DIPYRIDAMOLE ELECTROCARDIOGRAPHY TEST FOR THE
ASSESSMENT OF THE SEVERITY OF
CORONARY ARTERY DISEASE

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The purpose of this study was to investigate the relationship of dipyridamole-induced ST changes to the severity of coronary artery disease. The subjects were 100 patients without myocardial infarction who underwent coronary arteriography for the diagnosis of coronary artery disease. The dipyridamole injection test (D) (0.568 mg/kg/4 min), and symptom-limited treadmill exercise test (T) were performed separately. Body surface electrocardiographic mapping of 87 leads was performed in both tests. The incidences of significant ST depression $\geq 0.10 \text{ mV}$, number of leads showing significant ST depression (nST) and the maximal voltage of ST depression (maxST) in D and T were compared to the number of diseased coronary arteries. In patients without significant coronary stenosis (0VD group), the incidence of ST depression in the dipyridamole test was significantly lower than that in the treadmill test (D 9% vs T 47%, p < 0.01). While, in one vessel disease (1VD), two vessel disease (2VD), and three vessel disease (3VD) groups, there was no significant difference in the incidence of ST depression between the dipyridamole test and the treadmill test (in 1VD, D 44% vs. T 65%; in 2VD, D 67% vs. T 93%; and in 3VD, D 93% vs. T 96%). In the dipyridamole test, nST was 0.6 ± 2.4 in 0VD, 4.5 ± 6.9 in 1VD, 4.1 ± 4.5 in 2VD, and 10.6 ± 8.1 in 3VD. Significant differences were found between 0VD and 1VD (p < 0.05), 0VD and 3VD (p < 0.01), 1VD and 3VD (p < 0.01), and 2VD and 3VD (p < 0.01). The maxST in the dipyridamole test was 0.02 ± 0.04 mV in 0VD, 0.10 ± 0.12 mV in 1VD, 0.13 ± 0.11 mV in 2VD, and 0.22 ± 0.11 mV in 3VD. Significant differences were found between 0VD and 1VD (p < 0.01), 0VD and 2VD (p < 0.01), 0VD and 3VD (p < 0.01), 1VD and 3VD (p < 0.01), and 2VD and 3VD (p < 0.01). For the diagnosis of 3VD, the dipyridamole ECG test had a high sensitivity (93% vs 96%), higher specificity (68% vs 38%, p < 0.01), and higher predictive accuracy (75% vs 54%, p < 0.01) than the treadmill test. For the detection of one or more stenotic coronary arteries, the dipyridamole test had a lower sensitivity (70% vs 85%, p < 0.05), but higher specificity (91% vs 53%, p < 0.01), and as high a predictive accuracy (77% vs 74%) compared with the treadmill test. This study demonstrated that the dipyridamole ECG test was useful in stratifying the severity of coronary artery disease. Dipyridamole ECG was both sensitive and specific for the detection of 3VD. (Jpn Circ J 1992; 56: 223–234)

Key words:
Key words: Dipyridamole
Myocardial ischemia
ST depression
Number of diseased coronary artery

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INTRAVENOUS infusion of dipyridamole has been used to detect coronary artery disease by myocardial scintigraphy\(^1\)\(^-\)\(^7\) echocardiography\(^8\)\(^-\)\(^\)\(^12\) radionuclide ventriculography\(^13\) and also in electrocardiography\(^14\)\(^-\)\(^18\). Although it is an inexpensive, safe and feasible method not requiring a special technique, the dipyridamole electrocardiography test has not been used as much as dipyridamole scintigraphy or dipyridamole echocardiography. One of the problems associated with the dipyridamole electrocardiography is that the incidence of dipyridamole-induced ST depression varies according to the investigator\(^2\)\(^,\)\(^4\)\(^,\)\(^5\)\(^,\)\(^7\)\(^,\)\(^12\)\(^,\)\(^14\)\(^-\)\(^18\) from 3%\(^2\) to 90%\(^8\) of patients with coronary artery disease. Differences in the patient population, such as the prevalence of previous myocardial infarction and the severity of coronary artery disease might affect the incidence of ST depression in the dipyridamole test\(^9\)\(^,\)\(^17\).

To establish the clinical utility of the dipyridamole electrocardiography test, we studied the incidence, extent and severity of ST depression in relation to the number of diseased coronary arteries. In patients with coronary artery disease of varying severity and without myocardial infarction, the dipyridamole test and the symptom-limited treadmill test were performed by use of body surface electrocardiographic mapping. Electrocardiographic parameters of ST depression in the dipyridamole test were compared to those in the treadmill test in relation to the number of stenotic coronary arteries.

SUBJECTS AND METHODS

Subjects
The subjects were 100 consecutive patients (67 men and 33 women, aged 40 to 73 years, mean 60 years) who had no evidence of myocardial infarction and underwent coronary arteriography for the examination of chest pain in the Yamagata University Hospital. They had (1) no history of myocardial infarction as shown by typical clinical symptoms and serum enzyme changes; (2) no diagnostic Q wave in the standard 12 lead ECG except for lead aVR, and no tall R wave in V1 (R/S≥0.5); (3) no other heart disease such as congenital heart disease, myocardial disease, or valvular heart disease; and (4) no conduction disturbance such as right bundle branch block, left bundle branch block, Wolff-Parkinson-White syndrome, or QRS duration longer than 120 msec. Patients with vasospastic angina were excluded from the study.

The subjects were divided into 4 groups according to the number of stenotic coronary arteries those without significant coronary artery stenosis (0VD group), one vessel disease (1VD) group, two vessel disease (2VD) group, and three vessel disease (3VD) group. Coronary stenosis equal to or greater than 70% of the luminal diameter was considered significant.

Informed consent was obtained from all the subjects before the study. The study protocol was approved by the Ethical Committee of the Yamagata University.

Coronary arteriography
Selective coronary arteriography was carried out in multiple projections according to the Judkins technique. Coronary angiograms were recorded on 35 mm film taken at 50 frames/sec using the Toshiba 9-inch image amplifier system (Angiorex/u-arm), and were evaluated by 2 or more examiners, who had no knowledge of the patients clinical history or the results of other tests. The percentage of stenosis in the luminal diameter was measured manually for each of the major coronary arteries; right coronary artery (RCA), left main trunk (LMT), left anterior descending artery (LAD), and left circumflex artery (LCX). Coronary stenosis equal or greater than 70% of the luminal diameter was considered significant. Patients with a stenosis in LMT were treated as having stenoses in both LAD and LCX.

Study protocol
All the patients underwent the dipyridamole infusion test and the treadmill test separately, within two weeks before or after the coronary arteriography. All medications, except for the sublingual use of nitrates, were stopped at least 24 hours before each test. The normal volunteers also underwent the dipyridamole test and the treadmill test separately.

Dipyridamole infusion test
Dipyridamole was infused at the rate...
TABLE I  CLINICAL CHARACTERISTICS OF THE SUBJECTS

<table>
<thead>
<tr>
<th></th>
<th>0VD</th>
<th>1VD</th>
<th>2VD</th>
<th>3VD</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>23</td>
<td>15</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>age (mean±SD)</td>
<td>57±8</td>
<td>61±8</td>
<td>60±5</td>
<td>63±6</td>
<td>60±7</td>
</tr>
<tr>
<td>gender (men/women)</td>
<td>19/15</td>
<td>19/4</td>
<td>11/4</td>
<td>18/10</td>
<td>67/33</td>
</tr>
</tbody>
</table>

VD = vessel disease, n = number of patients, NS = not significant.

of 0.568 mg/kg/4 min according to the method of Albro et al. into the antecubital vein. Blood pressure was measured before in fusion and at 1 min intervals after initiation of the injection. ECG (CM5) was monitored continuously and heart rate was measured at 30 sec intervals. Body surface mapping was recorded before and at 5, 10, 15, and 20 min after initiation of the injection. Aminophylline (125–250 mg i.v.), which specifically blocks the vasodilating action of dipyridamole, was administered when moderate to severe angina appeared.

**Treadmill exercise test**

All the subjects underwent symptom-limited exercise on a treadmill according to Bruce’s protocol. The exercise was terminated when moderate to severe angina, leg fatigue, dizziness, hypotension, 3 or more successive ventricular arrhythmias, or ST depression of 0.2 mV or more, were encountered. Blood pressure was measured before and at 1 min intervals during exercise. ECG (CM5) was monitored continuously and heart rate was measured at 30 sec intervals. Body surface mapping was recorded before, and 1.5 min after, the termination of the exercise.

**Body surface electrocardiographic mapping**

Body surface maps were recorded with an HPM-5100 unit (Fukuda Denso Co., Tokyo, Japan) or a VCM-3000 unit (Fukuda Denso Co., Tokyo Japan). Eighty-seven ECG leads were placed over the torso; 59 leads on the anterior chest and 28 on the back. The 87 ECGs were sampled simultaneously with the Wilson’s central terminal as reference, at a rate of 250 samples/sec (HPM-5100) or 1000 samples/sec (VCM-3000). The standard 12-lead ECGs were also sampled simultaneously. The flat portion of the PQ segment was chosen for the baseline. The data were recorded on a magnetic cassette tape in digital format. The resolution was 0.01 mV (HPM-5100) or 0.005 mV (VCM-3000) in the dynamic range of ±5 mV (HPM-5100) or ±10 mV (VCM-3000). The data were sampled at the resting expiratory level in the supine position.

Each lead was analyzed for ST-segment depression. Horizontal or downsloping ST depression of 0.10 mV or more, lasting 0.08 sec, was considered to be significant. The voltage of ST depression was measured at 0.04 sec after the J-point. The number of leads with significant ST depression (nST) and the maximal voltage of ST depression among the 87 leads (maxST) were examined for each recording. In the dipyridamole test, the greatest maxST recording either 5, 10, 15 or 20 min after the injection was chosen for each subject.

Also, the incidences of significant ST depression were examined by the 87-lead ECG mapping (MAP) and by the standard 12-lead ECG in the dipyridamole test and in the treadmill test. The test was judged to be positive when significant ST depression was found in at least one lead.

**Statistical analysis**

Quantitative data were expressed as mean±SD. Statistical comparisons were made by the analysis of variance, one-way analysis of variance, and chi-square test; p < 0.05 was considered significant. The sensitivity, specificity, and predictive accuracy efficiency of the test were calculated as follows: sensitivity = TP/(TP + FN) × 100, specificity = TN/(TN + FP) × 100, predictive accuracy = (TP + TN)/(TP + FN + FP + TN) × 100; where TP = true positive, TN = true negative, FP = false positive, FN = false negative.
Fig. 1. Body surface distribution of ST depression in the dipyridamole test (0.568 mg/kg/4 min), and the treadmill exercise test in a patient of 3 vessel disease. Eighty-seven lead points were arranged lattice like (13 × 7 matrix), except for four lead points in both midaxillary regions. Columns A, E, and I were positioned in the right midaxillary, midsternal, and left midaxillary lines, respectively. Lead points E6 and E4 were located on the second and fifth intercostal space, respectively. Leads G4, H4, and I4 corresponded to leads V4, V2, and V6 respectively. ECG leads with significant ST depression were surrounded by solid line. At rest (a), ST depression was not observed in any lead. In the dipyridamole test (b), 10 min after the beginning of injection, significant ST depression was observed on the left anterior to lateral chest as well as in the treadmill test (c).
Fig. 2. Body surface distribution of ST depression in a patient without significant coronary artery stenosis. Significant ST depression was not found in any lead at rest (a) and in the dipyridamole test (b). However, in the treadmill test (c), ST depression was found in four leads on the left anterior chest.

RESULTS

Number of Stenotic Vessels and the Clinical Characteristics

The 100 subjects were divided into 0VD, 1VD, 2VD, and 3VD groups according to
TABLE II INCIDENCE OF ST DEPRESSION IN THE DIPYRIDAMOLE TEST AND IN THE TREADMILL TEST

<table>
<thead>
<tr>
<th></th>
<th>0VD</th>
<th>1VD</th>
<th>2VD</th>
<th>3VD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>23</td>
<td>15</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>MAP D</td>
<td>3 (9%)**</td>
<td>10 (44%)</td>
<td>10 (67%)</td>
<td>26 (93%)</td>
<td>49 (49%)**</td>
</tr>
<tr>
<td>T</td>
<td>16 (47%)</td>
<td>15 (65%)</td>
<td>14 (93%)</td>
<td>27 (96%)</td>
<td>72 (72%)</td>
</tr>
<tr>
<td>12-lead D</td>
<td>2 (6%)*</td>
<td>10 (44%)</td>
<td>8 (53%)</td>
<td>24 (86%)</td>
<td>44 (44%)**</td>
</tr>
<tr>
<td></td>
<td>8 (24%)</td>
<td>14 (61%)</td>
<td>11 (73%)</td>
<td>24 (86%)</td>
<td>57 (57%)</td>
</tr>
</tbody>
</table>

VD=vessel disease, n=number of patients, MAP=body surface ECG mapping, D=dipyridamole test, T=treadmill test.
*: p<0.05 vs. T; **: p<0.01 vs. T.

TABLE III EXTENT AND SEVERITY OF THE ST DEPRESSION IN THE DIPYRIDAMOLE TEST AND IN THE TREADMILL TEST

<table>
<thead>
<tr>
<th></th>
<th>0VD</th>
<th>1VD</th>
<th>2VD</th>
<th>3VD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>23</td>
<td>15</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>nST D</td>
<td>0.6±2.4*</td>
<td>4.5±6.9</td>
<td>4.1±4.5*</td>
<td>10.6±8.1</td>
<td>4.8±6.9*</td>
</tr>
<tr>
<td>T</td>
<td>2.2±3.6</td>
<td>4.4±6.4</td>
<td>8.0±5.5</td>
<td>11.2±7.8</td>
<td>6.1±6.9</td>
</tr>
<tr>
<td>maxST (mV) D</td>
<td>0.02±0.04**</td>
<td>0.10±0.12</td>
<td>0.13±0.11</td>
<td>0.22±0.14</td>
<td>0.11±0.13**</td>
</tr>
<tr>
<td>T</td>
<td>0.08±0.07</td>
<td>0.13±0.13</td>
<td>0.16±0.06</td>
<td>0.22±0.11</td>
<td>0.14±0.15</td>
</tr>
</tbody>
</table>

Values are expressed in mean±SD.
VD=vessel disease, n=number of patients, MAP=body surface ECG mapping, D=dipyridamole test, T=treadmill test, nST=number of leads with significant ST depression, maxST=maximal voltagle of ST depression among the 87 leads.
*: p<0.05 vs T; **: p<0.01 vs T.

The clinical characteristics of each group are shown in Table I. There was no statistically significant difference in the age and gender among the four groups.

Electrocardiographic Changes in the Dipyridamole Test and in the Treadmill Test

Electrocardiographic changes of representative cases are shown in Fig. 1 and Fig. 2. In a patient with 3VD, Fig. 1, significant ST depression was observed on the left anterior to lateral chest in the dipyridamole test as well as in the treadmill test. However, in a patient with 0VD, Fig. 2, no ST depression was observed in the dipyridamole test. In the treadmill test, ST depression was found in several leads on the left anterior chest.

Incidence of ST depression
The incidence of significant ST depression in the dipyridamole test and in the treadmill test are shown in Table II. By the 87-lead mapping (MAP), in the 0VD group, the incidence of ST depression in the dipyridamole test was significantly lower than that in the treadmill test (D 9%, T 47%, P<0.01). While, in the 1VD group and the 2VD group, the incidence of ST depression in the dipyridamole test was lower but had no significant difference compared to the treadmill test (in the 1VD group, D 44% vs T 65%, and in the 2VD group, D 67% vs T 93%). In the 3VD group, the dipyridamole test had as high an incidence as the treadmill test (D 93% vs T 96%). The total incidence of ST depression in this study group was 49% in the dipyridamole test and significantly lower dipyridamole test and 57% in the treadmill test (p<0.01). The incidence of ST depression, was the same for 12-lead ECG as MAP. In the 0VD group, the incidence of ST depression in the dipyridamole test was lower than that in the treadmill test.
Diprydamole ECG test in CAD

![Graphs showing changes in ST and maxST](image)

**Fig.3.** Group mean value of nST in the diprydamole test and the treadmill test.

**Fig.4.** Group mean value of maxST in the diprydamole test and the treadmill test.

**Table IV** Changes in blood pressure, heart rate, and pressure products in the diprydamole test and the treadmill test

<table>
<thead>
<tr>
<th></th>
<th>0VD</th>
<th>1VD</th>
<th>2VD</th>
<th>3VD</th>
<th>Total</th>
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<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>23</td>
<td>15</td>
<td>28</td>
<td>100</td>
</tr>
<tr>
<td>D rest HR (min)</td>
<td>65.3 ± 10.9</td>
<td>62.5 ± 8.5</td>
<td>59.4 ± 10.6</td>
<td>64.9 ± 10.5</td>
<td>63.7 ± 10.3</td>
</tr>
<tr>
<td>peak HR (min)</td>
<td>80.9 ± 14.2**</td>
<td>81.1 ± 15.7*</td>
<td>74.0 ± 14.2**</td>
<td>77.1 ± 12.9**</td>
<td>78.9 ± 14.3**</td>
</tr>
<tr>
<td>rest sBP (mmHg)</td>
<td>134.2 ± 19.1</td>
<td>151.3 ± 26.7</td>
<td>137.0 ± 15.6</td>
<td>150.4 ± 28.7</td>
<td>143.0 ± 24.5</td>
</tr>
<tr>
<td>peak sBP (mmHg)</td>
<td>129.8 ± 18.2</td>
<td>149.7 ± 25.5*</td>
<td>135.0 ± 22.3</td>
<td>151.0 ± 22.5**</td>
<td>141.1 ± 23.7</td>
</tr>
<tr>
<td>rest PRP (10^6 mmHg/min)</td>
<td>0.87 ± 0.18</td>
<td>0.94 ± 0.19</td>
<td>0.81 ± 0.15</td>
<td>0.97 ± 0.20</td>
<td>0.91 ± 0.18</td>
</tr>
<tr>
<td>peak PRP (10^6 mmHg/min)</td>
<td>1.05 ± 0.23**</td>
<td>1.23 ± 0.39**</td>
<td>1.01 ± 0.29**</td>
<td>1.17 ± 0.29**</td>
<td>1.11 ± 0.31**</td>
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<tr>
<td>T rest HR (min)</td>
<td>75.1 ± 9.7</td>
<td>69.1 ± 9.1</td>
<td>70.7 ± 13.8</td>
<td>74.3 ± 10.5</td>
<td>72.9 ± 10.5</td>
</tr>
<tr>
<td>peak HR (min)</td>
<td>132.5 ± 26.6**</td>
<td>122.7 ± 24.4*</td>
<td>116.8 ± 17.4**</td>
<td>107.6 ± 21.8**</td>
<td>120.9 ± 23.6**</td>
</tr>
<tr>
<td>rest sBP (mmHg)</td>
<td>135.8 ± 21.6</td>
<td>146.0 ± 28.9</td>
<td>135.2 ± 20.6</td>
<td>148.4 ± 23.3</td>
<td>141.6 ± 24.2</td>
</tr>
<tr>
<td>peak sBP (mmHg)</td>
<td>170.6 ± 26.7**</td>
<td>176.2 ± 31.1**</td>
<td>160.8 ± 37.1**</td>
<td>164.9 ± 27.6**</td>
<td>168.8 ± 29.7**</td>
</tr>
<tr>
<td>rest PRP (10^6 mmHg/min)</td>
<td>1.02 ± 0.22</td>
<td>1.00 ± 0.17</td>
<td>0.95 ± 0.20</td>
<td>1.11 ± 0.22</td>
<td>1.02 ± 0.21</td>
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<tr>
<td>peak PRP (10^6 mmHg/min)</td>
<td>2.25 ± 0.56**</td>
<td>2.16 ± 0.60**</td>
<td>1.90 ± 0.60**</td>
<td>1.77 ± 1.48**</td>
<td>2.05 ± 0.59**</td>
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</table>

Values are expressed as mean ± SD.

Abbreviations: HR = heart rate, sBP = systolic blood pressure, PRP = pressure rate products.

*; p < 0.05 vs. 0VD, **; p < 0.01 vs. 0VD, ***; p < 0.01 vs. rest.

(D 6% vs. T 24%, p < 0.05). In the 1VD, 2VD, and 3VD groups, there was no significant difference between the incidences in the diprydamole test and the treadmill test.

The extent and maximal voltage of ST depression

*Japanese Circulation Journal  Vol.56, March 1992*
TABLE V SENSITIVITY, SPECIFICITY AND PREDICTIVE ACCURACY OF THE DIPYRIDAMOLE TEST FOR 3VD

<table>
<thead>
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<th>sensitivity (%)</th>
<th>specificity (%)</th>
<th>predictive accuracy (%)</th>
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<tr>
<td>MAP D</td>
<td>93</td>
<td>68**</td>
<td>75**</td>
</tr>
<tr>
<td></td>
<td>96</td>
<td>38</td>
<td>54</td>
</tr>
<tr>
<td>12-lead D</td>
<td>86</td>
<td>72*</td>
<td>76*</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>54</td>
<td>63</td>
</tr>
</tbody>
</table>

MAP = body surface ECG mapping, D = dipyridamole test, T = treadmill test.
*; p<0.05 vs T, **; p<0.01 vs. T.

TABLE VI SENSITIVITY, SPECIFICITY AND PREDICTIVE ACCURACY OF THE DIPYRIDAMOLE TEST FOR ONE OR MORE STENOTIC ARTERIES

<table>
<thead>
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<th>specificity (%)</th>
<th>predictive accuracy (%)</th>
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</thead>
<tbody>
<tr>
<td>MAP D</td>
<td>70*</td>
<td>91**</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>53</td>
<td>74</td>
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<tr>
<td>12-lead D</td>
<td>64</td>
<td>94*</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>74</td>
<td>76</td>
<td>75</td>
</tr>
</tbody>
</table>

MAP = body surface ECG mapping, D = dipyridamole test, T = treadmill test.
*; p<0.05 vs T, **; P<0.01 vs. T.

test, the extent of the ST depression, nST by the dipyridamole test was significantly smaller in the 0VD group (p<0.05), and in the 2VD group (p<0.05). But in the 1VD and 3VD groups, there was no significant difference between the nST in the dipyridamole test and the treadmill test. The maxST in the 0VD group was significantly smaller than in the treadmill test. However, no significant difference was observed between maxST for both tests in the 1VD, 2VD, and 3VD groups.

Fig. 3 compares the group mean value of nST in the dipyridamole test and the treadmill test among 0VD, 1VD, 2VD and 3VD groups. The nSTs in the dipyridamole test, were significantly different 0VD vs 1VD (p<0.05), 0VD vs 3VD (p<0.01), 1VD vs 3VD (p<0.01), and 2VD vs 3VD (p<0.01). Significant difference were also found in nST of treadmill test 0VD vs 2VD (p<0.01), 0VD vs 3VD (p<0.01), and 1VD vs 3VD (p<0.01). 2VD vs 3VD, nST had significant differences in the dipyridamole test but not in the treadmill test.

Fig. 4 compares the group mean values of maxST in the dipyridamole test and the treadmill test. For maxST in the dipyridamole test, significant differences were found 0VD vs 1VD (p<0.01), 0VD vs 2VD (p<0.01), 0VD vs 3VD (p<0.01), 1VD vs 3VD (p<0.01), and 2VD vs 3VD (p<0.01). In the treadmill test, maxST had difference between 0VD vs 1VD (p<0.05), 0VD vs 2VD (p<0.01), 0VD vs 3VD (p<0.01), and 1VD vs 3VD (p<0.01). With the exception of 1VD vs 2VD, maxST of each group in the dipyridamole test differed. However, there was no significant difference between the maxST in the treadmill test between neither and 3VD, nor between 1VD and 2VD. Thus, as for 2VD vs 3VD, only nST and maxST in the dipyridamole test showed a significant difference, while those in the treadmill test did not.

Changes in heart rate, blood pressure, and pressure rate products

The changes in heart rate (HR), systolic blood pressure (sBP), and pressure rate product (PRP) of the dipyridamole test and the treadmill test for each subgroup are shown in Table IV. In the dipyridamole test, HR and
PRP increased slightly, while sBP did not show a significant changes. In the treadmill test, HR, sBP and PRP increased significantly.

**Diagnostic ability for 3VD and 0VD**

We tested the diagnostic ability of the dipyridamole test for 3VD and all coronary artery disease in comparison to the treadmill test. Significant ST depression in one or more leads was assigned to be positive. The sensitivity, specificity, predictive accuracy as found by 87-lead ECG mapping (MAP) and by standard 12-lead ECG (12 lead) are shown in Tables V and VI.

In the diagnosis of 3VD (Table V), the sensitivity of ST depression in the dipyridamole test was 93%, and comparable to that in the treadmill test (96%). The specificity of the dipyridamole test was 68% and significantly superior to the treadmill test (38%, p < 0.01). Also, the dipyridamole test was superior to the treadmill test in the predictive accuracy (D 75%, T 54%, p < 0.01). By use of the 12-lead ECG, the dipyridamole test had as high a sensitivity, and higher specificity and predictive accuracy than the treadmill test.

Table VI shows the diagnostic ability of the two tests for the detection of one or more stenotic coronary arteries. By MAP, the dipyridamole test had lower sensitivity (D 70% vs T 85%, p < 0.05), but higher specificity (D 91% vs T 53%, p < 0.01) than the treadmill test. There was no significant difference between the predictive accuracies of the two tests (D 77% vs T 74%). By 12-lead ECG, the dipyridamole test had higher specificity and as high sensitivity and predictive accuracy as the treadmill test. The higher specificity for coronary artery stenosis was characteristic of the dipyridamole ECG.

**DISCUSSION**

The dipyridamole electrocardiographic test

Because of its safety and inexpensiveness, ECG is used as a screening test for heart diseases. Since Tauchert et al. first demonstrated the ECG changes after dipyridamole injection in 1976, several studies have demonstrated the usefulness of the dipyridamole ECG test for diagnosis of coronary artery disease. However, few have investigated the relationship between the ECG changes and the severity of coronary artery disease in a large population. Such data are needed if the dipyridamole ECG test is to be used as a screening test of coronary artery disease. The purpose of this study was to examine the incidence, extent and the severity of ST depression in relation to the number of diseased coronary arteries.

In this study, we excluded patients with previous myocardial infarction. Because patients with myocardial infarction probably already have coronary artery disease, the screening of coronary disease in such a population might not be significant. Also, the incidences of dipyridamole-induced ST depression as well as exercise-induced ST depression in patients with myocardial infarction, lower than that of patients without myocardial infarction.

The results of this study revealed that the incidence of ST depression in the dipyridamole test was 9% in 0VD, 44% in 1VD, 67% in 2VD, and 93% in 3VD. Compared with the treadmill test, the incidence of ST depression in the dipyridamole test was lower in 0VD, tended to be lower but had no statistical difference in 1VD and 2VD, and was almost the same in 3VD. In the dipyridamole test, nST, the extent of ST depression, and maxST, the maximal voltage of ST depression became greater as the number of diseased coronary arteries increased. For nST, significant differences were found in 0VD vs 1VD, 0VD vs 3VD, 1VD vs 3VD, and 2VD vs 3VD. For maxST, significant differences were found in 0VD vs 1VD, 0VD vs 2VD, 0VD vs 3VD, 1VD vs 3VD, and 2VD vs 3VD. Although neither nST nor maxST in the treadmill test could distinguish 2VD and 3VD, there was a significant difference between 2VD and 3VD using the dipyridamole test. It is thought that the parameters of ST depression in the dipyridamole test reflect the severity of coronary artery disease.

The reported incidence of dipyridamole-induced ST depression varies among investigators: 3%, 10%, 31%, 34%, 44%, 59%, 61%, 71%, and 90% of patients with coronary artery disease. Several factors other than the given dose of dipyridamole might account for these discrepancies. First, in patients with previous myocardial infarc-
tion, the incidence of dipyridamole-induced ST depression was lower than in those without myocardial infarction\(^{16,17}\). Second, as this study indicated, the severity of coronary disease influenced the incidence of ST depression. The incidence of positive dipyridamole tests increased as the number of diseased coronary arteries increased.

Third, antianginal drugs might influence the results of the dipyridamole test. Our previous studies\(^{11,12,27}\) demonstrated that premedication with a Ca antagonist or long-acting nitrate suppressed dipyridamole-induced ST depression.

Fourth, the number of electrocardiographic leads might have affected the incidence of dipyridamole-induced ST depression. With only one to three leads, the ST depression might be missed in some cases. A standard 12-lead ECG must be employed to assess ECG changes in the dipyridamole test. Body surface mapping also improves the sensitivity of electrocardiography in the exercise test\(^{24}\) and the dipyridamole test\(^{17}\).

**Diagnostic ability of the dipyridamole ECG test in the coronary artery disease**

The results of our study show that the dipyridamole ECG test was highly positive in 3VD, and highly negative in 0VD. Then, we tried to use the dipyridamole ECG test for two purposes; for the detection of 3VD, and for the exclusion of 0VD. For the diagnosis of 3VD, the dipyridamole ECG test using 87-lead mapping had as high sensitivity (93% vs. 96%), higher specificity (68% vs. 38%, \(p<0.01\)), and higher predictive accuracy (75% vs. 54%, \(p<0.01\)) than the treadmill test. Using the 12-lead ECG, the dipyridamole test also had excellent diagnostic ability; the sensitivity, specificity and predictive accuracy were 86%, 72% and 76%, respectively. For the prediction of 3VD, the dipyridamole ECG test had high sensitivity and specificity and was better than the treadmill test.

On the other hand, for the detection of one or more stenotic coronary arteries, the dipyridamole test had lower sensitivity (70% vs. 85%, \(p<0.05\)), but higher specificity (91% vs. 53%, \(p<0.01\)), and as high predictive accuracy (77% vs. 74%) compared with the treadmill test. Also by the 12-lead ECG dipyridamole test, the sensitivity, specificity and the predictive accuracy were 64%, 94% and 74%, respectively. The higher specificity of the dipyridamole ECG test suggested that the test might be useful to rule out patients without coronary stenosis.

Cates et al\(^{13}\) also reported that dipyridamole test using radionuclide ventriculography had a lower sensitivity but higher specificity for coronary artery stenosis. In their study, the sensitivity and specificity of dipyridamole ventriculography were 67% and 92%, compared with 89% and 67% for exercise ventriculography, respectively. Their study and our study suggested that invasiveness dipyridamole sometimes failed to provoke myocardial ischemia in patients with less severe coronary artery disease.

The mechanism of dipyridamole-induced myocardial ischemia is supposed to be that vasodilatation by dipyridamole causes maldistribution of coronary blood flow and provokes reduction of coronary flow in regions served by stenotic coronary arteries\(^{10,25,26}\). However, Rossen et al\(^{27}\) demonstrated that the standard dose of dipyridamole (0.56 mg/kg/4 min) does not always result in maximal coronary dilation in patients with coronary artery disease. It is possible that dipyridamole-induced coronary vasodilation was sometimes submaximal and failed to provoke myocardial ischemia in patients with less severe coronary artery disease.

**Clinical implications**

This study has shown a possibility that nST and maxST of the dipyridamole test could be used to assess the severity of coronary artery disease. Further prospective studies should be performed to establish diagnostic criteria. In this study, we chose the number of stenotic arteries as a parameter of the severity of coronary artery disease, because it is widely used clinically. However it is well known that the severity of coronary artery disease is determined not only by the number of stenotic coronary arteries, but also by the degree of stenoses, the site of stenoses, the existence of collateral vessels etc. Further studies will be made in the near future about these points.

In conclusion, the dipyridamole electrocardiographic test, especially using 87-lead mapping, had high sensitivity and high specificity for the diagnosis of 3VD. Also, the
The dipyridamole test using 12-lead ECG had enough diagnostic ability for a clinical purpose. The dipyridamole electrocardiographic test is thought to be a useful method for screening of severe coronary artery disease, especially in patients who cannot perform adequate exercise, for peripheral vascular disease, arthritis, neurologic deficits, and orthopedic abnormalities. Also, it may be useful to non-invasively stratify the risk for future coronary events in patients with coronary artery disease.

REFERENCES


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