Prognostic Value of Dipyridamole Echocardiography Testing

Noémi Gruber, M.D., Tamás Forster, M.D., F.I.C.A., Albert Varga, M.D., Angela Borthaiser, M.D., Miklós Csanády, M.D.

2nd Department of Medicine, Albert Szent-Gyorgyi Medical University, Szeged, Hungary

Abstract. The aim of this study was to follow the results of dipyridamole echocardiography testing (DET) in 105 patients (mean age 53.2 ± 8.5 years) with suspected ischemic heart disease. The follow-up period was 31.4 ± 4.2 months. Twenty-nine patients had a positive DET result, and 76 a negative one. Fifty-two of the 105 underwent coronarography, and the remainder had no heart catheterization. In the follow-up study, the patients' subjective condition and the new heart events (angina, infarction, coronary bypass surgery, and death) were registered. The new heart events were more frequent in the DET-positive group than the negative one (45% vs 22%; p < 0.05). In the coronarography-positive and -negative group these values were 77% and 10%, respectively (p < 0.001). In the coronarography- and DET-positive group the frequency of new cardiac events was 69%. This value was only 10% in the coronarography- and DET-negative group. The difference between the true-positive and true-negative groups was highly significant (p < 0.001). Coronarography was found to be a good predictor of future cardiac events, however, the noninvasive dipyridamole echocardiography testing was also an appropriate method for follow-up.

Introduction

Pharmacological stress tests are well-known, nondangerous methods in the diagnosis of ischemic heart disease [1-4]. Dipyridamole or dobutamine stress tests monitored by two-dimensional echocardiography and/or perfusion scintigraphy are offered especially to those patients who are unable to perform adequate physical exercise, bicycle ergometry, or treadmill [5,6]. The diagnostic value of these pharmacological tests is similar to that of ergometry, with monitoring by imaging techniques [5,7,8]. Dobutamine stress echocardiography is also advised for the assessment of cardiac risk before noncardiac surgery [9]. Further, these pharmacological tests are widely used for the identification of viable myocardium or for the assessment of the prognostic value of future cardiac events after myocardial infarction [10,11].

The aim of our study was to estimate the value of dipyridamole echocardiography testing (DET) in predicting future cardiac events in patients with suspected ischemic heart disease. Therefore, patients were followed up after the test to reveal late cardiac complications (angina, myocardial infarction, bypass surgery, or cardiac death).

Patients and Methods

The study population comprised 105 patients who were referred to our department with the suspicion of ischemic heart disease. Patients with clinically important valvular heart disease, heart failure, previous PTCA or aorto-coronary bypass surgery, and recent myocardial infarction were excluded (12 patients had an earlier myocardial infarction in the case history). The mean age of the patients (70 men and 35 women) was 53.2 ± 8.5 years.

Dipyridamole Test

Patients were instructed to fast after midnight, and to avoid ingesting products containing caffeine for 24 hours before the test (because of the dipyridamole antagonist effect of the methylxanthine component). Oral theophyllin, nitrates, and calcium antagonists were also discontinued 24 hours before the investigation. Subjects were placed in the left lateral position. A cannula was introduced into the antecubital vein. Twelve-lead ECG, blood pressure, and two-dimensional echocardiographic views of the left ventricular wall motion were obtained. The test was continued from 8 minutes with a dose of 0.28 mg/body weight kg for 2 minutes (i.e., a total dose of 0.84 mg/body weight kg for 10 minutes). Two-dimensional echocardiographic views of the left ventricular wall motion were monitored at the beginning of the test, and continued for 3 minutes after dipyridamole
injection, with Toshiba SSH-65A equipment, using apical views (2 chamber, 4 chamber, and apical long-axis views).

**Evaluation of Two-dimensional Echocardiography Test**

The left ventricular motion was carefully analyzed by two independent observers, who assessed videotape recordings. For anatomic localization of wall motion abnormalities, the left ventricular myocardium was divided into 14 segments, and the wall motion abnormalities were scored according to Edwards et al. [12].

**Hemodynamic Investigation**

The Seldinger technique was performed in 52 of the 105 patients. After left ventricular angiography, selective right and left coronaryography were carried out with different views. The results were evaluated by two independent observers. Stenosis of over 70% of the diameter of at least one of the main vessels was regarded as significant. The time that elapsed between the exercise test and coronaryography was less than a week.

**Follow-up**

The patients were followed up for an average of 31.4 ± 4.2 months (range: 24.5-42.8, median 31) after DET. Each patient’s subjective condition was evaluated on the basis of personal communication. The patient’s medical reports on the heart events (angina, infarction, bypass surgery, or death) were also reviewed. Only the most severe event was considered in each patient. Physical examination, the 12-lead ECG, and, in relevant cases, two-dimensional echocardiography were also recorded.

**Statistical Analysis**

Fisher’s exact test was used for statistical analysis. For a larger number of samples, we preferred the chi-square test with Yates correction. In both tests, a probability of \( p < 0.05 \) was regarded as indicating statistically significant differences.

**Results**

Twenty-nine of the 105 patients were DET positive and 76 were DET negative. The mean score index ± SEM in the DET-positive group (29 patients) was 1.13 ± 0.03 and 1.30 ± 0.03 before and after DET, respectively (\( p < 0.001 \)). During the follow-up study, 13 of the 29 patients giving positive tests had new heart events (45%). The corresponding number in the DET-negative group was 17 of 76 patients (22%). The difference in the number of heart events was statistically significant (\( p < 0.05 \)) between the DET-positive and negative groups. In the study group, 52 patients underwent coronaryography: 22 patients had at least one-vessel significant stenosis, and 30 had negative results. The coronaryography results revealed a significant difference between the coronaryography-positive and negative groups during the follow-up: 17 of the 22 positive cases and 3 of the 30 negative ones exhibited a progression (\( p < 0.001 \)). The sensitivity and specificity of DET were found to be 16/22 (73%) and 20/30 (67%), respectively. During the follow-up, 11 of the 16 true-positive cases and 2 of the 20 true-negative ones had a new heart event (\( p < 0.001 \)) (Table 1). The types of the new heart events were analyzed in all 105 patients. One patient suffered from anginal pain, 10 patients had aorto-coronary bypass surgery, and 2 patients died because of cardiac reasons (i.e., a total of 13 of the 29 DET-positive tests). In the DET-negative group, 7 patients had angina, 4 suffered myocardial infarction, 5 underwent aorto-coronary bypass surgery, and 1 patient had cardiac death (i.e., a total of 17 cases) (Table 2). It is questionable whether anginal pain can be used as a prognostic sign. Consequently, we also evaluated the “hard events” (myocardial infarction, bypass surgery, or death). The difference between the DET-positive and negative groups was then even more significant (\( p < 0.005 \)) (Table 3).

**Discussion**

DET is well known to have an acceptable sensitivity and good specificity in the diagnosis of ischemic heart disease [13]. This stress-testing procedure has no serious side effects, it is relatively simple, and it is not expensive [14]. In 1989, Picano et al. [15] reported the prognostic value of DET. A study group of 539 patients (341 of them underwent coronaryography) were followed up for 3 years. There was a good prognostic value of DET positivity followed by pathological coronaryography; this was not influenced by the occurrence of previous myocardial infarction. Picano et al. discussed whether PTCA or coronary bypass surgery should be considered as cardiac events. Clearly, they probably reflect the presence of severe coronary vessel disease. Severi et al. [16] compared the prognostic impact of stress testing in coronary artery disease. They concluded from their preliminary data, obtained with a high dose of dipyridamole, that DET positivity was a more powerful predictor than exercise electrocardiography. The combination of these tests allowed a better prognostic stratification than that for either of the tests alone: the positivity of both tests was indic-

---

**Table 1. Prognostic values**

<table>
<thead>
<tr>
<th></th>
<th>With Heart Events</th>
<th>Without Heart Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>DET positivity (n = 29)</td>
<td>13 (45%)</td>
<td>16 (55%)</td>
</tr>
<tr>
<td>DET negativity (n = 76)</td>
<td>17 (22%)</td>
<td>59 (78%)</td>
</tr>
<tr>
<td>Coronarogr. positivity (n = 22)</td>
<td>17 (77%)</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>Coronarogr. negativity (n = 30)</td>
<td>3 (10%)</td>
<td>27 (90%)</td>
</tr>
<tr>
<td>DET true positive (n = 16)</td>
<td>11 (69%)</td>
<td>5 (31%)</td>
</tr>
<tr>
<td>DET true negative (n = 20)</td>
<td>2 (10%)</td>
<td>18 (90%)</td>
</tr>
</tbody>
</table>

The sensitivity and specificity of DET were 16/22 and 20/30, respectively.