Beneficial Effect of Coronary Artery Bypass Grafting as Assessed by Quantitative Gated Single-Photon Emission Computed Tomography

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The development of quantitative gated single-photon emission computed tomography (SPECT) has enabled the assessment of left ventricular perfusion, function and wall thickness in a single examination. Accordingly, the present study used gated SPECT to assess the benefit of coronary artery bypass grafting (CABG) in patients with coronary artery disease; 47 of those patients were evaluated before and 5 months after CABG. As a result of coronary revascularization, a significant improvement was observed in global ejection fraction (50±12 vs 53±11%; p<0.05). In 107 revascularized territories, the average regional reversible defect score (0.8±0.5 vs 0.2±0.3; p<0.0001), average regional perfusion score at rest (0.6±0.6 vs 0.3±0.4; p<0.0001), average regional wall motion score (0.9±0.7 vs 0.7±0.5; p<0.05), and end-diastolic wall thickness (8.1±1.3 vs 8.6±1.5 mm; p<0.0005) all improved significantly. Even in 34 non-revascularized territories, the average regional reversible defect score (0.5±0.7 vs 0.2±0.5; p<0.03), average regional wall motion score (0.8±1.1 vs 0.5±1.0; p<0.03) and end-diastolic wall thickness (8.0±1.4 vs 9.1±2.0 mm; p<0.03) all improved significantly. These results indicate that improvement in myocardial ischemia, hibernation and left ventricular function with CABG can be assessed in detail with gated SPECT. (Circ J 2003; 67: 499–504)

Key Words: Coronary artery bypass grafting; Coronary artery disease; Coronary revascularization; Myocardial viability; Quantitative gated single-photon computed tomography

Methods

Subjects

The subjects of this study were 47 patients with CAD who underwent elective CABG: 36 men and 11 women, with a mean age of 65±9 years. Sixteen patients had a previous myocardial infarction; 1-vessel CAD was observed in 3 patients, 2-vessel CAD in 14, and 3-vessel CAD in 30. The number of affected vessels for which revascularization was performed was 1 in 6 patients, 2 in 22 and 3 in 19. Patients with a history of acute myocardial infarction or unstable angina within 1 month prior to the study were excluded.

Stress Myocardial Scintigraphy

Stress myocardial scintigraphy was performed twice for each patient, first within 2 months prior to, and then 5 months after CABG, using the same radioisotopes. All the patients were in sinus rhythm during the scintigraphic study. In 12 patients, exercise myocardial scintigraphy with 99mTc-sestamibi was performed using the 2-day protocol. 14 Symptom-limited multistep exercise using a bicycle ergometer was undertaken by 11 patients. 99mTc-sestamibi (740 MBq) was administered when submaximal heart rate, chest pain, ST depression of ≥0.1 mV or leg fatigue developed and the exercise was then continued for 1 min at the same level. At 30 min after the last exercise session, image acquisition was started. In the remaining patient, adenosine triphosphate disodium (0.16 mg·kg⁻¹·min⁻¹) was administered intravenously for 6 min and 3 min later, 99mTc-sestamibi (740 MBq) was given intravenously. Imaging started 30 min after that. On the following day, the patients

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were given 99mTc-sestamibi (740 MBq) while at rest and 30 min later, ECG-gated myocardial SPECT images were acquired.

Using 201Tl (111 MBq), myocardial scintigraphy was performed in 35 patients; in 23 patients, scintigraphy was performed during exercise, and the remaining 12 patients underwent adenosine triphosphate-loading myocardial scintigraphy. The protocols to stress these patients were similar to the previous methods.\textsuperscript{15–17} Delayed images were acquired 4 h later. For all 35 patients, ECG-gated SPECT data were acquired when the delayed images were obtained. The number of diseased vessels, left ventricular ejection fraction, the preoperative frequency of myocardial infarction and the method of revascularization used did not differ between the group of patients in whom 99mTc-sestamibi was used and the group in whom 201Tl was used as the radioisotope (Table 1).

Data were acquired with a 2- or 3-detector gamma camera (Prism2000XP or Prism3000XP, Picker, Cleveland, OH, USA) for 180- or 360-degree arcs (in 20–30 six-degree-wide directions, taking 30 s per direction). For both radioisotopes, a low-energy high-resolution parallel multi-hole collimator was used. The maximum matrix size was 64×64. When taking the ECG-gated images, the R-R interval was divided by the R wave trigger into 8 equal portions. End-diastolic and end-systolic images were thus obtained. All patients were in sinus rhythm during the imaging. SPECT images were reconstructed from the data by a data processor (Odyssey VP, Picker) combined with a Butterworth filter (order 8; cutoff frequency 0.25 for 99mTc-sestamibi and 0.2 for 201Tl) and a ramp filter.

According to a method reported elsewhere\textsuperscript{18} each SPECT image was divided into 20 segments, with segments 1–3, 7–9, 13–14 and 19–20 corresponding to the areas perfused by the left anterior descending coronary artery, segments 4, 10 and 15–16 corresponding to the areas perfused by the right coronary artery, and segments 5–6, 11–12 and 17–18 corresponding to the areas perfused by the left circumflex coronary artery (Fig 1). The accumulation of radioisotope in the myocardium was visually evaluated by 2 cardiologists using a 5-grade scale: 0 (normal), 1 (slight reduction of uptake), 2 (moderate reduction of uptake), 3 (severe reduction of uptake) or 4 (absent of radioactive uptake). The total of the scores for all the segments during exercise and at rest was designated the summed stress score (SS) and the summed rest score (RS), respectively. The summed difference score (DS) was defined as summed SS minus summed RS. Disagreements in image interpretation were resolved by consensus. The radioactivity scores in each area perfused by different coronary arteries were defined as the regional SS, regional RS and regional DS values were calculated and divided by the number of segments involved, to yield the average regional SS, RS and DS.

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CABG and Gated SPECT

Wall motion score divided by the number of areas involved were calculated as well. The time-course of changes in the wall motion score for the entire left ventricle, as well as that for the revascularized and non-revascularized territories was compared. In addition, computer software developed by Nakata et al.4 was used to calculate the left ventricular end-diastolic wall thickness and end-systolic wall thickness, and the changes in these parameters following revascularization were analyzed (Fig 3).

Coronary Angiography

All patients underwent multi-direction coronary angiography, performed according to the Judkins’ method, before CABG. The degree of coronary artery stenosis was visually rated according to the AHA criteria.19 Significant stenosis was deemed as present when ≥75% narrowing of the diameter was noted. The presence or absence of collaterals was rated according to criteria reported previously.20

CABG

For all patients who undergo cardiac catheterization in Tokyo Medical University, the treatment strategy is discussed in clinical conference with the primary physicians, nuclear cardiologists, interventional cardiologists and surgeons. When coronary bypass surgery is indicated, CABG using standard techniques with complete revascularization is performed if technically and anatomically feasible.

Statistical Analysis

Results

Improvements in LV Blood Flow, Volume and Function Following CABG

Analysis of myocardial perfusion before and after CABG revealed that the summed DS (14.7±9.7  3.3±5.3; p<0.0001), the summed SS (26.2±14.9  9.6±9.9; p<0.0001), and the summed RS (11.5±9.9  6.3±5.3; p<0.0001) decreased significantly (Fig 4). Although the preoperative summed SS was <4 in 5 patients (11%), 4–13 in 14 (30%), and >13 in 28 (59%), the postoperative summed SS was <4 in 14 patients (30%), 4–13 in 20 (43%), and >13 in 13 (27%). The global wall motion score, as evaluated visually on gated SPECT images, decreased significantly (6.6±5.0  4.8±3.8; p<0.03) by CABG (Fig 4). Furthermore, as calculated from quantitative gated SPECT, end-diastolic volume (91.6±40.0  73.1±30.4 ml; p<0.0001, ESV=48.9±31.6  35.7±20.7 ml; p<0.0001, EF=50.4±11.6  53.4±11.2%; p<0.05) increased significantly (50.4±11.6  53.4±11.2%; p<0.05) after coronary artery bypass grafting.

Fig 3. End-diastolic and end-systolic wall thickness measurements. The segments of the SPECT images were assigned as follows, depending on each coronary territories: segments in the mid-portion of the anteroseptal area were assigned to the left anterior descending artery (LAD), segments in the mid-portion of the infaroposterior area to the right coronary artery (RCA), and segments in the mid-portion of the area lateral to the left circumflex artery (LCX).

Fig 4. Serial changes in the global summed stress score (SSS), summed rest score (SSR), summed differential score (SDS) and wall motion score (WMS) between before (open bars) and after (solid bars) coronary artery bypass grafting.

Fig 5. Changes in the end-diastolic volume, end-systolic volume and ejection fraction after coronary artery bypass grafting. EDV=91.6±40.0  73.1±30.4 ml; p<0.0001, ESV=48.9±31.6  35.7±20.7 ml; p<0.0001, EF=50.4±11.6  53.4±11.2%; p<0.05

Fig 6. Improvement in end-diastolic volume (ΔEDV), end-systolic volume (Δ ESV) and ejection fraction (ΔEF) in the segments with hypokinetic wall motion (solid bars) and the segments with normal wall motion (open bars) after coronary artery bypass grafting.

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fraction after revascularization being ≥50% in 33 patients (70%) and <35% in 4 (9%). In 23 patients with hypokinetic left ventricular wall motion before CABG, end-diastolic volume, end-systolic volume and ejection fraction improved more significantly after the bypass surgery than the improvement observed in the 24 patients without hypokinetic wall motion (Fig 6). After CABG, end-diastolic volume (99.7±25.3 vs 63.9±26.6 ml; p=0.0002) and end-systolic volume (50.3±16.6 vs 30.7±19.7 ml; p=0.004) was larger with 99mTc-sestamibi in comparison with 201TI, whereas the difference in the end-diastolic volume, end-systolic volume and ejection fraction with the revascularization, were similar (–6.7±27.3 vs –22.6±22.5 ml; p=NS, –6.8±14.7 vs –15.3±18.4 ml; p=NS, 0.3±6.6 vs 3.8±10.6%; p=NS, respectively).

**Improvement in Blood Flow, Wall Motion and Wall Thickness in the Revascularized Territories**

Among 141 coronary territories evaluated, 107 territories in 47 patients were revascularized and 34 territories in 28 patients were not, excluding 19 patients who underwent revascularization of all the 3 coronary arteries. The average regional DS, RS and wall motion score for the 107 revascularized territories decreased significantly after CABG (0.8±0.5 vs 0.2±0.3; p<0.0001, for DS, 0.6±0.6 vs 0.3±0.4; p<0.0001, for RS and 0.9±0.7 vs 0.7±0.5; p<0.05, for wall motion score) (Fig 7). The left ventricular end-diastolic wall thickness measured in the revascularized territories increased significantly postoperatively (8.1±0.8 vs 9.3±1.5 mm; p<0.0005), but the left ventricular end-systolic wall thickness did not change (13.0±1.7 vs 13.6±2.0 mm; p=NS) (Fig 8).

**Changes in Blood Flow, Wall Motion and Wall Thickness in the Non-Revascularized Territories**

After CABG, significant decreases were seen in the average regional DS (0.5±0.7 vs 0.2±0.5; p<0.03), average regional RS (0.5±0.8 vs 0.3±0.5; p<0.03) and average regional wall motion score (0.8±1.1 vs 0.5±1.0; p<0.03) of the 34 non-revascularized territories (Fig 7). The left ventricular end-diastolic wall thickness increased significantly postoperatively (8.0±1.4 vs 9.1±2.0 mm; p<0.03), whereas the left ventricular end-systolic wall thickness did not change (13.8±2.4 vs 13.9±2.5 mm; p=NS) (Fig 8). Of the 34 non-revascularized territories, 28 had been hypokinetic before CABG and in 8 of them, the wall motion improved after CABG. In these 8 territories, there was more collateral circulation than in the 20 territories in which no improvement of wall motion was observed (8/8 vs 5/20; p<0.0003).

**Discussion**

Using quantitative gated SPECT to evaluate 47 CAD patients before and after CABG, we were able to observe in detail the beneficial effects of coronary revascularization on the entire left ventricle, as well as its regional effects on the revascularized and non-revascularized territories. When the focus was on the entire left ventricle, coronary revascularization not only abolishes myocardial ischemia, but also increased myocardial blood flow at rest. It also reduced the left ventricular volume and increased the ejection fraction. These improvements were particularly significant in patients whose left ventricular wall motion had been hypokinetic before CABG. In patients whose wall motion has been normal before CABG, the main benefit of bypass surgery was reduced symptoms of myocardial ischemia. In contrast, in patients with abnormal wall motion before CABG, bypass surgery is expected to improve systolic wall motion by increasing the blood supply to hibernating myocardium. In the present study, a ≥5% increase in ejection fraction was found in 34% of the patients. Although careful assessments were not undertaken in a considerable number of patients before CABG, the results of the present study suggest that if the indications for CABG are determined from a thorough evaluation of myocardial ischemia, cardiac function, and myocardial viability using gated SPECT, this revascularization procedure will result in improved cardiac function in many patients.

Using gated SPECT before and after CABG can confirm the effectiveness of the treatment and can also predict the prognosis after the surgery. Adachi et al reported the usefulness of myocardial scintigraphy for predicting long-term outcome after CABG, using only perfusion data without functional assessment. Among the indicators that are obtained from gated SPECT, the summed SS, left ventricular ejection fraction and left ventricular end-systolic volume can serve as prognostic factors. In the present study of patients with CAD who required CABG, the summed SS improved to <4 in one-third of the patients after revascularization, and the left ventricular ejection fraction improved to ≥50% in two-thirds. In contrast, ≤30% of the patients had a summed SS of >13 and/or ejection fraction of <35%. These results suggest that gated SPECT may also help to
better stratify CAD patients even after CABG, though the actual prognosis of this patient cohort remains to be determined.

Gated SPECT can evaluate blood flow and function of the entire left ventricle, as well as regional left ventricular wall motion and thickness. Therefore, the emphasis of the present study was placed on comparing the changes observed after CABG between revascularized and non-revascularized territories. In the revascularized territories, not only was there alleviation of inducible myocardial ischemia, but improvements in myocardial blood flow at rest, end-diastolic wall thickness and regional wall motion were also observed. These improvements were also observed in non-revascularized territories. In most of the patients showing these improvements, there was adequate collateral development to the non-revascularized territories and it is apparent that blood flowed via these collaterals from the revascularized to the non-revascularized territories in sufficient volume to improve cardiac function. However, because the magnitude of the improvements in the myocardial perfusion scores of the non-revascularized territories were less than those of the revascularized territories, blood flow through the collaterals was probably less than the antegrade flow.

Study Limitation
In the present study, 99mTc-sestamibi and 201Tl were used for the gated SPECT studied before and after CABG. 99mTc-sestamibi is used frequently because of its high energy level, but although 201Tl is also used clinically for this purpose, its accuracy has not been established. 28,29 In the present study, the number of diseased vessels and the cardiac function at baseline were similar in the group of patients in whom 99mTc-sestamibi or 201Tl was used as the radioisotope. In these 2 groups, the degree of improvement in left ventricular volume and function after CABG was similar, except for smaller actual left ventricular volume as measured by 201Tl. Thus, even though some small differences existed between the 99mTc-sestamibi and 201Tl gated SPECT measurements, these radioisotopes have approximately similar results when used in an evaluation of the beneficial effect of CABG on myocardial function.

Conclusion
Coronary bypass surgery benefits most patients either by reducing the symptoms of myocardial ischemia or by increasing blood supply to hibernating myocardium to improve systolic wall motion. To evaluate the latter case, functional assessment using echocardiography is commonly done. However, the present study demonstrated that during a single examination using gated SPECT before and after CABG, the beneficial effects of bypass surgery regarding cardiac function, regional wall motion and wall thickness on the entire left ventricle, as well as its differential effects on revascularized and non-revascularized territories of the left ventricle, can be assessed in detail. Gated SPECT, therefore, is a powerful tool, particularly for assessing CAD patients who are candidates for bypass surgery.

References


