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# Left ventricular mass index measured by quantitative gated myocardial SPECT with <sup>99m</sup>Tc-tetrofosmin: a comparison with echocardiography

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**Objective:** Left ventricular mass is an important determinant of diagnosis and prognosis in patients with heart disease. The aim of the present study was to validate measurement of the left ventricular mass index (LVMI) by quantitative gated myocardial SPECT (QGS) with 99mTc-tetrofosmin by comparing it with echocardiography. Methods: QGS and M-mode echocardiography (Echo) were performed within one month of each other in 179 patients. M-mode echocardiography was carried out according to Devereux's method. QGS images were acquired one hour after injection of <sup>99m</sup>Tctetrofosmin at rest. Myocardial volume was defined as the volume between the endocardial and epicardial surface in the end-diastolic phase. LVMI (g/m<sup>2</sup>) was defined as myocardial volume divided by myocardial specific density and corrected for body surface area. QGS LVMI measurements were performed twice by the same observer and independently by two different observers. Regional hypoperfusion in the group of patients with old myocardial infarction (n = 26) was evaluated semiquantitatively on the basis of the total defect score on the resting 99mTc-tetrofosmin SPECT images. Results: Among the patients as a whole QGS LVMI was significantly correlated with Echo LVMI (r = 0.96, p < 0.001). Intra-observer and inter-observer analyses showed significant reproducibility (r = 0.99 and r = 0.98, respectively, p < 0.001). In the patients with old myocardial infarction, but QGS LVMI was significantly lower than Echo LVMI (p < 0.001), and the magnitude of the underestimation was closely related to the severity of the perfusion defect on the resting SPECT images. Conclusions: Measurements of LVMI by 99mTc-tetrofosmin QGS are reproducible and consistent with echocardiograpic estimates. Underestimation in patients with severe perfusion defects must be taken into consideration.

**Key words:** left ventricular mass, quantitative gated myocardial SPECT, <sup>99m</sup>Tc-tetrofosmin, M-mode echocardiography, perfusion

# **INTRODUCTION**

LEFT VENTRICULAR MASS is an important determinant of diagnosis and prognosis in patients with left ventricular

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hypertrophy (LVH) or coronary heart disease.<sup>1–3</sup> Patients with LVH are at high risk of subsequent cardiovascular morbidity and mortality.<sup>4</sup> The results of the 'Framingham Heart Study' demonstrated significantly increased rates of cardiac events and death in middle-aged patients with electrocardiographically<sup>5,6</sup> or echocadiographically determined LVH.<sup>2</sup> Angiotensin-converting enzyme inhibitors and beta-adrenergic blocking agents may reduce the left ventricular mass in patients with congestive heart failure<sup>7</sup> and survivors of acute myocardial infarction.<sup>8</sup> Assessment of left ventricular mass is critical to the management of hypertensive patients, particularly when

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the effect of antihypertensive drugs is being monitored.

A number of imaging techniques have been developed to measure the left ventricular mass. Ungated computed tomography (CT)<sup>9,10</sup> and ultra fast CT<sup>11</sup> utilize contrast agents that may induce a variety of side effects in some patients. Angiographic evaluation of left ventricular mass is an invasive technique,<sup>12</sup> and electrocardiographic (ECG) estimation of LVH is convenient but qualitative.<sup>13</sup> Echocardiaography is the most widely used means of measuring left ventricular mass in clinical practice, but it samples only a diastolic dimension measured by the Mmode of a long-axis view of the left ventricle and may be inaccurate in some myocardial infarction patients because of deformity of the cardiac chamber. Good-quality echocardiograhic recordings are sometimes difficult to acquire in patients with pulmonary disease or obesity. When breath-hold magnetic resonance imaging (MRI), which is an established method for estimating left ventricular mass is used,<sup>14</sup> several factors, including myocardial blood content and fat signals, affect the accuracy of mass determination. It has recently become possible to perform real-time MRI without ECG triggering or breath holding, but this method has been reported to underestimate the left ventricular mass, and the presence of fatty epicardial or paracardial fringes may make it difficult to identify the edge of the epicardium.<sup>15</sup> MRI cannot be used in patients with metalic implants, for example, coronary stents or artificial joints.

Electrocardiography-gated myocardial single-photon emission computed tomography (SPECT) has recently come to be widely used for non-invasive assessment of regional myocardial perfusion and left ventricular function, and several studies have shown that it can be used to measure the left ventricular ejection fraction and cavity volume by means of automatic-processing software for gated perfusion SPECT (quantitative gated SPECT [QGS], version 2; Cedars-Sinai Medical Center, Los Angeles, CA).<sup>16–18</sup> In contrast to CT, MRI and the echocardiogram, QGS mainly estimates the volume of perfusable tissue. Accurate estimation of the left ventricular mass by OGS depends on setting the myocardial border, the tracers used, and the methods of ECG gating, and it is important to compare the QGS-determined left ventricular mass with the left ventricular mass estimated by other methods in various types of heart diseases.

The goal of this study was to validate the QGS as a method for quantifying the left ventricular mass and to clarify its clinical feasibility and usefulness in patients with heart disease.

#### **METHODS**

#### Patient population

We studied 179 patients with suspected of heart disease, 113 men and 66 women, age  $59 \pm 13$  years, referred to Osaka University Hospital. The patients were subdivided into 6 groups: a control group, an ischemic heart disease group, an old myocardial infarction group, a dilated cardiomyopathy group, a hypertrophic cardiomyopathy, and a hypertensive heart disease group. Each group had the following characteristics. The control group (n = 74,34 men and 40 women) had normal systemic blood pressure, normal 99mTc-tetrofosmin SPECT images at rest and exercise, normal echocardiograms and ECGs within normal limits. The ischemic heart disease group (n = 39, 32 men and 7 women), defined as patients having more than 75% stenosis of a major coronary artery confirmed by coronary angiography and normal 99mTctetrofosmin SPECT images at rest but local hypoperfusion during exercise. The old myocardial infarction group (MI, n = 26, 20 men and 6 women) had a past history of myocardial infarction and exhibited a perfusion defect or hypoperfusion area on 99mTc-tetrofosmin SPECT images at rest. The dilated cardiomyopathy group (DCM, n = 10, 8 men and 2 women) had DCM diagnosed by the absence of significant coronary artery disease and the absence of specific heart muscle disease and the absence of active myocarditis confirmed by endomyocardial biopsy. The hypertrophic cardiomyopathy group had HCM (HCM, n = 10, 8 men and 2 women) diagnosed by the echocardiographic finding of left ventricular wall thickening of unknown origin. The hypertensive heart disease (HHD, n = 20, 10 men and 10 women) group had essential hypertension with a mean seated systolic blood pressure in the 140 to 200 mmHg range and diastolic pressure in the 95 to 115 mmHg range and had normal perfusion SPECT images. All patients in the present study had sinus rhythm and a heart rate of  $76 \pm 13$  beats/min, ranging from 51 to 96 beats/min.

# *Left ventricular mass index estimated by echocardiography (Echo)*

We measured the following parameters on the M-mode echocardiogram: left ventricular diastolic dimension (LVDd, cm), interventricular septum thickness (IVS, cm), and left ventricular posterior wall thickness (LVPW, cm). The echocardiograms were performed in accordance with the Penn convention.<sup>19</sup> LV mass was calculated according to Devereux's formula<sup>19</sup>:

left ventricular mass (g)  
= 
$$1.04 \times [(LVDd + IVS + LVPW)^3 - (LVDd)^3]$$
  
- 13.6,

where 1.04 (g/cm<sup>3</sup>) is the specific gravity of the myocardium. The measurements were obtained at the peak of the R wave on the ECG. The left ventricular mass index (LVMI, g/m<sup>2</sup>) was defined as left ventricular mass divided by body surface area (m<sup>2</sup>).

Left ventricular mass index estimated by SPECT at rest Gated SPECT images were acquired with a triple-detector gamma camera (GCA 9300A/HG; Toshiba Medical Co., Tokyo, Japan) equipped with a low-energy general-purpose collimator. One hour after injection of 370-740 MBq (10-20 mCi) 99mTc-tetrofosmin at rest, 20 projection images were acquired for 90 sec each in 6° increments over 120° and were stored in a 64 × 64 matrix. Ten ECGgated frames per cardiac cycle were acquired at each projection angle. The projection datasets were prefiltered with a two-dimensional Butterworth filter (order = 8 and critical frequency = 0.28 cycles/pixel) and reconstructed by filtered back projection with a Shepp and Logan filter. No attenuation correction or scatter correction was applied. The reconstructed transaxial image sets were reoriented into vertical long-axis, horizontal long-axis, and short-axis sets by using an operator-specified left ventricular long-axis of the heart. The left ventricular shortaxis slices were then used in the automatic QGS algorithm developed at Cedars-Sinai Hospital in Los Angeles by Germano et al.<sup>16</sup>

The algorithm was based on geometric analysis of the left ventricular surface. Endocardial and epicardial boundaries were automatically traced. Left ventricular volume can be automatically calculated from the endocardium by using the Cedars-Sinai original program. In this study, we also calculated the volume surrounded by automatically traced epicardial boundaries. Myocardial mass volume was defined as the volume of the difference between the endocardial surface and the epicardial surface. The myocardial edge can be manually traced, even when the infero-posterior myocardium is adjacent to glittering abdominal organs. Gated SPECT data of the end-diastole were used to measure LVMI. The QGS-based left ventricular mass index (QGS LVMI) was calculated thus:

$$QGS LVMI (g/m2) = \frac{Myocardial volume (cm3) \times 1.04 (g/cm3)}{body surface area (m2)}$$

The SPECT data in the end-systolic and the enddiastolic phases were used for the analysis in 35 randomly selected patients to test the dependency of the QGS LVMI on the cardiac cycle.

In the QGS analysis, an observer is requested to determine the axis of the left ventricle before automatic processing. To evaluate the intraobserver reproducibility of the QGS analysis, the same observer was asked to determine the long axis of the left ventricle of 35 patients randomly selected from all of the patients, twice, at least one week apart. To evaluate the interobserver reproducibility, the long axis of the left ventricle was independently determined in 35 patients by 2 observers.

#### Semiquantitative analysis of perfusion defects

Regional perfusion SPECT images at rest were analyzed in patients with old myocardial infarctions. Short-axis slices from the apical, middle and basal ventricular levels were divided into 6 segments each, and the apex of the vertical long-axis slices was divided into 2 segments. The severity of the hypoperfusion was evaluated on a fivepoint grading scale (0 = normal perfusion, 1 = mild



**Fig. 1** Intraobserver (A) and interobserver reproducibility (B) of determination of left ventricular mass index by quantitative ECG-gated SPECT in the diastolic phase of 35 patients with masses ranging from 63 to 157 g/m<sup>2</sup>. A, Linear regression analysis of intraobserver variability (n = 35, y = 0.9x + 1.2, r = 0.99, p < 0.01). B, Linear regression analysis of interobserver variability (n = 35, y = 1.02x - 0.8, r = 0.98, p < 0.01).

| Table 1 QGS LVMI versus Echo LVM |
|----------------------------------|
|----------------------------------|

| Subgroup            | QGS LVMI (g/m <sup>2</sup> ) | Echo LVMI (g/m <sup>2</sup> ) | p-value | (QGS LVMI-Echo LVMI) (g/m <sup>2</sup> ) |
|---------------------|------------------------------|-------------------------------|---------|--|
| Control $(n = 74)$  | $83.0 \pm 8.5$               | $83.6 \pm 9.4$                | < 0.01  | $-0.64 \pm 1.01$                         |
| Ischemia $(n = 39)$ | $86.8 \pm 11.7$              | 89.1 ± 13.3                   | < 0.01  | $-2.71 \pm 6.23$                         |
| MI (n = 26)         | $99.9 \pm 20.4$              | $115.5 \pm 18.3$              | < 0.01  | $-15.94 \pm 10.38^{*}$                   |
| DCM $(n = 10)$      | $139.5 \pm 31.9$             | $145.0 \pm 35.4$              | < 0.01  | $-5.53 \pm 5.38$                         |
| HCM $(n = 10)$      | $104.5 \pm 26.8$             | $115.2 \pm 37.9$              | n.s.    | $-1.66 \pm 6.73$                         |
| HHD $(n = 20)$      | $117.4 \pm 31.6$             | $124.5 \pm 33.6$              | < 0.01  | $-7.13 \pm 7.39 **$                      |

Values are expressed as means and standard deviations of left ventricular mass index (LVMI) determined by quantitative ECG gated SPECT (QGS) and echocardiograpy (Echo). p: paired t-test, MI: myocardial infarction, DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, HHD: hypertensive heart disease. Data presented are mean value and standard deviations of the difference between QGS LVMI and Echo LVMI. \*p < 0.001 versus other groups. \*\*p < 0.01 versus control group.

hypoperfusion, 2 = moderate hypoperfusion, 3 = severe hypoperfusion, 4 = defect). The total defect score is the sum of the points of all segments.

#### Data statistical analysis

Data are presented as the means  $\pm$  SD. Correlations were assessed by means of Pearson's correlation coefficients and Fisher's method. Spearman's rank correlation was used for non-parametric estimations for paired groups. Paired and unpaired Student's t-tests were used to assess differences. Linear regression analysis was used to evaluate correlations between the first and the second QGS analysis by the same observer and by different observers. A Bland-Altman<sup>20</sup> plot was also used to demonstrate agreement between the QGS and Echo LVMI. Scheffe's ANOVA (analysis of variance) was used to test for significant differences between QGS and Echo LVMI in the patient groups. The correlation between the LVMIs of the two methods and total defect scores of myocardial infarction patients was assessed by linear regression analysis and Spearman's rank correlation test. P < 0.05 was considered indicative of a statistically significant difference.

#### RESULTS

# Comparison of QGS LVMI in the end-diastolic phase and end-systolic phase

The correlation between the end-diastolic and end-systolic measurements of QGS LVMI in 35 patients, was statistically significant (r = 0.99, p < 0.001), and the end-diastolic phase was used to estimate QGS LVMI in other analyses.

### Reproducibility

Figure 1A shows the intraobserver reproducibility of measurement of QGS LVMI and a fairly good correlation was observed between the first and the second estimations (r = 0.99, p < 0.001). Figure 1B shows interobserver reproducibility, and a good correlation was found between the two observers (r = 0.98, p < 0.001).

Gender difference and age dependency of QGS LVMI Left ventricular mass was significantly greater in men (mean  $\pm$  SD: 147  $\pm$  19 g) than in women (mean  $\pm$  SD: 127  $\pm$  16 g, p < 0.01), and LVMI was also significantly greater in men (85  $\pm$  8 g/m<sup>2</sup>) than in women (81  $\pm$  9 g/m<sup>2</sup>, p < 0.05). A weak correlation was found between age distribution and both left ventricular mass weight (r = -0.33, p = 0.02) and QGS LVMI (r = -0.24, p = 0.03) in the range from 25 to 77 years old, with a mean of 59  $\pm$  13 years old ( $\pm$  SD).

#### Comparison between QGS LVMI and Echo LVMI

In Figure 2A QGS LVMI is plotted against Echo LVMI for all patients (n = 179). These two measurements were significantly correlated (y = 0.87x + 8.9, r = 0.96, p < 0.01), and the correlations were statistically significant in each of the patient groups (p < 0.01).

The mean QGS LVMI value  $(94 \pm 24 \text{ g/m}^2)$  in almost all patients was significantly smaller than the Echo LVMI  $(99 \pm 27 \text{ g/m}^2, \text{ p} < 0.001)$ . Table 1 summarizes the mean QGS LVMI and Echo LVMI values for each patient group, and the mean values for QGS LVMI were significantly lower than those for Echo LVMI in all of them except HCM (p < 0.01). Table 1 also shows the differences between QGS and Echo LVMI and compares the groups with each other. The myocardial infarction group showed the largest difference between the left ventricular mass index measured by QGS and Echo (mean ± SD:  $-15.9 \pm 10.4 \text{ g/m}^2$ ). The other groups, except the HCM group, also showed significant differences ranging from -0.64 to -7.13 g/m<sup>2</sup>. Significant differences were observed between the MI group and the other groups in regard to the differences between QGS and Echo LVMI, and between the HHD group and the control group (p < p0.001, p < 0.01, respectively).

In Figure 2B, the differences between QGS and Echo LVMI were plotted against the averages of the QGS and Echo LVMI. Under conditions that excluded myocardial infarction, the difference between the LVMI values of 146 (95%) of the 153 patients were within 2SD (10.4 g/ $m^2$ ).

In Figure 3, the differences between Echo LVMI and QGS LVMI are plotted against the total defect scores in



**Fig. 2** Scattergram showing the correlation between quantitative ECG-gated SPECT (QGS) and echocardiographic (Echo) measurements of left ventricular mass index (LVMI) in all patients (n = 179). A, The solid line is the regression line; the broken line is the line of the identity. The correlation statistics were: y = 0.87x + 8.9, r = 0.96. B, Bland-Altman plot for LVMI. QGS versus Echo. The solid line is the mean difference; the broken lines are 2SD of the mean difference (2SD = 15). X's indicate control subjects (n = 74), open circles indicate ischemia patients (n = 39), solid squares indicate infarction patients (n = 26), solid circles indicate dilated cardiomyopathy patients (DCM, n = 10), open squares indicate hypertrophic cardiomyopathy patients (HCM, n = 10), open diamonds indicate hypertrophic heart disease patients (HHD, n = 20). The values of QGS LVMI in the myocardial infarction group were lower than the Echo LVMI values.



**Fig. 3** Relationship between the differences between quantitative-ECG-gated SPECT (QGS) and echocardiography (Echo) LVMI values and the total defect scores of 26 patients with myocardial infarction represented by solid squares. The solid line represents the regression equation generated from these data (y = -0.56x - 3.4, r = -0.56, p < 0.01). The QGS LVMI values tended to be smaller than the corresponding Echo LVMI values according to the increasing total defect score.



Fig. 4 Control case. The quantitative ECG-gated SPECT (QGS) LVMI value (87 g/m<sup>2</sup>) is similar to the echocardiography (Echo) LVMI value (89 g/m<sup>2</sup>). A: Short-axis of mid-ventricular, B: Horizontal long-axis, C: Vertical long-axis images. D: End-diastolic phase. E: End-systolic phase. The white lines are the result of tracing the myocardial surface. D, E: Right anterior oblique images measured by the QGS program in the end-diastolic phase (D) and the end-systolic phase (E). The broken outer line is the line of the epicardium in the end-diastolic phase, and the broken inner line is the line of the endocardium. The surface of the colored area represents the epicardium.



**Fig. 5** Myocardial infarction case. A 71-year-old male with a history of anterior, apical, septal, and lateral old myocardial infarction. The total defect score was high (42). The region with severe defects was traced inside the true edge of the endocardium (*red arrow*). The value of the QGS LVMI (89 g/m<sup>2</sup>) was lower than that of the Echo LVMI (115 g/m<sup>2</sup>) (difference: -26 g/m<sup>2</sup>). The description of the figures is the same as in Figure 4.

patients with old myocardial infarction. The correlation was statistically significant (r = 0.56, p < 0.01).

Typical cases in the control group and infarction group are shown in Figure 4 and Figure 5, respectively.

# DISCUSSION

The results of this study demonstrated that left ventricular mass measured by QGS with <sup>99m</sup>Tc-tetrofosmin is consistent with measurements made by M-mode echocardiography, but that perfusion defects in patients with old myocardial infarction cause underestimation of left ventricular mass by an average of 15% compared with echocardiography.

Left ventricular mass has been measured by myocardial perfusion SPECT with <sup>201</sup>Tl<sup>21-27</sup> and <sup>99m</sup>Tc-MIBI (hexakis 2-methoxyisobutyl isonitrile).<sup>28-30</sup> Pioneering studies with <sup>201</sup>Tl SPECT indicated that SPECT methods allow quantification of left ventricular mass in canine myocardium,21-24,30 in a phantom model mimicking cardiac wall motion,<sup>27</sup> and in patients with heart disease.<sup>25,26,28</sup> Wolfe et al. reported initially determining the epicardial and endocardial boundaries of tracer accumulation by applying a threshold of 50% of the maximal pixel count within the entire myocardium on ungated <sup>201</sup>Tl SPECT images and found that the SPECT left ventricular mass (mean: 204 g) corresponded closely with the left ventricular mass determined by left ventricular angiography (mean: 208 g) in 12 patients with normal coronary arteries and left ventricular function (r = 0.82).<sup>25</sup>

Narahara et al. reported that left ventricular mass estimated from non-gated SPECT images by the edge detection method, which yielded a mean value of  $247 \pm 88.6$  g, was close to angiography estimates, which yielded a mean value of  $234 \pm 79.2$  g, in 21 patients with and without ischemic heart disease, and that the r value for the correlation was 0.97.<sup>26</sup>

Williams et al. measured left ventricular mass by <sup>99m</sup>Tc-MIBI gated SPECT. Their study indicated that left ventricular mass was influenced by the setting of the background threshold.<sup>31</sup> When a 35% threshold and 37.5% threshold were used, left ventricular mass in the end-diastolic phase was 381 g and 144 g, respectively, and much larger and smaller than the left ventricular mass determined echocardiographically (200 g).

In contrast to the threshold-derived detection of myocardial boundaries,<sup>22,23,25,27,29–31</sup> QGS employed a nonthreshold method for epicardial and endocardial surface detection.<sup>17,32</sup> The QGS method automatically determines the limits of the search for endocardial and epicardial surfaces by using radioactivity counts and count gradients. Even if there is only slight myocardial perfusion in the defect area (up to 5% of the maximum count pixel level), its distribution is tracked by an automatically generated contour.<sup>33</sup>

The weight of left ventricular mass in the control group

was  $137 \pm 20$  g by QGS, and  $138 \pm 19$  g estimated by echocardiography, and mean left ventricular weight in the men  $(147 \pm 19 \text{ g})$  was 16% higher than in the women (127 g) $\pm$  16 g). Reiner et al.<sup>34</sup> found that the mean left ventricular (left ventricular free wall + interventricular septum) mass in men (155 g) was 34% higher than in women (115 g) in normal hearts at autopsy. In our study, left ventricular mass in the control group based on QGS was 147 g in men and 127 g in women, and these values are 50% of the average total heart weight of Japanese men (290 g) and 55% of the average total heart weight of Japanese women (230 g) at autopsy.<sup>35</sup> In our study, left ventricular mass was 53% of total heart weight, which consisted of the weight not only of the left ventricle but also of the right ventricle, atria, and epicardial fat, and slightly higher than in the autopsy studies by Reiner et al.<sup>34</sup> and Bove et al.<sup>36</sup> Their reported ratios of left ventricular free wall + interventricular septum mass to total heart weight in adults ranged from 0.47 to 0.39, and may partially validate the accuracy of the QGS method for measuring left ventricular mass.

Although myocardial mass should remain unchanged throughout the cardiac cycle, Williams et al. reported that end-diastolic measurements resulted in significantly higher left ventricular mass values (381 g) than end-systolic measurements (268 g).<sup>31</sup> Nevertheless, Germano et al. mentioned that QGS program constrained myocardial volume was constant in the cardiac cycle.<sup>32</sup> We confirmed that left ventricular mass determined by the QGS method remained unchanged between end-diastole and end-systole. This may be due to the anatomical constraint of the constant myocardial volume in the cardiac cycle in the original QGS program.

Good reproducibility of QGS for determination of left ventricular chamber volume<sup>17,18</sup> and the ejection fraction has been reported,<sup>16,18</sup> and in this study we confirmed that QGS also provides highly reproducible estimates of left ventricular mass. One of the limitations of this study is the lack of data to compare two imagings in the same patient. Although the inter-observer and intra-observer reproducibility was fairly good, we have not confirmed the reproducibility of repeated QGS. Devereux reported the interobserver reproducibility of the echocardiography measurements of myocardial mass was good and echocardiography measurements with true left ventricular mass obtained at biopsy correlated well.<sup>19</sup>

A disadvantage of the QGS method was found in patients with myocardial infarction. <sup>99m</sup>Tc-tetrofosmin SPECT principally estimates perfusable myocardium alone, whereas echocardiography measures both perfusable and non-perfusable tissue. This methodological difference may cause a discrepancy in estimated left ventricular mass in patients with old myocardial infarction. In the presence of severe perfusion defects, especially when they included the apex or base of the myocardium, QGS underestimated the LVMI relative to

echocardiography (Fig. 5). QGS incorrectly traces inside the true edge of the myocardium (Fig. 5B, indicated by arrow). Another reason for the QGS underestimation of LVMI in infarction patients is that the edge in the region with a low myocardial count was traced inside between the endocardium and epicardium. This underestimation can be ascribed to the erroneous tracking of the true myocardial boundaries.

There were several other limitations to estimating left ventricular mass by the QGS method. First, high hepatic accumulation of 99mTc-tetrofosmin may impair determination of the appropriate cardiac contour. Manual tracking of myocardial radioactivity might be an effective means of improving the estimations. Second, there is a partial volume effect for calculating the left ventricular mass index.<sup>37</sup> A small heart causes severe partial volume effects. The QGS method tended to underestimate the left ventricular chamber volume compared with left ventricular angiography.<sup>38</sup> In our study, only 15 patients (8% of all patients) had a small heart, defined as one with an enddiastolic left ventricular chamber volume of less than 50 ml. Third, it is difficult to apply ECG-gated SPECT to patients with arrhythmia, and only echocardiographic measurement of LVMI was possible. Fourth, patient motion artifacts during SPECT acquisition is a source of error in scan interpretation. Motion with triple-head detectors moving will causes artifacts.<sup>39</sup> Patient motion during acquisition is likely to cause blurring of that projection and misalignment with the other projections, resulting in underestimation of QGS LVMI. Fifth, our study did not include patients with a left ventricular aneurysm, mural thrombi, or an enlarged right ventricle. But myocardial deformity is a potential source of error in the QGS method.

In conclusion, QGS-based measurements of left ventricular mass were found to be reproducible in the interobserver and intraobserver analyses, independent of the cardiac cycle, and consistent with the echocardiographic estimations. In addition to myocardial perfusion and function, left ventricular mass can be reliably estimated by the QGS method, but underestimation of left ventricular mass should be taken into consideration in patients with old myocardial infarction who have large perfusion defects.

#### REFERENCES

- Casale PN, Devereux RB, Milner M, Zullo G, Harshfield GA, Pickering TG. Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. *Ann Intern Med* 1986; 105: 173–178.
- Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990; 322: 1561–1566.

- Sullivan JM, Vander Zwaag RV, el-Zeky F, Ramanathan KB, Mirvis DM. Left ventricular hypertrophy: effect on survival. *J Am Coll Cardiol* 1993; 22: 508–513.
- Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *J Am Coll Cardiol* 1998; 32: 1454–1459.
- Kannel WB, Gordon T, Offutt D. Left ventricular hypertrophy by electrocardiogram. Prevalence, incidence, and mortality in the Framingham study. *Ann Inter Med* 1969; 71: 89–105.
- Kannel WB, Gordon T, Castelli WP, Margolis JR. Electrocardiographic left ventricular hypertrophy and risk of coronary heart disease. The Framingham study. *Ann Intern Med* 1970; 72 (6): 813–822.
- Hall SA, Cigarroa CG, Marcoux L, Risser RC, Grayburn PA, Eichhorn EJ. Time course of improved in left ventricular function, mass, geometry in patients with congestive heart failure with beta-adrenergic blockade. *J Am Coll Cardiol* 1995; 25: 1154–1161.
- 8. The SOLVD investigators. Studies of left ventricular dysfunction (SOLVD) rationale, design and methods: two trials that evaluate the effect of enalapril in patients with reduced ejection fraction. *Am J Cardiol* 1990; 66 (3): 315– 322.
- 9. Skioldebrand CG, Lipton MJ, Mavroudis C, Hayashi TT. Determination of left ventricular mass by computed tomography. *Am J Cardiol* 1982; 49: 63–70.
- Peck WW, Mancini GBJ, Slutsky RA, Mattrey RF, Higgins CB. *In vivo* assessment by computed tomography of the natural progression of infarct size, left ventricular mass, and function after myocardial infarction in the dog. *Am J Cardiol* 1984; 53: 929–935.
- Feiring AJ, Rumberger JA, Reiter SJ, Skorton DJ, Collins SM, Lipton MJ, et al. Determination of left ventricular mass in dogs with rapid-acquisition cardiac computed tomographic scanning. *Circulation* 1985; 72 (6): 1355–1364.
- 12. Bexley WA, Dodge HT, Sandler H. A quantitative angiocardiograhic study of left ventricular hypertrophy and the electrocardiogram. *Circulation* 1968; 37: 509–517.
- Levy D, Labib SB, Anderson KM, Christiansen JC, Kannel WB, Castelli WP. Determinants of sensitivity and specificity of electrocardiographic criteria for left ventricular hypertrophy. *Circulation* 1990; 81 (3): 815–820.
- Lorenz CH, Walker ES, Morgan VL, Klein SS, Graham TP Jr. Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. *J Cardiov Magn Res* 1999; 1: 7–21.
- Schalla S, Nagel E, Lehmkuhl H, Klein C, Bornstedt A, Schnackenburg B, et al. Comparison of magnetic resonance real-time imaging of left ventricular function with conventional magnetic resonance image and echocardiography. *Am J Cardiol* 2001; 87: 95–99.
- Germano G, Kiat H, Kavanagh PB, Moriel M, Mazzanti M, Su HT, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 1995; 36: 2138–2147.
- Germano G, Kavanagh PB, Kavanagh JT, Wishner SH, Berman DS, Kavanagh GJ. Repeatability of automatic left ventricular cavity volume measurements from myocardial perfusion SPECT. *J Nucl Cardiol* 1998; 5: 477–483.

- Yoshioka J, Hasegawa S, Yamaguchi H, Tokita N, Paul AK, Xiuli M, et al. Left ventricular volumes and ejection fraction calculated from quantitative electrocardiographicgated <sup>99m</sup>Tc-tetrofosmin myocardial SPECT. *J Nucl Med* 1999; 40: 1693–1698.
- 19. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. *Circulation* 1977; 55: 613–618.
- 20. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307–310.
- Keyes JW Jr, Brady TJ, Leonard PF, Svetkoff DB, Winter SM, Rogers WL, et al. Calculation of viable and infarcted myocardial mass from thallium-201 tomograms. *J Nucl Med* 1981; 22: 339–343.
- 22. Holman BL, Moore SC, Shulkin PM, Kirsch CM, English RJ, Hill TC. Quantitation of perfused myocardial mass using TI-201 and emission computed tomography. *Invest Radiol* 1983; 18: 322–326.
- 23. Wolfe CL, Corbett JR, Lewis SE, Buja LM, Willerson JT. Determination of left ventricular mass by single-photon emission computed tomography. *Am J Cardiol* 1984; 53: 1365–1368.
- Narahara KA, Thompson CJ, Maublant JC, Criley JM, Mena I. Estimation of left ventricular mass in normal and infarct canine hearts using thallium-201 SPECT. *J Nucl Med* 1987; 28: 1315–1321.
- 25. Wolfe CL, Jansen DE, Corbett JR, Lipscomb K, Gabliani G, Filipchuk N, et al. Determination of left ventricular mass using single-photon emission computed tomography. *Am J Cardiol* 1985; 56: 761–764.
- 26. Narahara KA, Thompson CJ, Maublant JC, Brizendine M, Mena I. Thallium-201 single-photon emission computed tomographic estimates of left ventricular mass in patients with and without ischemic heart disease. *Am Heart J* 1987; 114: 84–90.
- Machac J, Vaquer R, Levin H, Horowitz SF. The effect of heart rate and contractility on the measurement of left ventricular mass by <sup>201</sup>Tl SPECT. *Eur J Nucl Med* 1987; 13: 446–449.
- 28. Narahara KA, Villanueva-Meyer J, Thompson CJ, Brizendine M, Mena I. Comparison of thallium-201 and technetium-99m hexakis 2-methoxyisobutyl isonitrile single-photon emission computed tomography for estimating the extent of myocardial ischemia and infarction in coronary artery disease. *Am J Cardiol* 1990; 66: 1438–

1444.

- Wolfe CL, O'Connell JW, Sievers RE, Cobb C, Dae MW, Botvinick E. Assessment of perfused left ventricular mass in normal, ischemic, and reperfused myocardium by means of single-photon emission computed tomography of technetium-99m isonitrile. *Am Heart J* 1993; 126; 1275–1286.
- 30. Leon AR, Eisner RL, Martin SE, Schmarkey LS, Aaron AM, Boyers AS, et al. Comparison of single-photon emission computed tomographic (SPECT) myocardial perfusion imaging with thallium-201 and technetium-99m sestamibi in dogs. J Am Coll Cardiol 1992; 20: 1612–1625.
- Williams KA, Lang RM, Reba RC, Taillon LA. Comparison of technetium-99m sestamibi-gated tomographic perfusion imaging with echocardiography and electrocardiography for determination of left ventricular mass. *Am J Cardiol* 1996; 77: 750–755.
- 32. Germano G, Erel J, Lewin H, Kavanagh PB, Berman DS. Automatic quantitation of regional myocardial wall motion and thickening from gated technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol 1997; 30: 1360–1367.
- Germano G, Berman DS. On the accuracy and reproducibility of quantitative gated myocardial perfusion SPECT. J Nucl Med 1999; 40: 810–813.
- Reiner L, Mazzoleni A, Rodriguez FL, Freudenthal RR. The weight of the human heart. *Arch Pathol* 1959; 68: 58– 73.
- 35. Fujita T. Human Anatomy. Nankoudou 1993; 41: 304-305.
- Bove KE, Rowlands DT, Scott RC. Observations on the assessment of cardiac hypertrophy utilizing a chamber partition technique. *Circulation* 1966; 33: 558–568.
- Nakajima K, Taki J, Higuchi T, Kawano M, Taniguchi M, Maruhashi K, et al. Gated SPET quantification of small hearts: mathematical simulation and clinical application. *Eur J Nucl Med* 2000; 27: 1372–1379.
- Toba M, Kumita S, Cho K, Mizumura S, Kijima T, Nakano H, Kumazaki T. Comparison of Emory and Cedars-Sinai methods for assessment of left ventricular function from gated myocardial perfusion SPECT in patients with a small heart. *Ann Nucl Med* 2000; 14 (6): 421–426.
- Matsumoto N, Berman DS, Kavanagh PB, Gerlach J, Hayes SW, Lewin HC, et al. Quantitative assessment of motion artifacts and validation of a new motion-correction program for myocardial perfusion SPECT. *J Nucl Med* 2001; 42: 687–694.