Quantitative Evaluation of Exercise Tl-201 Myocardial Scintigraphy Before and After Transluminal Coronary Angioplasty
A Preliminary Report

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SUMMARY
Quantitative evaluation of exercise Tl-201 myocardial scintigraphy was carried out to determine the effect of transluminal coronary angioplasty (TCA) in 15 patients with critical coronary artery stenoses (≥70%). Thirteen lesions were successfully dilated (reduction in stenosis by more than 30%); two were unsuccessful. Calculated indices from Tl-201 myocardial scintigraphy, using a semi-automatic computer image processing system, included washout factor (WF), vitality index (VI) and redistribution factor (RDF). No changes were noted in WF before and after dilatation. The VI increased in successfully dilated patients from 66.3±8.5% (mean±SD) to 77.8±10.9% (p<0.001) in the areas perfused by the vessels containing the lesions. The RDF decreased significantly after dilatation from 4.4±6.1% to 1.2±2.8% (p<0.05) 1 hour after exercise and from 10.4±7.5% to 4.1±4.2% (p<0.01) 3–4 hours after exercise. From these results, we conclude that the perfusion of ischemic areas distal to critical coronary artery stenoses improves following successful dilatation. Tl-201 myocardial scintigraphy was shown to be very useful in the evaluation of TCA.

Additional Indexing Words:
Exercise Tl-201 myocardial scintigraphy Transluminal coronary angioplasty Myocardial perfusion Critical coronary artery stenosis

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THE technique of transluminal angioplasty, devised by Dotter and Judkins for the treatment of atheromatous obstruction of the femoral artery was introduced in modified form by Gruntzig for the treatment of coronary artery disease. This method can effectively reduce highly stenotic coronary lesions and provide early recovery of ischemic but viable myocardium.

Exercise Tl-201 myocardial scintigraphy has been widely used for the evaluation of regional myocardial ischemia. Non-invasive visualization of myocardial ischemia yields useful information on both the presence and localization of stenotic coronary artery lesions. In addition, the results of therapeutic interventions can be evaluated by this method. The purpose of the present investigation was to quantitatively assess the effects of transluminal coronary angioplasty (TCA) in exercise Tl-201 myocardial scintigraphy.

Methods

Patients

Fifteen patients (3 women and 12 men) with critical coronary artery stenoses were studied both before and within 1 week after TCA. They ranged in age from 31 to 60 years, with a mean age of 48 years. All patients had angina pectoris and ST-segment depression in the exercise electrocardiogram (ECG). They had 70% or greater obstruction of at least one major coronary artery. Thirteen patients had single-vessel disease; 1 had double-vessel disease and 1 had triple-vessel disease. Five patients had a history of previous myocardial infarction including ECG changes. In 13 patients, the acute results of TCA showed a reduction of the critical coronary artery stenoses by more than 30%.

Coronary arteriography

Selective coronary arteriography using Sones technique was performed immediately before and after TCA in all patients. The lesions in the left anterior descending (LAD, 11 patients), left circumflex (LCX, 1 patient) and right coronary artery (RCA, 4 patients) were found suitable for TCA, and the procedure was performed within a week. Pre- and post-TCA angiograms were interpreted by at least 2 experienced cardiologists who were not directly involved with the scintigraphic studies.

Exercise Tl-201 myocardial scintigraphy

Exercise Tl-201 myocardial scintigraphy (TMS) was performed 3 days before and 4 days after the TCA using an arm-assisted step test with continuous monitoring of leads V₄₋₆ and, when necessary, of additional limb leads. Work loads ranged from 50 to 200 watts with a mean of 110 watts.
Written informed consent was obtained in each patient. All antianginal drugs were discontinued at least 10 hours before the TMS.

A 2mCi bolus of thallous chloride (Tl-201) followed by a 5 ml normal saline flush was injected into a butterfly cannula placed in the forearm when angina, ischemic ST-depression of more than 1 mm, maximum fatigue or dyspnea appeared during exercise. Exercise was continued for 30–60 sec following the injection. The same work load was used in individual patients for comparison before and after the TCA. After TCA, Tl-201 was injected at 5.5 min if the above mentioned criteria for the cessation of exercise were not satisfied.

Myocardial imaging was begun within 5–10 min after intravenous administration of Tl-201 using a computer-assisted, monocrystal gamma camera (Dynacamera, Picker 4/11, interfaced on line to SIMIS 3 Informatek) with general purpose parallel-hole collimators in anteroposterior (AP), left anterior oblique 45° (LAO) and LAO 80°. Counting was carried out using a one-channel analyzer, with the window centered at 75 keV at a window width of 25%. Careful adjustment of field homogeneity was carried out before every investigation.

**Quantitative analysis**

The scanning time for each view was 400 sec. Scans were repeated 1 hour and 3–4 hours after exercise images. Images were acquired in a 64×64 matrix on magnetic disk. Data were imaged on a digital display matrix of 128×128 pixels (8 bit depth, 16K). The collected images analyzed after a single nine-point weighed smoothing without background subtraction. Each image was divided into 3 segments for a total of 9 segments numbered 1–9 (Fig. 1) and the region of interest (ROI) was determined visually. The size of the ROI was always adjusted to 4×4 channels (1 cm²), equivalent to the spatial resolution capability of our gamma camera.

The relationship between Tl-201 fixation abnormalities of the left ven-
tricular segments and the obstructed coronary arteries were determined as follows: abnormalities of the postero-septal myocardial area to RCA or LAD coronary artery disease; septum and anterior wall to LAD lesions; inferior with RCA disease; posterior segment with RCA or LCX lesions and posterolateral with LCX lesions.

**Determination of Tl-201 washout factors (WF)**

The washout of Tl-201 from the myocardium was determined over the region of maximum Tl-201 uptake (ROI\text{max}) as the ratio of count rates 1 hour and 3–4 hours after exercise (crtt\text{1,2}) and immediately after exercise (crtt\text{0}), carefully adjusting the same site in the same view.

\[
WF_{1,2} (%) = \left[ \frac{crtt_{1,2}}{crtt_0} \right]_{\text{ROI}_{\text{max}}} \times 100
\]

where, WF\text{1,2} are the washout factors at 1 hour and 3–4 hours after exercise, respectively.

**Determination of vitality index (VI)**

The VI is the ratio of the average count density in the ROI to the region of maximum uptake in the same image. This parameter was derived from the image obtained immediately after exercise. A region was considered abnormal if its average count rate was less than 85% of the average count rate for the maximally dense region of the same image; i.e. suggesting myocardial ischemia or fibrosis. VI is calculated as follows:

\[
VI (%) = \left[ \frac{(crtt_0)_{\text{ROI}}}{(crtt_0)_{\text{ROI}_{\text{max}}}} \right] \times 100
\]

For the patients with successful TCA, VI was determined visually in all ischemic segments. These ischemic segments were compatible with areas nourished by the "stenotic" coronary artery. For the 2 control patients (unsuccessful TCA), all 9 segments were calculated and 6 representative segments (anterior, apical, septal, inferior, posterolateral and posterior) were demonstrated. For the anterior segment of both groups, the lesser value of segments 1 or 2 (Fig. 1) was taken; the lesser value of segments of 2, 5, or 8 was taken for the apex. The same sites were carefully compared before and after TCA.

Regions of previous myocardial infarction were also included for the calculation of VI, because scintigraphic defects do not necessarily imply the presence of myocardial fibrosis or scars.

**Determination of the Tl-201 redistribution factor (RDF)**

The RDF represents the relationship between Tl-201 redistribution in the ROI 1 hour and 3–4 hours after exercise (RDF\text{1,2}) and the distribution of Tl-201 immediately after exercise. These parameters were expressed as
Case reports of typical patients

Case 1. E.B. a 47-year-old male patient with exertional angina of recent onset. Coronary arteriography disclosed 80% stenosis of the proximal segment of the LAD (Fig. 2). Exercise TMS was performed with a work load of 110 watts. At 4 min during exercise, the patient complained of chest pain; an ST-depression of 2 mm was seen in the ECG. Exercise was halted after 5 min. Initial Tl-201 scans revealed a lack of activity in the septum and a marked decrease of Tl-201 concentration in the apex and anterior wall. Delayed images showed a late accumulation of Tl-201 in anterior and septal segments (Fig. 3a).

The 80% LAD lesion was dilated to 20% (Fig. 2). After TCA, the patient performed an exercise test without any symptoms. The Tl-201 scans immediately after exercise showed almost normal perfusion (Fig. 3b). Quantitative analysis of these findings compared with pre- and post-TCA, are shown in Fig. 4.

Case 2. P.T. a 48-year-old male patient with an 8-month history of severe exertional angina. Coronary arteriography revealed a 95% stenosis of the right coronary artery and complete occlusion of the left circumflex branch. Exercise TMS was carried out with a work load of 80 watts. After
1 min of exercise, the ECG showed an ST-depression of 2 mm in leads $V_4$-$6$; angina pectoris appeared after 3 min. Exercise was terminated after 3 min 30 sec. Tl-201 scans 5 min after exercise revealed complete absence of tracer in the inferior, posterolateral and posterior segments (Fig. 5a). No redistribution was noted 1 hour after exercise. However, a marked redistribution in the inferior and posterior segments was noted 3.5 hours after
exercise.

TCA successfully reduced the obstruction of the RCA from 95 to 50% (Fig. 6). Tl-201 scans 5 min after exercise showed normal perfusion in the inferoposterior segments and slightly decreased tracer concentration in the posterolateral wall (Fig. 5b). Quantitative findings before and after TCA are shown in Fig. 7.

Results of TCA in the total patient population

The clinical, angiographic and Tl-201 scintigraphic data for all 15 patients included in this study are listed in Tables I and II. Data are expressed as mean±SD. Statistical analysis was done using a paired t test and considered significant at p<0.05.

Washout factor (WF)

The statistical calculation of WF was based upon the data from all 15 patients, because the Tl-201 washout rate from normal myocardium is the same in successfully and unsuccessfully treated patients. The WF 1 hour after exercise was 84.3±7.1% before TCA and 81.1±7.1% after TCA. WF 3–4 hours after exercise was 62.3±7.1% and 63.2±8.3%, respectively. These values are not statistically different (Fig. 8).

Vitality index (VI)

The VI increased in 21 of 24 segments (88%) studied. In 10 of 13 successfully treated patients, the VI increased by more than 10% in the
Fig. 5a. Case 2. Exercise Tl-201 images prior to TCA. Upper panel showing 5 min after exercise, middle 1 hour and lower panel 3.5 hours after exercise. Note an absence of activity in the inferior and posterior segments in early images with marked redistribution in the inferior and posterior walls in delayed images.

Fig. 5b. Post-TCA exercise Tl-201 images 5 min after exercise of the Case 1 patient. Note the marked improvement in Tl-201 activity in the inferior and posterior walls compared to pre-TCA.

regions supplied by the dilated vessels. The average VI was $66.3 \pm 8.5\%$ before the dilatation and it increased to $77.8 \pm 10.9\%$ after the procedure $(p<0.001, \text{Fig. 9})$. This indicates an immediate increase of coronary blood flow after successful dilatation.

In the two unsuccessful procedures, the VIs of 12 segments were evaluated
Fig. 6. Coronary arteriography of the patient described in Case 2. Ninety-five stenosis of the right coronary artery (left) was dilated to 50% after TCA.

STATISTICAL ANALYSIS OF TL-201

Fig. 7. Quantitative analysis of Tl-201 images of Case 2. The marked improvement in myocardial perfusion was noted after TCA which appears as an increase in the vitality index (VI) in the inferior and posterior segments and a significant reduction in the redistribution factor (RDF).

Statistically. The average VI was unchanged before (82.8±9.3%) and after TCA (82.4±9.3%), as shown in Fig. 9. These findings demonstrate the satisfactory reproducibility in the quantitative evaluation of TMS.

Redistribution factor (RDF)

In the successfully treated patients, the pre-TCA RDF 1 hour and 3–4
<table>
<thead>
<tr>
<th>No. of case, age, sex</th>
<th>Work load (watts)</th>
<th>% Stenosis of CA</th>
<th>Washout factor (%)</th>
<th>Vitality index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LAD</td>
<td>LCX</td>
<td>RCA</td>
<td>1 hour</td>
</tr>
<tr>
<td>6. 41 M</td>
<td>Before 170</td>
<td>80</td>
<td>0</td>
<td>81 &amp; 60</td>
</tr>
<tr>
<td>7. 47 M</td>
<td>After 170</td>
<td>40</td>
<td>0</td>
<td>84 &amp; 65</td>
</tr>
<tr>
<td>8. 57 M</td>
<td>Before 110</td>
<td>80</td>
<td>0</td>
<td>74 &amp; 61</td>
</tr>
<tr>
<td>9. 59 F</td>
<td>After 110</td>
<td>80</td>
<td>0</td>
<td>74 &amp; 61</td>
</tr>
<tr>
<td>10. 41 M</td>
<td>Before 170</td>
<td>70</td>
<td>0</td>
<td>78 &amp; 61</td>
</tr>
<tr>
<td>11. 60 M</td>
<td>After 170</td>
<td>40</td>
<td>0</td>
<td>84 &amp; 60</td>
</tr>
<tr>
<td>12. 46 M</td>
<td>Before 110</td>
<td>80</td>
<td>0</td>
<td>91 &amp; 71</td>
</tr>
<tr>
<td>13. 48 M</td>
<td>After 110</td>
<td>30</td>
<td>0</td>
<td>91 &amp; 71</td>
</tr>
</tbody>
</table>

Abbreviations: CA=coronary artery; LAD=left anterior descending; LCX=left circumflex; RCA=right coronary artery; Ant=anterior; Ap=apical; Sep=septal; Inf=inferior; Post=posterior.
hours after exercise were $4.4\pm 6.1\%$ and $10.4\pm 7.5\%$, respectively. These values decreased significantly after TCA to $1.2\pm 2.8\%$ and $4.1\pm 4.2\%$, respectively (Fig. 10). In the unsuccessfully treated patients, the pre-TCA RDF 1 hour and 3-4 hours after exercise were $1.3\pm 1.4\%$ and $5.2\pm 4.4\%$, respectively (Fig. 11). There was a tendency toward higher RDF after dilatation ($4.0\pm 2.5\%$ and $7.8\pm 5.4\%$).

**DISCUSSION**

*Percutaneous transluminal coronary angioplasty*

TCA is the non-operative dilatation of critical coronary artery stenosis using a balloon catheter system. Gruntzig et al. reported that the average luminal obstruction was reduced from 84 to 43% ($p<0.001$) and the average pressure gradient from 58 to 19 mmHg ($p<0.001$) in 32 patients; our results (83 to 36%, $p<0.001$) are similar.
Table II. Coronary Angiography and Computerized

<table>
<thead>
<tr>
<th>No. of case, age, sex</th>
<th>Work load (watts)</th>
<th>% Stenosis of GA</th>
<th>Washout factor (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>LAD</td>
<td>LCX</td>
</tr>
<tr>
<td>14. 57 M</td>
<td>Before 140</td>
<td>—</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>After 140</td>
<td>—</td>
<td>30</td>
</tr>
<tr>
<td>15. 40 M</td>
<td>Before 110</td>
<td>100</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>After 110</td>
<td>100</td>
<td>—</td>
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</table>

Abbreviations: Post. lat = posterolateral. Others are the same as in Table I.

**Vitality Index**

**Tl-201 myocardial scintigraphy**

Myocardial imaging using TMS is widely used in the diagnosis of coronary artery disease and the evaluation of aorto-coronary bypass surgery, especially in questions of bypass graft patency. Currently, Tl-201 myocardial scintigrams are interpreted visually and qualitatively. However, there are many factors which limit subjective interpretations and evaluations. For example, complete agreement in the visual interpretation of unprocessed
Tl-201 Images in 2 Patients with Unsuccessful TCA

<table>
<thead>
<tr>
<th>Vitality index (%) (Redistribution factor : %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ant</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>94 (1, 3)</td>
</tr>
<tr>
<td>94 (0, 0)</td>
</tr>
<tr>
<td>89 (2, 2)</td>
</tr>
<tr>
<td>91 (4, 4)</td>
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</tbody>
</table>

Fig. 10. Redistribution factors before (left panel) and after TCA (right panel). Note the marked reduction in the redistribution factors after successful TCA.

images was reported to be only 67% among 4 experienced investigators. Therefore, quantitative analysis is recommended to correct observer bias.

The sensitivity of Tl-201 myocardial images, incorporating analog and computerized scintigrams, ranges from 68 to 95% with a mean of 81%. The specificity is between 84 and 100% with a mean of 94%. Although there is obviously no difference in specificity between analog and computerized imagings, the sensitivity of computer-assessed imagings is superior to that of analog images. In addition, the sensitivity is influenced by the location of coronary artery stenosis. The sensitivity is highest for LAD lesions (89%), decreasing to 78% and 48% for RCA and LCX lesions, respectively. Our group comprised 11 LAD, 5 RCA lesions, and 1 LCX stenosis.

Reproducibility

The reproducibility of the exercise Tl-201 myocardial scintigram was
No significant changes were noted before and after the TCA.

The possible reasons for some reports claiming non-reproducibility of Tl-201 imagings include differences in myocardial uptake of Tl-201 on separate occasions, inadequate exercise techniques and data collection methods, the processing and display of data, and observer variability. In this study, washout factors were identical in coronary heart disease before and after TCA. Vitality indices in 12 segments (6 segments each of 2 patients) of unsuccessfully dilated patients did not change significantly. These findings support the reproducibility of the quantitative analysis of Tl-201 myocardial scintigrams in our study.

**Quantitative evaluation of Tl-201 imaging washout factors**

According to Hör et al., the post-exercise WFs in healthy subjects were $88\pm12\%$ and $79\pm10\%$ after 1 and 2 hours, respectively. In 25 patients with coronary artery disease, the washout factors were $86\pm10\%$ and $76\pm10\%$, respectively. No significant differences were noted between these 2 groups. In our subjects with critical coronary artery disease, the WF 1 hour after exercise was $84\pm7\%$, which was consistent with the other values.10)

**Vitality index**

The normal values of the minimal myocardial Tl-201 uptake ratio are reported to be more than 80% at rest and 75–80% by exercise imagings.18),22)–29) However, Buell et al.20) stated that although the minimal
myocardial Tl-201 uptake ratio (defined as the mean value minus twice the standard deviation) is close to 75%, the normal values are different in segments. Therefore, it is risky to use a uniform normal value in all left ventricular segments. In this study, we considered segments to be hypoperfused if the activity was below 85%, because we did not perform background subtraction. Hirzel et al. studied Tl-201 uptake before and within 3 weeks of TCA and reported VI values of 66±4% before the procedure and 86±5% after dilatation. We obtained similar values in our study.

Redistribution factor

The redistribution of Tl-201, with the filling-in of defects which is noted on delayed images, shows that the transient defects are due to stress-induced myocardial ischemia or underperfusion. The disappearance of these transient defects on serial imagings were found to result in the accumulation of Tl-201 in previously ischemic zones as well as in a more rapid washout from normal myocardium. In 19 patients with coronary artery disease, Hör et al. obtained exercise redistribution factors of 15±10% and 18±8% after 1 and 2 hours, respectively. In our study, cases with greater redistribution tended to improve more after successful dilatation.

The role of Tl-201 imagings in TCA

Tl-201 imagings play three roles in TCA. First, Tl-201 imagings are important in evaluating the condition of the myocardium to establish the indication for TCA. The viability of ischemic areas is assessed. Secondly, the effects of TCA can be evaluated by comparing pre- and post-TCA Tl-201 imaging, as in our study. Thirdly, the relationship between the patency of the dilated coronary artery and the ultimate prognosis may be established after a certain period of time. Generally speaking, the quantitative results of interpretation of the standard thallium set of photos are sufficient for daily clinical use. However, it is difficult to separate confidently subtle defects from normal by visual interpretation. Therefore, the quantitative interpretation methods presented here provide very useful information to follow up serial myocardial perfusion after TCA.

In our results, no relationship was detected between the increased thallium perfusion index assessed by VI and the percent stenosis dilatation. The reason for this is that there are many factors in addition to arterial luminal caliber that determine regional myocardial perfusion, such as elimination of collateral flow immediately after TCA. Also, although our cases are limited, the myocardial perfusion improved to the same degree both in LAD and RCA disease.
22. Lanaers A: Thallium-201 myocardial perfusion scintigraphy during rest and exercise.


