Quantitative gated myocardial perfusion single photon emission computed tomography improves the prediction of regional functional recovery in akinetic areas after coronary bypass surgery: Useful tool for evaluation of myocardial viability

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Objective: Assessment of myocardial viability in akinetic areas is essential in surgery for ischemic heart disease, including coronary artery bypass grafting and left ventriculoplasty. The aim of this study is to evaluate the utility of quantitative indices of perfusion uptake, wall motion, and wall thickening of each region calculated by quantitative electrocardiogram-gated single photon emission computed tomography (SPECT) for prediction of functional recovery after coronary artery bypass grafting.

Methods: Forty patients scheduled for coronary artery bypass grafting were prospectively included. Electrocardiogram-gated SPECT was performed before and 1 week and 3 months after operation, and coronary angiography was performed before and after operation. The myocardium was divided into 9 segments and myocardial viability, assessed by improvement of the wall motion score using a cine mode display, and evaluated by radionuclide criteria (perfusion uptake, wall motion, wall thickening). Twenty-four segments with moderate hypokinesis and 14 segments with akinesis with patent grafts were assessed.

Results: All segments with moderate hypokinesis except 1 (96%) had improved wall motion scores postoperatively, whereas of 14 segments with akinesis only 7 segments (50%) had improved wall motion scores. The preoperative perfusion uptake in the improved segments was significantly higher than in the nonimproved segments ($62.7\% \pm 15.6\%$ vs $46.4\% \pm 24.5\%$, $P = .01$). There was a significant difference in wall motion between the improved and nonimproved segments (3.8 ± 2.2 mm vs 1.4 ± 1.4 mm, $P = .001$), and the preoperative wall thickening of the improved segments was significantly higher than in the nonimproved segments ($27.2\% \pm 14.1\%$ vs $8.2\% \pm 10.3\%$, $P < .0001$). The optimal cutoff level of perfusion uptake was 50%, with the highest accuracy of 72%, and the optimal cutoff levels of wall thickening and wall motion were 10% and 1.5 mm, with the highest accuracies of 76% and 85%, respectively.

Conclusion: The regional functional index calculated by electrocardiogram-gated SPECT indicated that wall thickening was well correlated with functional recovery compared with wall motion or perfusion uptake. This suggests that the wall thickening calculated by electrocardiogram-gated SPECT may be more useful to predict functional recovery than regional myocardial perfusion. Or, it could suggest that in addition to perfusion uptake, wall thickening could enhance the objective assessment of myocardial viability.

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In patients with ischemic heart disease, detection of myocardial viability is of major clinical and prognostic importance and may significantly affect therapeutic decisions. Surgical revascularization has been shown to improve survival in patients with ischemic cardiomyopathy¹⁻³; however, perioperative mortality is high in this group of patients who do not have significant viable myocardium.⁴ In addition, some reports^{5,6} have suggested that endoventricular circular patch plasty, the so-called Dor operation, is effective in patients with akinetic areas as well as dyskinetic areas in ischemic cardiomyopathy with a dilated heart. However, it is important to determine whether the akinetic area is viable. For left ventriculoplasty in dilated cardiomyopathy, Suma and colleagues^{7,8} suggested that the volume reduction test was useful to detect residual contractile reserve and hence decide the area to be excluded. Thus, in patients with severe left ventricular (LV) dysfunction, preoperative quantification of viable myocardium is of the utmost importance to identify patients who can benefit from revascularization or ventriculoplasty instead of heart transplantation.

The detection of myocardial viability is currently based on the use of nuclear techniques, which show preserved tracer uptake and metabolism in viable myocardium, and echocardiographic methods, which detect the residual contractile reserve. Both techniques show similar sensitivity in predicting functional recovery after revascularization. Dobutamine stress echocardiography has higher specificity and therefore may be clinically more useful⁹ but requires a trained observer. Due to the limitations of current nuclear and echocardiographic methods in detecting myocardial viability, new developments are directed toward better quantification of viable myocardium and simultaneous assessment of myocardial metabolism, perfusion, and function. Quantitative electrocardiogram (ECG)-gated single photon emission computed tomography (SPECT; QGS) with combined evaluation of metabolism and perfusion seems to be one of the most promising and cost-effective methods for a comprehensive and objective assessment of myocardial viability. In this study, the myocardial viability of severely hypokinetic and akinetic areas was evaluated by the QGS after coronary artery bypass grafting (CABG).

Methods

Patients and Protocol

The study population consisted of 40 patients with angiographically proven coronary artery disease scheduled for CABG. There were 29 men and 11 women with a mean age of 65.8 ± 5.5 years (range from 46 to 79 years). Twenty-five had a history of myocardial infarction, and 3 patients had a history of congestive heart failure requiring hospitalization. On coronary angiography, 2 patients had 1-vessel disease, 12 had 2-vessel disease, and 26 had 3-vessel disease with stenosis of the major coronary artery of more than 75%. The LV ejection fraction assessed by left ventriculog-

Figure 1. Segmental division of left ventricle in long- and short-axis views.

TABLE 1. Bypass grafts used and their patency

Conduit	Number of grafts	Patency (%)
Left (right) ITA	43	98
RA	34	92
GEA	11	80
SV	42	88

ITA, Internal thoracic artery; RA, radial artery; GEA, gastroepiploic artery; SV, saphenous vein.

raphy was 52.1% ± 7.8% (n = 28, range from 19 to 72%). All patients underwent technetium Tc 99m (^{99m}Tc)-tetrofosmine-gated myocardial perfusion SPECT at rest preoperatively and at 1 week and 3 months after CABG. Coronary angiography was performed preoperatively and 2 to 3 weeks after CABG. Postoperative coronary angiography was performed after QGS in all patients, and the results of coronary angiograms were blinded to 2 examiners who evaluated the results of QGS postoperatively.

This study was approved by the institutional review board of the School of Medicine, Hokkaido University. Informed written consent for this study was obtained from all patients. The average number of bypasses was 3.3 ± 1.1 (range from 1 to 5). The grafts used in the bypass surgery and their patency rates are shown in Table 1.

Image Acquisition and Quantitation

Patients were injected with 740 MBq of ^{99m}Tc-tetrofosmine at rest and gated myocardial perfusion SPECT was performed 30 minutes later. Eight frames of data according to the averaged cardiac cycle were acquired with a 20% window centered over the 140-keV photopeak, using a dual-head 90° camera (Vertex; ADAC Laboratories, Milpitas, Calif). A ramp filter and a Butterworth filter of order 5 and cutoff frequency of 0.35 cycle/pixel were used for

Figure 2. Changes in LVEDV, LVESV, and LVEF calculated by QGS before and 1 week and 3 months after coronary artery bypass. *P* values are shown between 2 groups as indicated in the figure.

Figure 3. The preoperative percent uptake in the improved segments (open circles) and the nonimproved segments (closed circles). The optimal cutoff level of percent uptake was 50% with the highest accuracy (72%), and the sensitivity, specificity, and positive and negative predictive value were 80%, 50%, 82%, and 46%, respectively.

reconstruction. No attenuation or scatter correction was done. Tomographic transaxial images and gated surface images were reconstructed. The LV myocardium was divided into 9 segments

(Figure 1). In each of the 9 segments, the average quantitative values of segmental wall motion and wall thickening were determined using the QGS software developed by Germano and colleagues.¹⁰ Wall motion was calculated and expressed in millimeters, and wall thickening was expressed as the percentage of end-diastolic wall thickness. The entire process was performed automatically, without manual intervention. Regional perfusion (percent uptake) was also evaluated automatically using QGS software to average the quantitative values in the 9 segments. This algorithm has been reported to have reproducibility and clinical relevance.^{10,11}

The wall motion score was defined visually by a 4-point scale using the cine mode display of gated SPECT (0: normal, 1: mild hypokinesis, 2: moderate hypokinesis, 3: akinesis). Segments with scores 2 and 3 with patent grafts were selected for assessing improvement of wall motion after CABG. The septum (segments 6a and 6b in Figure 2) was excluded from the analysis because of its paradoxical motion after open cardiac surgery. Wall motion improvement was defined as improvement of the wall motion score by 1 or greater at 1 week and 3 months after CABG compared with preoperative evaluation.

Statistical Analysis

Results are expressed as mean value $\pm$ SD. Continuous data were compared using the Student 2-tailed *t* test. We have previously reported¹² the diagnostic criteria of perfusion uptake ($\geq 50\%$), wall motion (≥ 1.5 mm), and wall thickening ($\geq 10\%$) for prediction of functional recovery, and these criteria were used in this study. Specificity, sensitivity, positive and negative predictive values, and accuracy were calculated. Differences between quantitative values were evaluated with χ^2 analysis or the Fisher exact test when appropriate.

TABLE 2. Clinical and operative profiles in patients with segments of moderate hypokinesis (score 2) and/or akinesis (score 3)

Wall motion score	No. of segments studied	No. of patients	History of MI (no. of patients)	History of CHF (no. of patients)	EF (%) by QGS	No. of bypasses	Patency of graft (%)
Score 2	23	13	7	0	49-70	34	92
Score 2 and 3	12 and 6	6	6	2	13-56	23	96
Score 3	6	2	2	1	19-52	6	100

MI, Myocardial infarction; CHF, congestive heart failure; EF, ejection fraction; QGS, quantitative gated SPECT.

Results

Clinical Outcomes

There were no hospital or late deaths during this study. Although 2 patients had perioperative infarction with a new Q-wave in ECG, there was no hemodynamic deterioration at all. Two of 3 patients who had a history of congestive heart failure were moved to the medical ward to control heart failure before discharge, while others went home from the surgical ward. No patient had a recurrent ischemic episode after discharge.

LV Dimensions and Function

The changes in LV end-diastolic volume (EDV) and end-systolic volume (ESV) measured by QGS are shown in Figure 2. Both LVEDV and LVESV were significantly decreased ($P < .0001$) 1 week after operation, and after 3 months LVEDV was still significantly lower than the preoperative value ($P = .03$). The LV ejection fraction (EF), calculated by LVEDV and LVESV, was not significantly increased at 1 week after operation but was significantly improved at 3 months after operation ($P = .04$) compared with the preoperative value (Figure 2).

Myocardial Viability and Parameters Measured by QGS

There were 47 segments with a preoperative score of 2 (moderate hypokinesis; $n = 30$) or 3 (akinesis; $n = 17$) with patent grafts, and these segments were analyzed. Clinical characteristics of patients are shown in Table 2. After 3 months, 35 of these segments had improved regional function assessed by the cine mode display, whereas 12 segments did not have improved functional recovery compared with the preoperative score. The preoperative percent uptake in the improved segments was significantly higher than in the nonimproved segments ($62.7\% \pm 15.6\%$ vs $46.4\% \pm 24.5\%$, $P = .0103$; Figure 3). There was a significant difference of preoperative wall thickening between the improved and nonimproved segments ($27.2\% \pm 14.1\%$ vs $8.2\% \pm 10.3\%$, $P < .0001$; Figure 4), and the preoperative wall motion of the improved segments was significantly higher than in the nonimproved segments (3.8 ± 2.2 mm vs 1.4 ± 1.4 mm, $P = .0011$; Figure 5).

The optimal cutoff level of percent uptake was 50% with the highest accuracy (72%), which provided a sensitivity of

80%, specificity of 50%, positive predictive value of 82%, and negative predictive value of 46% (Figure 3). The optimal cutoff level of wall thickening was 10% with the highest accuracy (85%), which provided a sensitivity of 89%, specificity of 73%, positive predictive value of 91%, and negative predictive value of 67% (Figure 4). The optimal cutoff level of wall motion was 1.5 mm with the highest accuracy (76%); the sensitivity, specificity, and positive and negative predictive values were 74%, 83%, 93%, and 52%, respectively (Figure 5). Therefore, wall thickening of more than 10% had higher accuracy for predicting viable myocardium than percent uptake or wall motion. The myocardial viability assessed by preoperative perfusion uptake and wall thickening is shown in Figure 6, indicating that segments with less than 50% uptake and less than 10% wall thickening were less likely to recover after bypass grafting.

Changes of Functional Recovery of Segments

Functional recovery of segments with moderate hypokinesis is shown in Figure 7, A. There were 30 segments with a score of 2 (moderate hypokinesis) with patent grafts. One week after operation, functional recovery was obtained in 26 segments, including 14 with a score of 1 and 12 with a score of 0, whereas no functional recovery was seen in 4 segments. Three months after operation, further improvement was obtained in 4 segments, whereas the wall motion score was increased from 1 to 2 in 1 segment. Consequently, at 3 months, only 4 segments (4/30, 13%) did not show any improvement of the wall motion score compared with preoperative evaluation.

There were 17 segments with a score of 3 (akinesis) with patent grafts, as shown in Figure 7, B. One week after operation, functional recovery was obtained in 11 segments, including 2 with a score of 2, 5 with a score of 1, and 4 with a score of 0, whereas no functional recovery was seen in 6 segments. Three months after operation, further improvement was obtained in only 2 segments, but the wall motion score was increased in 2 segments, one from a score of 2 to 3 and one from a score of 1 to 3. Consequently, at 3 months, 8 of 17 segments (47%) did not exhibit any improvement of the wall motion score compared with preoperative evaluation. The rate of improvement of the wall motion score after 3 months was significantly lower in segments with moderate

Figure 4. The preoperative wall thickening calculated by QGS in the improved segments (*open circles*) and the nonimproved segments (*closed circles*). The optimal cutoff level of wall thickening was 10% with the highest accuracy (85%), and the sensitivity, specificity, and positive and negative predictive value were 89%, 73%, 91%, and 67%, respectively.

Figure 5. The preoperative wall motion (*WM*) calculated by QGS in the improved segments (*open circles*) and the nonimproved segments (*closed circles*). The optimal cutoff level of wall motion was 1.5 mm with the highest accuracy (76%), and the sensitivity, specificity, and positive and negative predictive value were 74%, 83%, 93%, and 52%, respectively.

hypokinesis than in those with akinesis (13% vs 47%, $\chi^2 = 6.49$, $P = .0165$).

Discussion

This study indicates that regional function was recovered in almost all segments with moderate hypokinesis after surgical revascularization, whereas functional recovery was obtained in only 8 of 17 segments with akinesis. To predict functional recovery in segments, wall thickening calculated by QGS is a useful indicator compared with perfusion uptake, which is currently used in assessment of myocardial viability with SPECT.

Surgical Options in Ischemic Cardiomyopathy

Recently, identification of viable hibernating myocardium has gained a substantial role in the evaluation and management of patients with ischemic LV dysfunction. The possibility of identifying patients with severely impaired LV function who may benefit from myocardial revascularization has received enormous clinical interest, leading to a large number of studies that assessed different modalities for distinguishing between reversibly dysfunctional (hibernating) and necrotic myocardium. As a result of this effort and of improved surgical techniques, it is now widely recognized that many patients with severely depressed systolic

function, but with a substantial amount of residual viable myocardium function, can be removed from the waiting list for heart transplantation to surgical revascularization at an acceptable perioperative risk.¹⁻³ Because perioperative mortality is high in the group of patients who do not demonstrate significant viable myocardium,⁴ the identification of viable hibernating myocardium is essential for therapeutic decisions. In addition to surgical revascularization, left ventriculoplasty, such as the Dor procedure,⁵ Batista operation,¹³ and overlapping of the left ventricle,¹⁴ is reported to be one of the therapeutic options in dilated ischemic cardiomyopathy. Not only scarred and thinned-out areas but also akinetic areas are isolated for exclusion to reconstruct an appropriately sized left ventricle; however, it is sometimes difficult to decide the area of resection, for instance, the posterior wall or anteroapical wall. Although palpation under heart beating can delineate the margin of contractility in scarred and thinned-out areas,⁶ it would not be accurate, particularly in akinetic areas. Suma and colleagues^{7,8} suggested that changes of LV wall motion and thickness can be evaluated by intraoperative cardiac echography when the left ventricle is decompressed under the cardiopulmonary bypass and the wall tension decreases. This volume-reduction test could be a useful method to predict myocardial

Figure 6. The relationships of myocardial viability with preoperative perfusion uptake and wall thickening are shown. The segments with less than 50% uptake and less than 10% wall thickening were less likely to recover after bypass grafting. Closed circles indicate the nonimproved segments.

viability and decide the area to be excluded; however, it would be better to quantify viable myocardium preoperatively and objectively. Therefore, preoperative evaluation of wall thickening calculated by QGS could identify patients who can benefit from revascularization and help to decide the area to be excluded when left ventriculoplasty is performed.

Wall Thickening Value Calculated by QGS as a Marker for Functional Recovery

For comprehensive and objective assessment of myocardial viability, ECG-gated SPECT with combined evaluation of metabolism and perfusion seems to be one of the most promising methods, and this study indicated that wall thickening calculated by QGS was a useful indicator compared with perfusion uptake, which is currently used in assessment of myocardial viability with SPECT.

Pathologic examinations have demonstrated that myocardial thinning occurs in areas of necrotic myocardium in chronic transmural infarction,¹⁵ whereas preserved wall thickness is seen in viable myocardium.¹⁶ Our data confirmed these findings. There have been a few reports about the utility of using wall thickening analysis to detect viable myocardium.¹⁷⁻²⁰ Most of these studies evaluated the wall thickening visually, but one study by Lazar and coworkers¹⁷ reported the quantitative changes in wall thickness assessed by epicardial echocardiography after CABG intraoperatively. They concluded that quantitative wall thickening, compared with visual qualitative changes of wall motion, was a more accurate technique to assess postoperative changes in regional function. Our study confirmed their findings that the quantitative changes in wall thickness were more objective and accurate than visual analysis. Compared with either epicardial or transesophageal echocardiography,

Figure 7. Changes in wall motion score in segments with severe hypokinesis (A) and akinesis (B). Wall motion score was evaluated by a cine mode display before and 1 week and 3 months after coronary artery bypass.

QGS is less invasive and can be repeated easily in long-term follow-up. In addition, the reproducibility of the algorithm of QGS is quite high,²¹ and wall thickening expressed as a percentage of end-diastolic wall thickness is less influenced by attenuation and noise than the absolute value of wall thickness because it is a relative value.

Previous studies demonstrated that perfusion uptake of more than 50% was an indicator of functional recovery after revascularization. Our results may partly support these studies. However, the accuracy of perfusion uptake was lower than that of wall thickening. This would suggest that in addition to perfusion uptake, wall thickening calculated by QGS could enhance the objective assessment of myocardial viability because the accuracy of perfusion uptake together with wall thickening may be higher than that of perfusion uptake or wall thickening alone, as shown in Figure 6.

Study Limitations and Cautions

Automatic quantification from QGS has the potential to simultaneously assess LV function and myocardial perfusion. Although many reported LV volumes and LVEF calculated by QGS correlate well with those evaluated by various imaging modalities, including echocardiography,

ventriculography, and magnetic resonance imaging, LV volumes and LVEF tend to be underestimated by QGS in small hearts.^{11,22} Because accurate delineation of the endocardial and epicardial contours on the reconstructed images is a prerequisite for reliable calculation, the accuracy of volumes and wall motions depend on the software program.

The other limitation of our study is the interval of follow-up after CABG. We did not evaluate the myocardium that would have recovered after 3 months. Long-term follow-up is required to clarify whether functional recovery of akinetic areas is obtained after revascularization, although in this study only half of such areas had improved wall motion after 3 months. Many patients with ischemic cardiomyopathy have a mixture of hibernating, stunned, remodeled, and scarred myocardium^{23,24} and may therefore exhibit variable degrees of improvement in ventricular function after revascularization. One report²³ provided interesting insights into the pathophysiology of ischemic cardiomyopathy, indicating that revascularizing viable myocardium might prevent or reverse the remodeling of nonischemic segments. Another study,²⁵ however, indicated that failure to improve LV function after CABG for ischemic cardiomyopathy was not associated with worse clinical outcomes of symptoms and survival. Therefore, myocardial viability should be considered a continuum, from full-thickness viability without any scar to full-thickness scarring without viable cells. Furthermore, recent studies^{26,27} suggest that the degree and timing of recovery of LV function after revascularization may be a continuum, depending on the underlying pathophysiologic substrate (ie, the preoperative ratio of viable-to-scarred myocardium). Clearly, repeated assessments by QGS will be required in the long term, particularly in segments that show no improvement in function 3 months after revascularization. Further studies are also required to elucidate whether the indices of wall thickening are correlated with clinical outcomes.

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