Correlations Between Resting Regional Wall Motion and Regional Myocardial Blood Flow (at Rest and During Exercise) in Infarct-Related Myocardium

— A Study With [\(^{13}\)N]Ammonia Positron Emission Tomography —

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We evaluated quantitatively the correlations between resting wall motion and regional myocardial blood flow (RMBF; at rest and during exercise) in infarct-related myocardium. The study was performed in 28 subjects: 21 patients who had previously suffered myocardial infarction of the anteroseptal wall, and 7 normal individuals. Positron emission tomography (PET) with \(^{13}\)N-ammonia was performed at rest and during low-grade exercise (bicycle ergometer fixed at 25 W for 6.5 min), and RMBF was measured quantitatively from the radioactivity in myocardial tissue and arterial blood. Resting regional wall motion was calculated using the centerline method on left ventriculographic findings. Resting regional wall motion was correlated with RMBF both at rest and during exercise in the infarct areas (anterior walls: y = \(-2.74 + 4.25 \times 10^{-2}x\), r = 0.43, at rest; and y = \(-2.48 + 3.04 \times 10^{-2}x\), r = 0.48, during exercise, p < 0.05; septal walls: y = \(-3.61 + 5.64 \times 10^{-2}x\), r = 0.62, at rest; and y = \(-3.46 + 4.31 \times 10^{-2}x\), r = 0.62, during exercise, p < 0.01). In each infarct-related wall, the coefficient (the slope) during exercise was smaller than that at rest (3.04 vs 4.25 and 4.31 vs 5.64 in each), and the infarct areas with preserved wall motion showed higher RMBF during exercise than those with reduced wall motion. Our results may show that wall motion depends on viable but ischemic myocardium in infarct-related walls.

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Key Words: Positron emission tomography; Regional myocardial blood flow; Regional wall motion; Ergometer exercise

Experimental studies have shown a correlation between regional wall motion and reduction in coronary blood flow\(^1\). In clinical studies using positron emission tomography (PET) with \(^{13}\)N-ammonia, a tracer, regional wall motion of infarct areas was related to the regional percent count increase in radioactivity from end-diastole to end-systole\(^2\) and to regional myocardial blood flow (RMBF)\(^3\). Furthermore, in recent studies using stress thallium-201 scintigraphy\(^3,4\) or stress PET with \(^{13}\)N-ammonia\(^5,6\), infarct areas with transient perfusion defects preserved regional wall motion compared with those with persistent perfusion defects. In the above studies, RMBF and regional wall motion in infarct areas were evaluated qualitatively by visual inspection. No attempt has been made to determine a correlation between regional wall motion and RMBF using quantitative estimates in a clinical study. We have developed methods of quantitatively evaluating RMBF using PET, making it possible to measure RMBF in infarct-related walls that...
show perfusion defects on thallium-201 scintigraphy.\textsuperscript{7,8} We measured RMBF at rest and during exercise using \textsuperscript{13}N ammonia PET in infarct-related anteroseptal walls, and evaluated quantitatively the correlations between RMBF (rest and exercise) and resting wall motion calculated using centerline methods on left ventriculography (LVG).

Methods

Study Patients

A total of 28 subjects (23 men and 5 women) were studied: there were 21 patients with myocardial infarction (MI) of anteroseptal walls and 7 normal subjects. The mean age was 60.1±8.6 years for MI subjects and 43.4±15.7 years for normal subjects. MI of the anteroseptal wall was diagnosed on the basis of clinical findings, the presence of an abnormal Q wave in leads V1 through V3 on electrocardiography (ECG), elevation of serum enzymes at the attacks, and stenosis of more than 50% of left anterior descending coronary artery as determined by coronary arteriography (CAG). The normal subjects were healthy and had no history of ischemic heart disease. PET, LVG, and CAG were performed about 1 month after the onset of MI. Informed consent was obtained from all patients. LVG was obtained in 30° right anterior oblique (RAO) and 60° left anterior oblique (LAO) projections. CAG was performed according to the Judkins method.\textsuperscript{9} The position and the degree of coronary artery stenosis were referenced visually using American Heart Association criteria\textsuperscript{10} from LVG findings. Ejection fraction (EF) was measured from LVG findings.

Analysis of Resting Regional Wall Motion

Resting regional wall motion was calculated using the centerline method on LVG as described by Sheehan et al.\textsuperscript{11} The end-diastolic and end-systolic phases were determined visually and, using these data, motion was measured along 100 chords drawn perpendicular to a centerline constructed midway between the end-diastolic and end-systolic contours. These data were measured automatically by the computer system. The motion of the 100 chords was normalized for heart size by dividing the length of the end-diastolic perimeter. As normal motion varies from chord to chord, the normalized motion at each chord was converted into units of normal standard deviation (SD) from the mean of normal wall motion, which had been obtained from 100 subjects with no previous coronary artery disease. The value of wall motion in each chord was expressed in SD of normal wall motion. The mean regional wall motion in each myocardial wall (the anterolateral, apical, posterobasal, posterolateral, midseptum) was calculated by averaging the chord data (SD) on myocardium for each view from RAO and LAO.

PET Study

RMBF was measured with \textsuperscript{13}N ammonia (half-life of \textsuperscript{13}N = 10 min) as a tracer, using a Headtome IV PET machine (Shimadzu). The spatial resolution for a static image at the center of the field of view was adjusted to 6 mm using a Butterfield filter. The PET study was performed at rest and during exercise. The exercise test was conducted in the supine position using a bicycle ergometer (Monark) at a fixed level of 25 W for a total period of 6.5 min. At both rest and exercise, we administered 370–740 MBq (10–20 mCi) of \textsuperscript{13}N ammonia by intravenous injection to the patient in the supine position. Immediately after injection of the tracer, arterial blood was sampled for 2 min at a constant rate of 10 ml/min, and 1 ml of the blood sample was taken to measure radioactivity with decay correction. At both rest and exercise, the PET scan was started 5 min after injection of the tracer, and was continued for 10 min. During exercise, \textsuperscript{13}N ammonia was injected intravenously 5 min after the beginning of exercise, and the patient continued to exercise for another 1.5 min. All of the PET data were automatically decay corrected in a computer and stored in the memory. The examination was performed in the same way as in previous studies.\textsuperscript{7,8}

Analysis of PET Images

Myocardial images with gated ECG were obtained by synchronizing the patient's R wave with the opening of the gate. The average R-R interval was divided into 5 frames. Data were collected from the first 4 frames. PET images of 5 slices were taken by 13-mm steps from the base of the left ventricle to the apex. Twenty images (transaxial images) were obtained from 4 frames of 5 slices. Of 5 images from the first time frame, which represented the end-diastolic phase of the left ventricle, 3 images were chosen for quantitative analysis of RMBF. The images of areas that correspond to the anterior, septal, lateral, and inferior walls of the left ventricle were allotted to the regions of interest (ROIs), and the radioactivity of each ROI was measured\textsuperscript{12}.

Quantitative Measurement of RMBF

The radioactivity of each ROI was presented as Q (cps/cm\textsuperscript{3}). \( \int_C \text{Ca}(t)dt \) (cps·min/ml) refers to the integration of radioactivity in the arterial blood withdrawn at a constant rate for 2 min. RMBF of
each ROI was calculated according to the equation of Hara et al.\textsuperscript{13}

\[
\text{RMBF (ml/min/100 cm}^3\text{)} = \frac{|Q/\text{E (Extraction)} - \int_0^t \text{Ca}(t)\,dt|}{100}
\]

where \text{E} represents extraction fraction, for which a value of 0.82 was used in our study.\textsuperscript{7,8,12} as described by Schelbert et al.\textsuperscript{14}

\textbf{Data Analysis}

Of the 3 analyzed PET images, the image at the apical slice level was used to evaluate the correlation between regional wall motion on LVG and RMBF, as shown in Fig 1. The septal area (wall) of the PET image was regarded as the wall of midseptum on LVG. The anterior area (wall) was regarded as the apical on LVG. RMBF at rest and during exercise were compared with regional wall motion on LVG in the anterior and septal walls. Comparison of the RMBF at rest and during exercise between infarct areas in patients with MI and normal areas of normal subjects was made using an unpaired Student's t test. In the comparison of resting regional wall motion and RMBF, statistical analysis revealed a linear correlation (coefficient value; \(r\)), and a paired Student's t test was used to compare variables. A \(p\) value of less than 0.05 was considered statistically significant. All data was presented as means \(\pm\) 1 SD.

\textbf{Results}

\textbf{Patient's Characteristics}

Table 1 shows CAG findings and EF in each patient. Of 21 patients with anterosertal MI, 14 patients had obstruction in segment 6 of the infarct-related vessel as revealed by CAG, and 7 patients had the obstruction in segment 7. Four patients had single-vessel disease, 5 had 2-vessel disease, and 12 had 3-vessel disease. Of

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Coronary arteriography (infarct-related vessel)</th>
<th>EF (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>M</td>
<td>Seg 6 99%</td>
<td></td>
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<tr>
<td>2</td>
<td>49</td>
<td>M</td>
<td>Seg 7 99%</td>
<td></td>
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<tr>
<td>3</td>
<td>43</td>
<td>M</td>
<td>Seg 7 100%</td>
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<tr>
<td>4</td>
<td>71</td>
<td>F</td>
<td>Seg 5 75%, Seg 6 100%</td>
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<tr>
<td>5</td>
<td>67</td>
<td>M</td>
<td>Seg 7 100%</td>
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<td>6</td>
<td>58</td>
<td>F</td>
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<td>M</td>
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<td>F</td>
<td>Seg 6 90%</td>
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<td>Seg 7 99%</td>
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<td>21</td>
<td>52</td>
<td>M</td>
<td>Seg 6 90%</td>
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\text{Abbreviations: LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; M, male; F, female; Seg, segment of obstructed coronary artery; EF, ejection fraction.}

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these, 7 patients showed an EF of more than 60% despite anteroseptal MI (mean EF 54.1±13.1%).

**Table 2** Regional Myocardial Blood Flow in Each Wall

<table>
<thead>
<tr>
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<th>RMBF (ml/min/100 cm³)</th>
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<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Exercise</td>
<td></td>
</tr>
<tr>
<td>Anterior wall</td>
<td>39.0±14.2***</td>
<td>45.7±22.0***</td>
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<tr>
<td>Infarction (n=21)</td>
<td>69.6±8.8</td>
<td>119.8±29.2**</td>
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<tr>
<td>Normal (n=7)</td>
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<td></td>
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<tr>
<td>Septal wall</td>
<td>60.3±20.4**</td>
<td>75.4±26.4***</td>
<td></td>
</tr>
<tr>
<td>Infarction (n=21)</td>
<td>88.0±14.2</td>
<td>136.9±26.9***</td>
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<tr>
<td>Normal (n=7)</td>
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</table>

* **p<0.01, ***p<0.001 (vs resting RMBF), ++p<0.01 (vs RMBF at rest or during exercise in normal areas). In 21 patients with prior myocardial infarction of anteroseptal wall, the infarct areas in the infarct-related anterior and septal walls were described as “Infarction”. In 7 normal subjects, the areas in the anterior and septal walls were described as “Normal.”

Abbreviations: RMBF, regional myocardial blood flow.

**Exercise Testing**

During low-grade exercise, no patient experienced chest pain. Both at rest and during exercise, there was no significant difference in heart rate and blood pressure at rest between 21 patients with MI and 7 normal subjects, but there was a significant difference in rate-pressure products (heart rate: 97±24 vs 113±13, p=NS; blood pressure: 157±26/83±19 vs 182±23/96±20, p=NS; and rate-pressure product: 15,295±4878 vs 20,600±3546, p<0.01).

**RMBF at Rest and During Exercise**

Table 2 shows the RMBF at rest and during exercise in the infarct areas (the anterior and the septal walls) in patients with anteroseptal MI. In each wall, the RMBF in these infarct areas was compared with the RMBF in normal subjects (the normal areas). The infarct areas showed significantly lower RMBF than the normal areas both at rest and during exercise (p<0.001). Exercise did not increase the RMBF in the infarct areas of anterior walls, but increased the

**Fig 2.** Correlation between resting regional wall motion measured by the centerline method on left ventriculography and regional myocardial blood flow (RMBF) measured by positron emission tomography (PET) with [¹⁵N]ammonia in the infarct-related anterior walls of 21 patients who had previously suffered myocardial infarction of the anteroseptal walls. Motion, RMBF at rest (top) and during exercise (bottom) are both correlated with wall motion. RMBF is shown on the abscissa and regional wall motion is shown on the ordinate. The numbers on each point of these graphs are patient numbers. The slopes and correlation coefficient (r) are shown. A p value of less than 0.05 was considered statistically significant.
INFARCT AREAS OF SEPTAL WALLS

Fig 3. Correlation between resting regional wall motion and regional myocardial blood flow (RMBF) in the infarct-related septal walls in 21 patients with prior myocardial infarction of anteroseptal walls, similarly to Fig 2. RMBF at rest (top) and during exercise (bottom) are both correlated with wall motion. RMBF is shown on the abscissa and regional wall motion is shown on the ordinate. Numbers on each point of these graphs are patient numbers. The slopes and correlation coefficient ($r$) are shown. A $p$ value of less than 0.05 was considered statistically significant.

RMBF in those of septal walls ($p<0.01$).

Correlation Between Resting Regional Wall Motion and RMBF in the Infarct-Related Walls

Fig 2 shows the correlation between resting regional wall motion and RMBF in the infarct-related anterior walls, and Fig 3 shows the correlation between those in the infarct-related septal walls. In each figure, RMBF at rest is shown at the top and RMBF during exercise is shown at the bottom. A linear correlation between resting regional wall motion and RMBF at rest was observed in the anterior walls (at rest: $y = -2.74 + 4.25 \times 10^{-2}x$, $r = 0.43$; during exercise: $y = -2.48 + 3.04 \times 10^{-2}x$, $r = 0.48$; $p < 0.05$). Similar results were obtained in the septal walls (at rest: $y = -3.61 + 5.64 \times 10^{-2}x$, $r = 0.62$; during exercise: $y = -3.46 + 4.31 \times 10^{-2}x$, $r = 0.62$; $p < 0.01$). The coefficients (the slopes) during exercise were smaller than those at rest (3.04 vs 4.25 in the anterior walls and 4.31 vs 5.64 in the septal walls). In the anterior walls, the group with severely reduced wall motion ($> -2.0$ SD, $n = 7$) showed lower RMBF both at rest and during exercise than the group with preserved wall motion ($\leq -2.0$ SD, $n = 14$) (29.8 ± 10.3 ml/min/100 cm$^3$ vs 43.5 ± 14.0 ml/min/100 cm$^3$ at rest and 32.3 ± 16.2 ml vs 52.4 ± 21.8 ml during exercise, $p < 0.05$). Similar results (regional wall motion $> -2.0$ SD, $n = 5$ vs $\leq -2.0$ SD, $n = 16$) were obtained in the septal walls (38.5 ± 15.3 ml vs 67.2 ± 17.0 ml at rest and 57.6 ± 21.9 ml vs 80.9 ± 25.8 ml during exercise, $p < 0.05$).

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Discussion

In the present study, the resting regional wall motion correlated linearly with RMBF in the infarct areas not only at rest but also during exercise. Tamaki et al. in their recent study, reported qualitatively that regional perfusion flow measured by $[^{13}]$NH$_3$ammonia PET and regional wall motion were relatively preserved in infarct-related walls, and that in those with transient perfusion defects on stress thallium-201 scintigraphy resting wall motion was better preserved than in those with persistent perfusion defects. However, they did not find a linear correlation between regional wall motion and RMBF. We observed linear correlations between resting regional wall motion and RMBF (at rest and during exercise) in the infarct areas using quantitative estimates. Furthermore, the coefficient (the slope) during exercise was smaller than that at rest, and infarct areas with preserved wall motion showed higher RMBF during exercise than those with reduced wall motion. Transient perfusion defect on stress thallium-201$_{15,16}$ or PET$_{17}$ myocardial perfusion imaging, and assessment of glucose utilization$_{18}$ in the infarct-related wall have been used to distinguish reversible ischemic myocardium from irreversible infarcted myocardium. The infarct-related wall that showed a large increase in RMBF induced by exercise was considered to be viable. Our results may show that wall motion depends on viable but ischemic myocardium in electrocardiographic Q wave regions.$^{19}$

In the present study, some infarct-related walls with reduced resting regional wall motion (value of regional wall motion $>about-2.0$ SD) showed high RMBF during exercise despite RMBF <50 ml at rest (patient No. 19 in the anterior wall, and patient No. 5 and 10 in the septal walls). Recent reports suggest that some myocardial walls with perfusion defects at rest as visualized by thallium scintigraphy or PET may contain substantial amounts of viable tissue.$^{17,20}$ In the chronic state, these infarct-related myocardia were considered to be viable despite severely reduced wall motion and low RMBF at rest. Thus, regional wall motion was correlated closely, but not completely, with RMBF because infarct-related wall was considered to show a different motion under the influence of the myocardial cellular process, which may prolong mechanical recovery.$^{21}$ In the present study, the rate-pressure products during exercise in patients with MI were lower than those in normal subjects. In the lateral walls of patients with MI, RMBF at rest in normal areas (which were perfused by coronary arteries without stenosis) that were distant from infarct areas (n=5) was not significantly different from RMBF in normal subjects (n=7); however, during exercise the remote areas showed lower RMBF than in normal subjects (at rest: $83.7 \pm 20.8$ ml/min/100 cm$^3$ vs $80.9 \pm 12.4$ ml/min/100 cm$^3$, p=NS; during exercise: $108.1 \pm 12.6$ ml vs $136 \pm 30$ ml during exercise, p<0.05). Rate-pressure product is a good indicator of the amount of energy (myocardial oxygen consumption; MVO$_2$) being used by the heart during exercise$^{22}$ similar to myocardial blood flow.$^{23}$ Our results may explain the difference in MVO$_2$ or cardiac function between patients with MI and normal subjects. In the present study we examined only the anteroseptal walls (obstruction of the left anterior descending coronary arteries), which were homogeneous, and we distinguished a different vascular distribution, which might influence the relation between wall motion and RMBF.$^{12}$

Our study has several limitations. Half of the 21 patients with anteroseptal MI had comparatively preserved function (EF $>$50%), and therefore the infarct-related walls were more likely to have had a viable myocardium. This might well have affected the results of our study. Our method of quantitation is detailed in our recent studies.$^{7,8}$ Low-grade and fixed exercise was used to quantitate RMBF (so as not to affect significantly the extraction of ammonia during exercise) in the present study, in the same way as in our previous study$^7$ which revealed a close relation between coronary artery stenosis and RMBF. A slight change in the extraction rate of $[^{13}]$NH$_3$ammonia by myocardium, which depended on perfusing flow$^{14,24}$ and a partial volume effect in myocardial perfusing image on PET influence the RMBF value.$^{25,26}$ We used ECG-synchronized gating to minimize a partial volume effect caused by wall motion of the myocardium. On the other hand, when the myocardial wall is thinner at the infarct area, the measured RMBF value may be lower than the actual RMBF even with the ECG-synchronized scan. Our procedure was not able to eliminate completely a partial volume effect, but this might not have imposed a serious problem clinically in our previous study.$^7$ Our method of quantitation (quantitative estimate) may be a compromise between numerical objectivity and visual distinction. In patients with relative flow defects, which have until now been evaluated by relative values, perfusion of remote myocardium influences the perfusion of infarct-related myocardium, particularly when the subject has 3-vessel disease. Furthermore, a large exercise-induced increase in RMBF in remote myocardium may underestimate the exercise-induced increase in RMBF in infarct-related myocardium. Regional wall motion in patients with multivessel coronary artery disease may
not reflect movement of the wall itself, because the movement of infarct-related walls is influenced by that of other walls. It is generally difficult to distinguish regional wall motion of the septal wall itself from abnormal antero-septal wall motion (akinesis or dyskinesis), and volume overload on the right ventricle affects septal wall motion. In the present study, the centerline method was used to analyze regional wall motion, because this method has been applied extensively for analyzing regional wall motion and comparing regional wall motion in different regions of the left ventricle, particularly in multivessel disease.

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References


