and the ejection fraction can be accurately measured by ^{99m}Tc-MIBI gated SPECT.[2-7] Also, the accuracy of ^{201}Tl gated SPECT for the assessment of volumes and ejection fraction is highly comparable with that of other studies, such as first-pass radionuclide angiography,[8,9] gated blood pool scan,[10] ^{99m}Tc-MIBI gated SPECT,[11-13] echocardiography,[14] and three-dimensional magnetic resonance imaging.[15]

The confidence with which the methods can be used depends upon their reproducibility as well as their accuracy. Moreover, we need accurate and reproducible methods for the assessment of clinical outcome. The reproducibility of the assessment of myocardial function was excellent by repeated acquisitions of ^{99m}Tc-MIBI gated SPECT in the same patients at the same status.[16,17] However, the reproducibility of ^{201}Tl gated SPECT for the assessment of myocardial function has not been thoroughly investigated.

In this study, we investigated the reproducibility of serial ^{201}Tl and ^{99m}Tc-MIBI gated SPECT for two groups that received either of the two tracers, ^{201}Tl or ^{99m}Tc-MIBI. And, we compared the reproducibility of ^{201}Tl and ^{99m}Tc-MIBI gated SPECT measurement of myocardial function using Germano algorithm.

Materials and Methods

1. Patient Selection

Patients referred for routine rest ^{201}Tl/dipyridamole ^{99m}Tc-MIBI stress SPECT to assess myocardial perfusion, and viability between May and December 1999 were enrolled in this study. Patients from May to August were included in the ^{201}Tl group, and patients from September to December in the ^{99m}Tc-MIBI group.

In the randomly selected ^{201}Tl group of 34 patients, sequential acquisitions of ^{201}Tl gated SPECT were performed repeatedly in same position. In the randomly selected ^{99m}Tc-MIBI group of 31 patients, sequential acquisitions of ^{99m}Tc-MIBI gated SPECT were performed repeatedly in same position.

2. Gated SPECT Imaging Protocol

In the Tl group, rest ^{201}Tl gated SPECT acquisition was initiated ten minutes after the injection of 111∼148 MBq (3∼4 mCi) of ^{201}Tl with the patient at rest. Repeated ^{201}Tl gated SPECT acquisition was sequentially performed in situ in the same position. In the ^{99m}Tc-MIBI group, stress ^{99m}Tc-MIBI gated SPECT acquisition was initiated one hour after injection of 1,110 MBq (30 mCi) of ^{99m}Tc-MIBI at peak dipyridamole stress (0.56 mg/kg for 4 min). Repeated ^{99m}Tc-MIBI gated SPECT acquisition was sequentially performed in situ in the same position.

Image acquisition was performed with a triple-detector gamma camera (MultiSPECT3: Siemens, Ohio, USA) with the cardio 90 collimators, and an electronic zoom of 1.45 provided a pixel size of 4.91 mm. Sixty projections were obtained from the left posterior oblique to the right anterior oblique over 180°, with an acquisition time of 30 sec (^{201}Tl), or 15 sec (^{99m}Tc-MIBI) for each projection, which resulted in a total acquisition time of approximately 18 min (^{201}Tl), or 9 min (^{99m}Tc-MIBI). For gating, a 64×64 pixel matrix with eight frames per cardiac cycle with a pre-fixed RR interval and a 35% window were used. The projection data was reconstructed using a Butterworth filter (order=5 and cutoff frequency=0.35 cycles/pixel for the ^{201}Tl images, order=5 and cutoff frequency of 0.40 cycles/pixel for the ^{99m}Tc-MIBI images).

3. Calculation of Volumes, EF and Reproducibility

EDV, ESV, and EF by gated SPECT were calculated by an independent operator using Cedars Quantitative Gated SPECT software. The same indices were obtained with the same images, regardless of whether they were ^{201}Tl or ^{99m}Tc-MIBI gated SPECT images. EF was not calculated in patients whose ESV was less than 30 ml on ^{201}Tl and ^{99m}Tc-MIBI gated SPECT.[15]

Bland Altman analysis and correlation analysis were performed. The coefficients of variation (CV) of repeated sequential ^{201}Tl and ^{99m}Tc-MIBI gated SPECT were calculated by dividing the SD by the mean of the two values. The root mean square (RMS) value of these CVs was calculated and used to represent reproducibility.

The RMS mean of CVs, Bland Altman analysis, and the correlation analysis of volumes and EF were performed in the same manner for the repeated sequential studies of ^{201}Tl and ^{99m}Tc-MIBI gated SPECT.

4. Statistical Analysis

Differences between volumes and EFs of measurements made by repeated ^{201}Tl and ^{99m}Tc-MIBI gated SPECT were evaluated using the paired t-test. Correlation of volumes and EFs between measurements made by repeated ^{201}Tl and ^{99m}Tc-MIBI gated SPECT were evaluated using Pearsons r value.

Bland Altman analysis[18,19] was used to test for bias and to determine the value of 2SD of repeated gated SPECT with ^{201}Tl and ^{99m}Tc-MIBI. We used MedCalc (MedCalc, Belgium) software to perform and display the Bland Altman analysis.

Results

1. Demographic Data

In a total number of 34 cases of ^{201}Tl gated SPECT, the QGS program succeeded in automatic edge detection and to calculate the volumes and EF. Thirty patients were analyzed for volumes and EFs on two repeated ^{201}Tl gated SPECTs, except for four patients whose ESVs were less than 30 ml.

In 29 of a total of 31 cases examined by ^{99m}Tc-MIBI gated SPECT, the QGS program succeeded in automatic edge detection. One failure was found in an AMI patient with severe and extensive defect in inferior wall and apex. The other failure was caused by the presence of gall bladder uptake with low myocardial counting statistics. Twenty-six patients were analyzed for volumes and EFs on repeated ^{99m}Tc-MIBI gated SPECT, except for three patients whose ESVs were less than 30 ml.

There was no significant difference between clinical characteristics of the ^{201}Tl group and the ^{99m}Tc-MIBI group patients ($p>0.05$) (Table 1).

2. Reproducibility of the Measurement of Myocardial Function between the Two Sequential ^{201}Tl Gated SPECTs

The first EDV ranged from 60−282 (120±52) ml, and the second from 68−288 (122±57) ml. The first ESV ranged from 31−240 (75±51) ml, and the second from 33-237 (78±54) ml. The first EF ranged from 15−66 (41±14)%, and the second from 14−63 (40±14)%. No statistical differences were found between repeated ^{201}Tl gated SPECTs in terms of volumes and EF.

The correlation for the volumes and EF was excellent between the repeated ^{201}Tl gated SPECTs ($r=0.928$ to 0.986; $p<0.05$) (Fig. 1A, B, and C).

Table 1. Demographic Subjects

	Group		
	^{201}Tl	^{99m}Tc-MIBI	p value
Total no. of subjects	30	26	
Sex			
Male	22 (73%)	17 (65%)	ns
Female	8 (27%)	9 (35%)	ns
Age (yr)	55±17	61±15	ns
Diabetes Mellitus	6 (20%)	8 (31%)	ns
History of MI	15 (50%)	13 (50%)	ns
Coronary artery disease	14 (47%)	15 (58%)	ns
Defect extent (% of LV)	19±22	19±18	ns

Bland Altman nalysis of this group showed no evidence of any asymmetric bias between the two ^{201}Tl gated SPECTs. On the Bland Altman plot, the 2 SD was 24.1 ml, 18.6 ml and 10.3% for the EDV, ESV, and EF (Fig. 2, A, B, and C) respectively. The RMS value of the CVs was 3.2 ml, 3.5 ml and 5.2% for the EDV, ESV, and EF respectively.

3. Reproducibility of the Measurement of Myocardial Function between Two Sequential ^{99m}Tc-MIBI Gated SPECTs

The first EDV ranged from 71−349 (136±68) ml, and the second from 71−341 (137±68) ml. The first ESV ranged from 31−276 (84±58) ml, and the second from 30−273 (84±60) ml. The first EF ranged from 18−67 (42±13)%, and the second from 19−67 (42±13)%. No statistical difference was found between repeated ^{99m}Tc-MIBI gated SPECTs in terms of volumes and EFs.

The correlation for the left ventricular volume and EF was excellent between the repeated ^{99m}Tc-MIBI gated SPECTs (r=0.979 to 0.997; $p<0.05$) (Fig. 3A, B, and C). Bland Altman analysis of this group showed no evidence of any asymmetric bias between the two ^{99m}Tc-MIBI gated SPECT results. On the Bland Altman plot, 2 SD was 14.1 ml, 9.4 ml, and 5.5% for EDV, ESV, and EF respectively (Fig. 4, A, B, and C). The RMS value of the CVs was 2.1 ml, 2.7 ml, and 2.3% for EDV, ESV, and EF respectively.

4. Comparison of Reproducibility between two Sequential ^{201}Tl Gated SPECTs and Two Sequential ^{99m}Tc-MIBI gated SPECTs

There was no statistical difference between ^{201}Tl and ^{99m}Tc-MIBI gated SPECTs in terms of volumes and EFs ($p>0.05$).

On the Bland Altman plot, the 95% limits of agreement (2 SD) for volumes and EFs between repeated ^{99m}Tc-MIBI gated SPECTs were tighter than the volumes and EFs between repeated ^{201}Tl gated SPECTs. The RMS values of the CVs between repeated sequential ^{99m}Tc-MIBI gated SPECTs for volumes and EFs were smaller than the corresponding volumes and EFs between repeated ^{201}Tl gated SPECTs.

Discussion

There are many different indications for the assessment of myocardial function in clinical

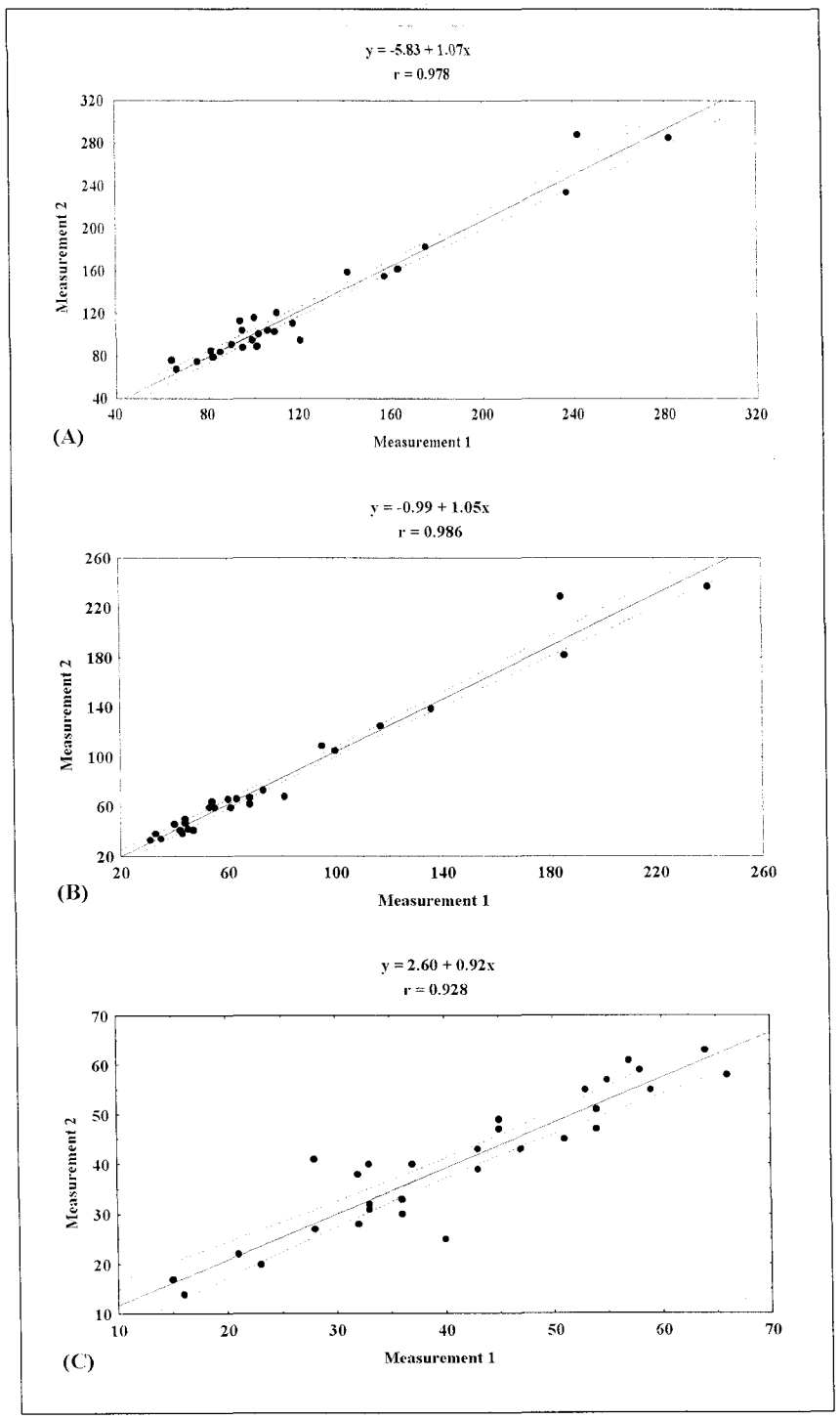

Fig. 1. Scatter plots are shown for (A) end-diastolic volume, (B) end-systolic volume, and (C) ejection fraction obtained by sequential imaging of ^{201}Tl gated perfusion SPECT.

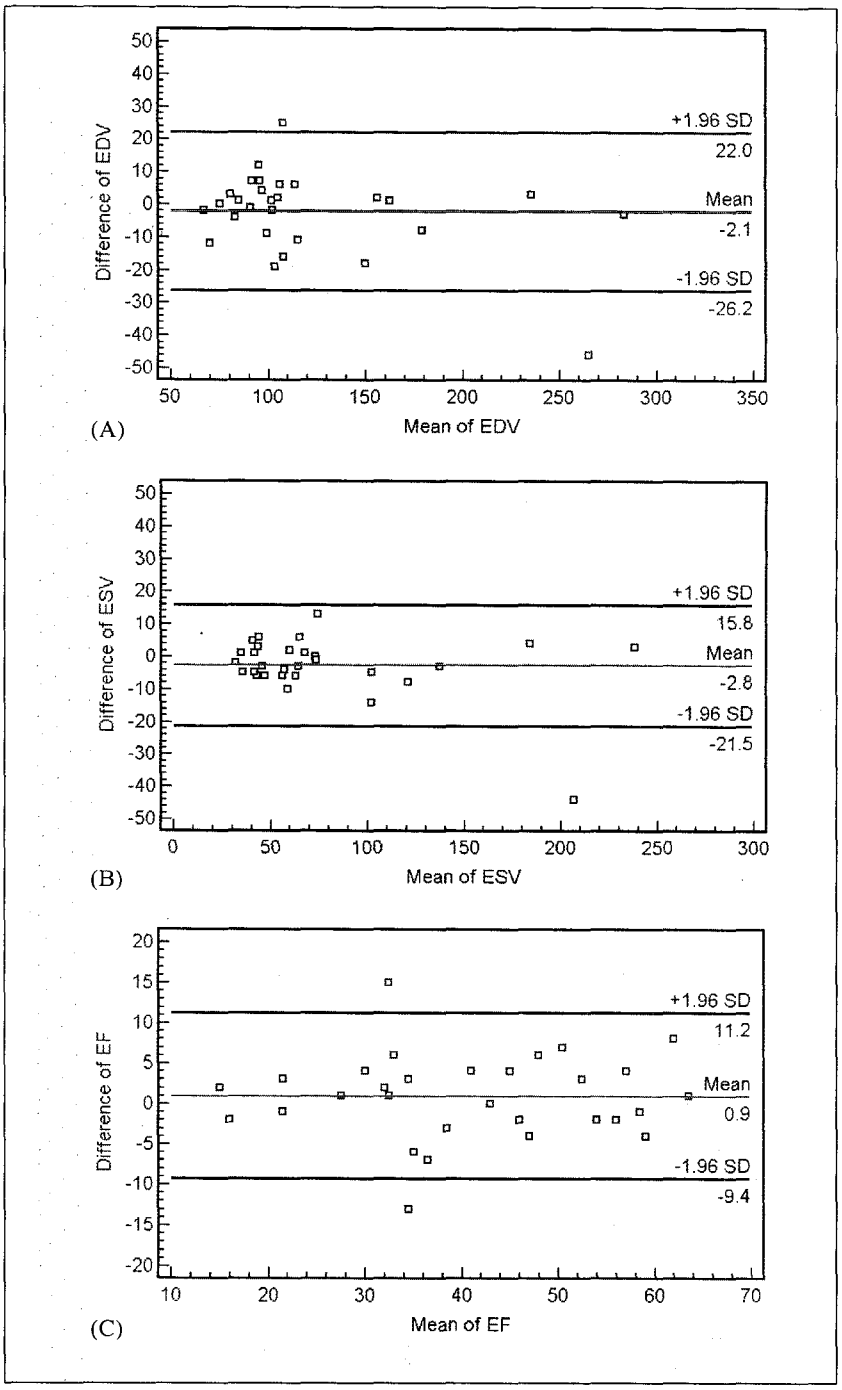

Fig. 2. Bland Altman analysis is shown for (A) end-diastolic volume, (B) end-systolic volume, and (C) ejection fraction obtained by sequential imaging of ^{201}Tl gated perfusion SPECT. The horizontal axis indicates the mean of the parameters obtained from two measurements, the vertical axis indicates the difference between the two measurements, and the upper and lower margins indicate 2 SD of the differences, and the 95% limits of agreement.

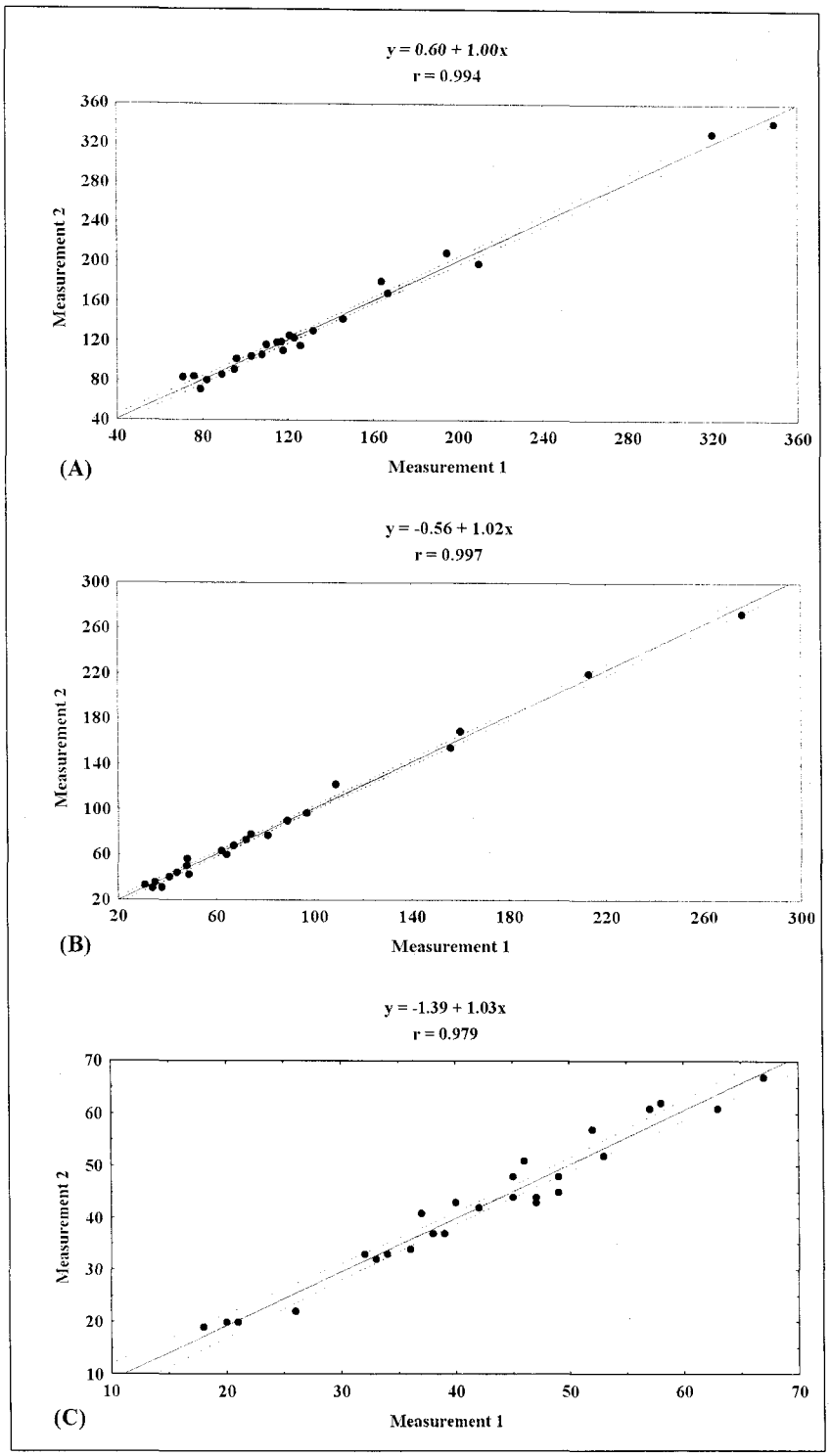

Fig. 3. Scatter plots are shown for (A) end-diastolic volume, (B) end-systolic volume, and (C) ejection fraction obtained by sequential imaging of ^{99m}Tc-MIBI gated perfusion SPECT.

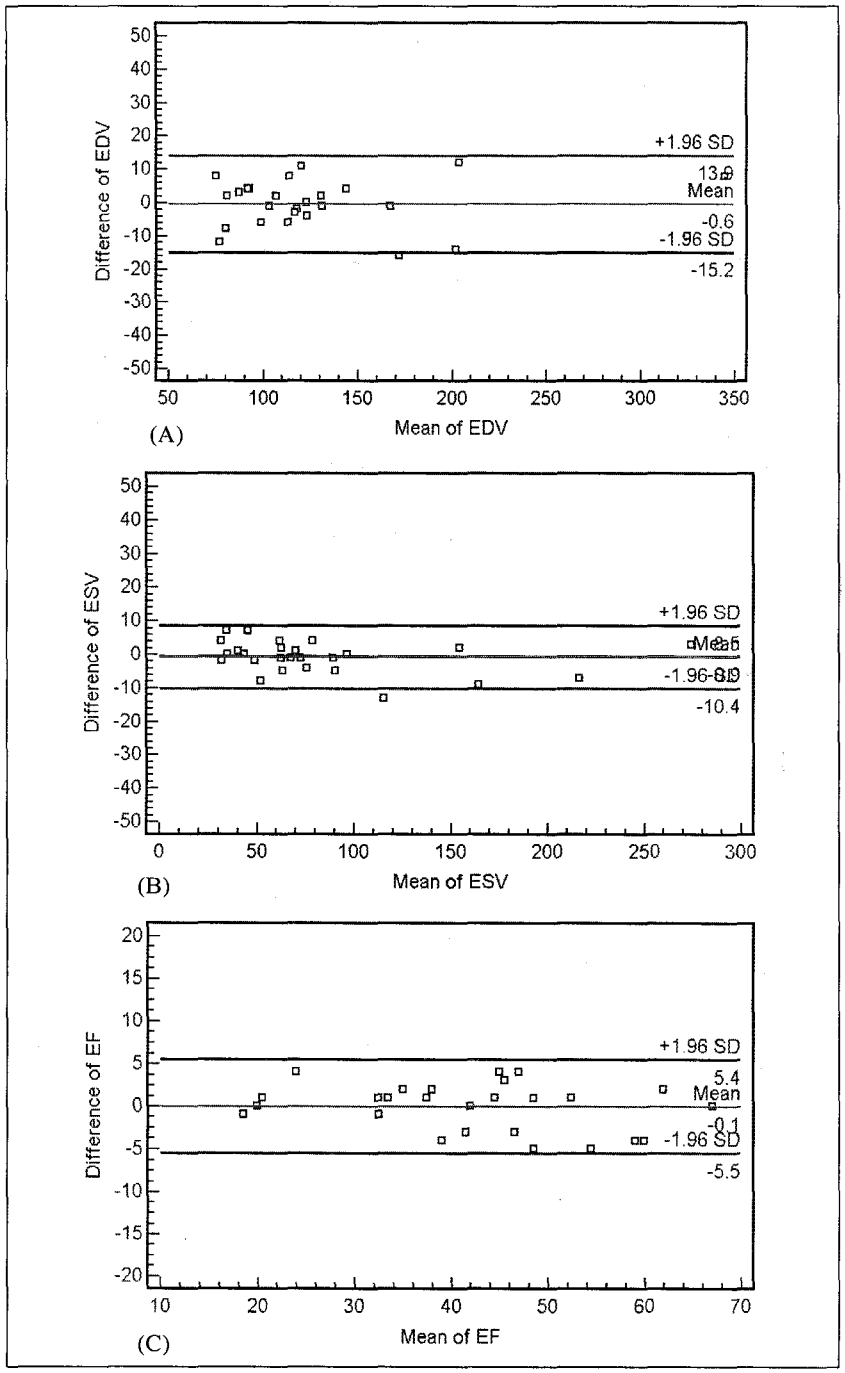

Fig. 4. Bland Altman analysis is shown for (A) end-diastolic volume, (B) end-systolic volume, and (C) ejection fraction obtained by sequential imaging of ^{99m}Tc-MIBI gated perfusion SPECT. The horizontal axis indicates the mean of the parameters obtained from two measurements, the vertical axis indicates the difference between the two measurements, and the upper and lower margins indicate 2 SD of the differences, and the 95% limits of agreement.

practice, and different requirements for levels of accuracy and reproducibility. In terms of accuracy, both ^{201}Tl and ^{99m}Tc-MIBI gated SPECT are satisfactory for the assessment of myocardial function. In view of reproducibility, Lee et al.[16] and Johnson et al.[17] reported ^{99m}Tc-MIBI gated SPECT was a method with excellent reproducibility. However, data is scant on the reproducibility of ^{201}Tl gated SPECT for the assessment of myocardial function.

Our results demonstrate that an excellent correlation exists between two sequential gated SPECTs with ^{201}Tl and ^{99m}Tc-MIBI. However, scatter plots showed that volumes and EF values on two repeated ^{99m}Tc-MIBI gated SPECTs were closer to regression line with 95% confidence than on two repeated ^{201}Tl gated SPECTs. On Bland-Altman analysis, there was no evidence of any asymmetric bias between these two sequential gated SPECT with either ^{201}Tl or ^{99m}Tc-MIBI. However, the reproducibility between two sequential gated SPECTs for volumes and EF assessed by 95% limits of agreement and the RMS values of the CVs was better with ^{99m}Tc-MIBI than ^{201}Tl. Tadamura et al.[15] reported that volumes and EF values estimated by reinjection ^{201}Tl or ^{99m}Tc-MIBI gated SPECT in combination with Germanos algorithm correlated and agreed well with those obtained by three-dimensional MRI, whereas ^{99m}Tc-MIBI gated SPECT provided more stable and accurate values of left ventricular performance with a shorter acquisition time. Lee et al.[20] recently reported that the estimates of volumes and EF made by ^{201}Tl gated SPECT were less reproducible than those of ^{99m}Tc-MIBI gated SPECT and suggested that the poorer reproducibility of ^{201}Tl gated SPECT was due to its lower count.

Patients with myocardial dysfunction present a quite different situation to those with normal myocardial function. Monitoring myocardial function with a more accurate and reproducible method may over time add confidence to clinical decisions in patients with myocardial dysfunction. Because indices of global left ventricular function, such as EF and ESV, are important prognostic indicators in patients with ischemic left ventricular dysfunction, functional recovery after revascularization of treatment for myocardial viability is also defined on an individual patient basis.[21] Moreover, the poorer reproducibility of ^{201}Tl gated SPECT is a limitation to the accurate monitoring of myocardial function for the purposes of assessing clinical outcome. And so, the estimates of volumes and EF made by ^{201}Tl gated SPECT are not interchangeable with those of gated ^{99m}Tc-MIBI SPECT in terms of monitoring myocardial function.

Recently, Vallejo et al.[24] showed that correlation of EF between repeated ^{99m}Tc-MIBI gated SPECT was poor after low-dose injection and it was fair after high-dose injection. Also, correlation was poor in the presence of significant background activity. In this study, correlation of EF was excellent between repeated ^{99m}Tc-MIBI gated SPECT. We suggest that repeated acquisitions one hour after high-dose injection in this study protocol result in satisfactorial reproducibility of QGS with ^{99m}Tc-MIBI

Although the acquisition time of ^{201}Tl gated SPECT was twice that for ^{99m}Tc-MIBI gated SPECT in this study, ^{201}Tl gated SPECT had poorer reproducibility than ^{99m}Tc-MIBI gated SPECT. Thus, a longer acquisition time is the another limitation of ^{201}Tl gated SPECT. Therefore, ^{201}Tl gated SPECT imaging may not be feasible in severely ill patients or busy laboratories.

Germano et al.[11] described a small artifactual increase in ^{201}Tl left ventricular EFs for left ventricular EFs >60, in the case of smaller left

ventricular cavity volume, and suggested it is not likely to be clinically significant. However, Mazzanti et al.[22] and Case et al.[23] reported that the automated algorithm tends to an underestimation of the ventricular volume when the chamber size is extremely small. In Tadamura's study,[15] patients whose ESVs was less than 30 ml were not included. In the current study, a 64×64 pixel matrix with an electronic zoom of 1.45 provided a pixel size of 4.91 mm. However, we observed four patients whose ESVs was less than 30 ml by ^{201}Tl and three by ^{99m}Tc-MIBI gated SPECT. In these patients whose ESVs was less than 30 ml, we met five patients with an artifactual increase in EFs >60. Moreover, three patients whose ESVs ≤10 ml showed EF >70. Therefore, some corrections may be required for accurate volume measurements of small ventricles. In future study, we plan to use the appropriate electronic zoom to increase the size of the heart for such patients.[11]

The present study shows that ^{99m}Tc-MIBI provides more reproducible volumes and EF than ^{201}Tl by repeated sequential gated SPECT. If an accurate objective monitoring of myocardial function is required for clinical outcome, ^{99m}Tc-MIBI gated SPECT is a suitable method, but in our opinion ^{201}Tl gated SPECT is not sufficiently reproducible for this purpose. It is important to decide upon the objectives of the measurement of myocardial function and choose appropriate radiotracers, ^{201}Tl, or ^{99m}Tc-MIBI for gated SPECT accordingly.

요 약

목적: Cedars 소프트웨어를 이용한 게이트 SPECT에서 ^{201}Tl와 ^{99m}Tc-MIBI 게이트 SPECT 두 방법으로 측정한 좌심실 부피와 구혈률의 재현성을 비교하였다. **대상 및 방법**: 휴식 ^{201}Tl/부하 ^{99m}Tc-MIBI 심근 관류 SPECT를 촬영한 환자 중에서 무작위로 추출된 30명은 같은 자리에서 휴식 ^{201}Tl 게이트 SPECT를, 26명은 부하 후 ^{99m}Tc-MIBI 게이트 SPECT를 한번 더 촬영하였다. Cedars 소프트웨어를 이용하여 연속해 측정된 좌심실 부피와 구혈률에 대하여 표준편차의 기하학적 평균과 Bland Altman 도표를 이용한 방법으로 ^{201}Tl과 ^{99m}Tc-MIBI 게이트 SPECT 방법의 재현성을 각각 평가하여 비교하였다. **결과**: 연속 촬영한 ^{99m}Tc-MIBI 게이트 SPECT로 얻은 확장기말 부피와 수축기말 부피, 구혈률에 대한 Bland Altman 도해의 2 표준편차에 상당하는 범위는 14.1 ml, 9.4 ml, 5.5%로 연속 촬영한 ^{201}Tl 게이트 SPECT로 얻은 24.1 ml, 18.6 ml, 10.3%보다 좁았다. 또한, 연속 촬영한 ^{99m}Tc-MIBI 게이트 SPECT로 얻은 확장기말 부피와 수축기말 부피, 구혈률에 대한 표준편차의 기하학적 평균은 2.1 ml, 2.7 ml, 2.3%로 연속 촬영한 ^{201}Tl 게이트 SPECT로 얻은 3.2 ml, 3.5 ml, 5.2%보다 작았다. **결론**: 같은 환자를 같은 위치에서 두 번 연속하여 촬영한 게이트 SPECT로 평가한 심근 기능의 재현성은 ^{99m}Tc-MIBI게이트 SPECT 방법에서 더 우수하였다. 그러므로, 기간별 변동과 약제의 효과를 보기 위한 좌심실 부피와 구혈률 측정에서 ^{201}Tl보다는 ^{99m}Tc-MIBI 게이트 SPECT 방법을 선택하는 것이 더 좋을 것으로 생각된다.

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