Improved Myocardial Ischemia and Left Ventricular Function during Exercise after Successful Percutaneous Transluminal Coronary Angioplasty

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Percutaneous transluminal coronary angioplasty (PTCA) was performed in 42 patients with effort angina, 28 (67%) of them underwent successful angioplasty. Treadmill exercise testing, thallium-201 myocardial scintigraphy and radionuclide ventriculography were performed before and after PTCA for evaluation of the improvement of myocardial ischemia and left ventricular function at rest and during exercise. The average exercise duration by treadmill testing in 14 successful cases increased from 14 ± 4 (mean ± S.D.) to 16 ± 2 minutes (p < 0.05).

Sixteen of 28 the patients were studied by thallium-201 myocardial scintigraphy. Before PTCA, regions of decreased thallium-201 uptake after exercise were observed in 12 of the 16 patients. After angioplasty, no distinct defects were recognizable in 9 of the 12 patients, and in the remaining three, a significant decrease in defects was recognized. Fifteen of the 28 patients were studied by radionuclide ventriculography. The mean ejection fraction was 61 ± 5% at rest and 56 ± 11% during exercise (N.S.) before PTCA. After angioplasty, the ejection fraction was unchanged at rest (61 ± 5 to 62 ± 4%), but increased significantly during exercise (62 ± 4 to 74 ± 4%, p < 0.001).

In conclusion, left ventricular function was improved by successful PTCA due to improvement of myocardial ischemia. The long term results require further study.

PERCUTANEOUS transluminal coronary angioplasty (PTCA) was introduced by Grünzig et al. in 1977 and has received widespread attention as a new treatment for selected patients with ischemic heart disease. In these patients, PTCA is an alternative management to coronary artery bypass operation. On the other hand, since complications with this method are by no means rare, care must be taken when selecting suitable patients for PTCA. The evaluation of the improvement of myocardial ischemia after PTCA is also thought to be important, but as yet it has not been well documented. In this study, we performed treadmill exercise testing pre- and post-PTCA for evaluation of the change of exercise capacity. Also, to determine the improvement of myocardial ischemia and left

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ventricular function during exercise, thallium-201 myocardial scintigraphy was performed at rest and during exercise before and after successful PTCA.

METHODS

Patient Selection

Between December 1980 and March 1984, PTCA was performed in 42 patients at the Heart Institute Japan, Tokyo Women's Medical College; they included 40 males and 2 females, with an average age of 51.6 years (range from 67 to 35).

All patients presented with effort-dependent angina and 13 had a history of myocardial infarction. Coronary arteriography (CAG) revealed a single lesion with more than 75% narrowing of the luminal diameter in the proximal portion of the left anterior descending artery in 30 patients, in the proximal portion of the left circumflex artery in one patient and in that of the right coronary artery in 8 patients. In the other patients, CAG revealed a double vascular lesion.

Coronary Angioplasty

About one week prior to PTCA, the patients received 250 mg of aspirin and 150 mg of dipyridamole for at least 2 days and one hour before, 10 mg of nifedipine and 10 mg of isosorbide dinitrate were given orally.

The PTCA was carried out according to the procedure described by Gruntzig et al. A bipolar pacing catheter (6F USCI) was placed either in the pulmonary artery or the right ventricle. A preformed guiding catheter (9F USCI or 9F ACS) was positioned at the appropriate coronary ostium and a coronary dilatation catheter (USCI, ACS or MEDITECH) with a 3.0 mm maximal balloon diameter was introduced through the guiding catheter.

Prior to dilatation, 0.3 mg of nitroglycerin was given sublingually and the dilatation was performed while the patient was receiving heparin (5000 IU). With the dilatation catheter positioned within the lesion, serial balloon inflations using controlled pressure of 8 to 10 atmospheres were performed.

Patients were monitored for at least 24 hours post-PTCA and discharged 7 to 10 days later. Aspirin, dipyridamole, nifedipine and isosorbide dinitrate were continued for one year. Follow-up CAG was performed 10 to 14 months post PTCA, or sooner, if clinically indicated.

PTCA was considered successful by angiographic criteria when there was more than a 20% decrease in the diseased luminal diameter.

Noninvasive Evaluation

Prior to PTCA, patients were evaluated by standard treadmill exercise testing, thallium-201 exercise and redistribution myocardial imaging, and radionuclide ventriculography at rest and during exercise unless clinically contraindicated. These studies were repeated 7 to 21 days after PTCA and again 12 months later.

Treadmill stress testing: 12 hours after discontinuation of nifedipine and isosorbide dinitrate, 14 patients underwent treadmill stress testing using a modified Bruce protocol. Cuff blood pressure and a standard 12-lead ECG were recorded every 3 minutes during exercise and for 9 minutes thereafter.

Myocardial scintigraphy: To perform myocardial imaging after exercise, 16 of the fasting patients exercised on a bicycle ergometer in the supine position until the appearance of angina or significant ischemic changes in the ECG, which was recorded continuously during the stress test, or until a submaximal heart rate was achieved under steady-state conditions. At this point, 3 mCi of thallium-201 chloride were injected i.v. and the patient continued to exercise for another 2 minutes. Exercise workloads, initially 15W, were increased stepwise in 15-W increments every minute. Imaging was started 5 minutes after exercise. Scintigrams were obtained in the 45° left anterior oblique, anterior and left lateral positions. Imaging was repeated after a 4-hour rest for identifying exactly the nature of perfusion defects on the exercise scintigrams.

Radionuclide ventriculography: 15 patients underwent radionuclide ventriculography at rest and during exercise. Before the procedure, 12 hours after discontinuation of nifedipine and any nitrates, technetium, 25 mCi was administered intravenously. Global left ventricular function was assessed by determining the ejection fraction, calculated from the ratio of radioactive emissions collected from the left ventricle. Electrocardiographic gating was employed in the organization of scintigraphic data into a series of images that spanned the average cardiac cycle. After studies were performed at rest, imaging was repeated during submaximal supine bicycle ergometer exercise.

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Fig. 1. Results of coronary angioplasty.
Angiographically unsuccessful cases are shown in the crosshatched area. Inability to cross the stenosis with the balloon catheter occurred in 12% and to enter the balloon catheter selectively occurred in 5% of patients. In 17% of patients, despite correct positioning of the balloon, the stenosis was unchanged (12%) or dilated insufficiently (5%) after balloon inflation.

Statistics
The results were expressed as mean ± standard deviation. The significance before and after PTCA was estimated by Student's unpaired t test.

RESULTS
Successful and Unsuccessful PTCA
PTCA was successful in 28 of the 42 patients (67%). In five of the 14 unsuccessful cases, the lesion could not be traversed due to its severity and rigidity. In two of them, catheters could not be selectively entered, and in the remaining seven cases, the lesion could not be dilated (5 cases) or was dilated insufficiently (2 cases) (Fig. 1).

In the 31 patients who had dilatation, the average degree of stenosis was 86.1 ± 9.1% before PTCA and was reduced to 47.1 ± 16.2% after angioplasty (p < 0.001). Angiographic results during follow-up (n = 10) performed 3 to 13.8 months (mean 9.1 months) after PTCA, demonstrate mean percent stenosis of 67.4 ± 23.9 of the four patients with recurrence of stenosis (defined as a more than 50% loss of gain in luminal diameter achieved with the previous PTCA). Two patients with worsened symptoms received bypass surgery (Fig. 2).

Complications
Four serious complications resulted from angioplasty in the total groups of 42 patients. One patient had coronary dissection after balloon inflation, two had acute coronary occlusion which was probably due to coronary spasm and the remaining patient had perforation of a coronary artery by a guide wire. In one of these four patients, emergency coronary bypass operation was performed and in another, elective bypass operation occurred two days later.
Fig. 4. Relationship between duration of pre-PTCA symptoms and PTCA results (B).
Among 31 patients with symptoms occurring less than one year pre-PTCA, 23 (74.2%) cases were successful. However, only 5 of patients (45.5%) with pre-PTCA symptoms of more than one year's duration underwent successful angioplasty.

Fig. 5. Exercise duration by treadmill exercise testing before and after PTCA.
Data represent increased exercise capacity after angioplasty in 13 patients, but decreased capacity in the remaining patient. The mean exercise duration is 14.4 minutes before and 16.2 after PTCA (p < 0.05).

Fig. 6. Comparison of exercise response after successful angioplasty in patients receiving exercise studies before and after angioplasty. Prior to PTCA, the mean peak heart rate at maximal exercise was 122.2 ± 22.2 beats/min and increased to 144.7 ± 22.2 beats/min following angioplasty (p < 0.005).

Relation of Successful PTCA to Duration of Prior Symptoms
In this series, there was certain relationship between duration of pre-PTCA symptoms and PTCA results. Mean duration of pre-PTCA symptoms in 28 patients with successful angioplasty was 8.7 ± 8.0 months (range 1 to 36 months), as compared with a mean duration of pre-PTCA symptoms of 12.6 ± 11.3 months (range 2 to 39 months) in 14 patients with unsuccessful PTCA (p < 0.05) (Fig. 3).

In other words, 23 of 31 patients (74.2%) whose pre-PTCA symptoms were of less than 1 year's duration were successfully dilated and 8 (25.8%) were unsuccessful; 5 of 11 patients (45.5%) with pre-PTCA symptoms of more than 1 year underwent successful angioplasty while in the remaining 6 (54.5%) it was unsuccessful.

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**Treadmill Stress Testing**

Fourteen of the 28 patients who subsequently had arteriographically determined successful PTCA underwent graded stress testing. Before angioplasty, eight patients stopped exercising because of angina, five because of ischemic ST changes and one because of leg fatigue. The average duration of exercise before angioplasty was $14.4 \pm 4$ minutes. After successful angioplasty, the duration of exercise increased to $16 \pm 2$ minutes ($p < 0.05$) (Fig. 5). Three of the 14 patients had angina during exercise after successful angioplasty, and one patient stopped exercising because of ischemic ST changes. The remaining 10 patients had no chest pain after PTCA, and they stopped because of leg fatigue or on attaining the target heart rate. Figure 6 demonstrates the change of maximum heart rate in these patients before and after angioplasty. Maximum heart rate improved significantly from $122.4 \pm 22.2$ to $144.7 \pm 13.1$ beats/min ($p < 0.005$). Estimated myocardial oxygen consumption at peak exercise, as judged by the heart rate-blood pressure product, also improved significantly from $19500 \pm 3300$ to $25300 \pm 3500$ ($p < 0.001$) (Fig. 7).

**Thallium-201 Exercise Scintigraphy**

Sixteen of 28 successful patients underwent thallium-201 exercise scintigraphy, which disclosed typical isolated zones of reduced activity after exercise that filled in as redistribution occurred in at least one projection in 12 patients. In four patients, however, no distinct abnormality was found on either the exercise or the resting scintigram. Of 12 patients with

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**TABLE 1 DATE OF THALLIM-201 EXERCISE SCINTGRAPHY BEFORE AND AFTER PTCA**

<table>
<thead>
<tr>
<th></th>
<th>Pre-PTCA</th>
<th>Post-PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M.T. Pos.: septal</td>
<td>Neg.</td>
</tr>
<tr>
<td>2</td>
<td>A.T. Pos.: anteroseptal anterolateral</td>
<td>Neg.</td>
</tr>
<tr>
<td>3</td>
<td>H.W. Pos.: septal apical</td>
<td>Neg.</td>
</tr>
<tr>
<td>4</td>
<td>K.U. Pos.: anteroseptal apical</td>
<td>Neg.</td>
</tr>
<tr>
<td>5</td>
<td>M.I. Pos.: anteroseptal apical</td>
<td>Neg.</td>
</tr>
<tr>
<td>6</td>
<td>A.M. Pos.: anteroseptal</td>
<td>Neg.</td>
</tr>
<tr>
<td>7</td>
<td>T.H. Pos.: anteroseptal apical</td>
<td>Neg.</td>
</tr>
<tr>
<td>8</td>
<td>T.M. Pos.: anteroseptal apical</td>
<td>Neg.</td>
</tr>
<tr>
<td>9</td>
<td>A.T. Pos.: inferior</td>
<td>Neg.</td>
</tr>
<tr>
<td>10</td>
<td>K.H. Pos.: anteroseptal</td>
<td>Pos.: apical (small)</td>
</tr>
<tr>
<td>11</td>
<td>S.S. Pos.: anteroseptal</td>
<td>Pos.: apical (small)</td>
</tr>
<tr>
<td>12</td>
<td>M.K. Pos.: anteroseptal apical</td>
<td>pos.: anteroseptal apical</td>
</tr>
<tr>
<td>13</td>
<td>M.I.</td>
<td>Neg.</td>
</tr>
<tr>
<td>14</td>
<td>K.S.</td>
<td>Neg.</td>
</tr>
<tr>
<td>15</td>
<td>I.I.</td>
<td>Neg.</td>
</tr>
<tr>
<td>16</td>
<td>S.W.</td>
<td>Neg.</td>
</tr>
</tbody>
</table>

Before PTCA, regions of decreased thallium-201 activity after exercise are observed in 12 patients. After successful angioplasty, no distinct defects are recognizable in 9 of 12 patients. In one patient, similar exercise-induced ischemia is seen before PTCA (case 12), and in the remaining two, a significant decrease of defects was seen (case 10, 11).

Neg. = negative; Pos. = positive
exercise-induced ischemia in the scintigrams, nine had normalization after angioplasty. In the three successful patients, the exercise-induced ischemia remained after angioplasty, and the ischemic region was either identical (one case) or only slightly less but still normal (two cases) (Table I).

Radionuclide Ventriculography
Fifteen of 28 successful patients were studied by radionuclide ventriculography at rest and during supine bicycle exercise before the procedure. The ejection fraction averaged 61 ± 5% at rest and 56 ± 11% (N.S.) during exercise before angioplasty (Fig. 8). The ejection fraction fell by 5% or more in nine patients, did not change in five, and increased by more than 5% in one patient (Fig. 9).

After successful angioplasty, the ejection fraction was unchanged at rest, remaining at 62 ± 4% (Fig. 8), but increased from 56 ± 11% to 74 ± 4% (p < 0.001) during exercise. The exercise ejection fraction after PTCA increased by more than 5% in all cases.

Fig. 8. Ejection fractions as determined by radionuclide left ventriculography at rest and during exercise, before and after PTCA. The average ejection fraction is 61 ± 5% at rest and 56 ± 11% during exercise (N.S.) before PTCA. After angioplasty, the exercise ejection fraction increases to 74 ± 4% (p < 0.001).

Fig. 9. Radionuclide left ventricular ejection fraction before and after PTCA at rest and with exercise.

The exercise ejection fractions after angioplasty increase by more than 5% in all cases.

DISCUSSION
Grüntzig et al.3 reported initial success in 64% of patients (cases) in their series in 1974, but the success rate was increased to 90% in 1982.4 It is thought that the success rate is increasing more and more in relation to advances in the technique and improvement of instruments. Accordingly, PTCA has proved to be an effective and safe procedure, and the indication for this procedure has expanded to include bypass grafts, multivessel disease and lesions which are usually difficult to dilate.5 But, because complication with this method are by no means rare, we have to be careful to select suitable patients for PTCA.

In our study, angioplasty was successful in 67% of patients with a considerable reduction of mean percent stenosis, from 86.1% to 47.1%. The success rate of PTCA in this series is relatively low and similar to that reported by Grüntzig et al.3 in 1979 (64% success) and by Stortzer et al.9 in 1979 (56% success). Following these preliminary results, the success rate should gradually increase.

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Criteria for our patient selection were adapted from those of Grünzig et al\textsuperscript{3} which are: (1) recent onset of angina, relatively refractory to medical therapy, compromised quality of life; (2) patients with objective evidence of reversible myocardial ischemia on electrocardiographic exercise testing, thallium-201 scintigraphy or gated blood pool scan; (3) patients with single vessel coronary atherosclerosis with lesions that were proximal, discrete, subtotal, relatively concentric and non-calcified. The lower success rate in this series, in spite of suitable patient selection, may have been due to lack of experience in the use of the technique.

Recurrence of stenosis has appeared in four of 10 patients. This is higher than that of other studies\textsuperscript{3,10} We thought that this higher recurrence rate might have originated from the small number of the follow up CAG. Of the four patients with restenosis, two patients received bypass surgery. Repeat PTCA has not been performed yet in this series, however if possible, we are going to try repeat PTCA because King et al\textsuperscript{11} found that the success rate of repeat PTCA is higher than that of the first procedure.

Similarly to Grünzig’s results\textsuperscript{3} there was a certain relationship between the duration of pre-PTCA symptoms and PTCA results (mean 8.7 months for successful, 12.6 months for unsuccessful) in our study. Of the patients with pre-PTCA symptoms in more than one year, the lesion could not be traversed in two patients, could not to dilated in four patients and was dilated insufficiently. There was no case in which the vessel could not be selectively entered. This observation suggests that duration of symptoms correlates with the softness or distortibility of an atheroma. However, Cowley et al\textsuperscript{12} suggested that duration of symptoms alone does not correlate with the softness or distortibility of an atheroma and does not become a restriction of patient selection. Sometimes, the patients with recent onset of symptoms may have unsuitable hard lesions. As mentioned above, the conclusion still remains obscure and awaits further studies.

Fourteen of successful patients underwent treadmill exercise testing. Before PTCA, 8 patients stopped exercise because of angina and 5 because of ischemic ST changes. After angioplasty, three patients had angina during exercise and another one stopped ischemic ST changes. Myocardial ischemia during exercise might be induced, because the luminal stenosis of these cases were remaining 60% or over in spite of successful angioplasty. The remaining 10 patients whose stenoses were improved less than 50%, stopped exercising because of leg fatigue or attained target heart rate. Furthermore, the exercise duration, maximum heart rate and myocardial oxygen consumption at peak exercise were improved significantly, although myocardial ischemia was induced after angioplasty.

We performed thallium-201 exercise scintigraphy in 16 of 28 successful patients. In four patients, no distinct abnormal perfusion defects were found on the exercise and the resting scintigrams before PTCA. The reason why the myocardial perfusion defect did not appear, these coronary stenoses of luminal diameter might be 70% narrowing or less.

After angioplasty, no distinct perfusion defects were recognizable in 9 cases. But in the remaining three cases, the exercise-induced perfusion defect was apparent. These defects had decreased significantly in the two patients (case 10, 11) and had been unchanged in the other. The perfusion abnormality remained since the luminal stenosis continued to be 75% or over in two cases. In one patient (case 12), typical abnormal perfusion defect was found to equal that of pre-PTCA, although the degree of stenosis was reduced from 90% to 50% after angioplasty. He had no chest pain and appeared to have no ischemic ST changes during treadmill stress testing, performed 5 days after PTCA. It is thought that a recurrent stenosis at the early stage of follow up or exercise induced spasm. We recommended that he underwent a repeat CAG, but he would only agree to have the CAG one year later. As Hirzel et al\textsuperscript{13} mentioned, thallium-201 exercise scintigraphy is the most popular technique. It clearly provides the best documentation of changes in regional myocardial activity after PTCA and proves it usefulness in documenting the success of angioplasty. It is also thought that thallium-201 scintigraphy can be used for serial studies since it is completely noninvasive and provides the documentation of ongoing changes in myocardial perfusion after coronary dilatation.

Radionuclide ventriculography was performed on 15 patients who had successful results at angiography. The mean ejection fraction during exercise increased from 56 ± 11 to 74 ± 4% and the exercise ejection fraction increased by more than 5% in all cases after PTCA. It is noted that coronary artery bypass surgery does not improve
myocardial function at rest but does improve the function of myocardial segments with exercise-induced myocardial ischemia. Similar improvement of reversible myocardial ischemia can be achieved by coronary angioplasty on the basis of the results presented in this study. Ken et al.\textsuperscript{15} reported a change of myocardial function before and after PTCA, and their results were the same as ours. In addition, they referred to the changes in not only global ejection fraction but in regional function during exercise before and after PTCA. It is important to examine the segmental function of the ventricular wall during exercise, since its improvement will be caused by an augmented capacity of the dilated coronary artery to deliver blood to previously ischemic myocardium, sufficient data was not available to allow for an inclusion in this investigation.

PTCA remains a promising technique for non-operative relief of symptomatic coronary stenoses in patients with ischemic heart disease. However, before PTCA is undertaken, the risks of emergency bypass surgery, myocardial infarction and rapid disease progression at the dilatation site should be considered. The management of the patients who have undergone PTCA must await further examination to determine long-term results and comparative evaluation with medical and surgical therapy in patients with coronary artery disease.

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