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Short-Term Reproducibility of Dipyridamole-Echocardiography Test

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Summary: The aim of this study was to assess the short-term reproducibility of dipyridamole-echocardiography test (DET) consisting of two-dimensional echo monitoring during dipyridamole infusion (up to 0.84 mg/kg in 10 min). The diagnostic end-point of the test is the detection of new onset or worsening regional asynergy. A group of 87 patients with rest and/or effort angina performed two DETs on two consecutive days. All 60 patients with a positive DET had a positive repeat test, and the 27 negative DETs were also negative on the following day. The timing of the asynergy was also very similar between the two tests, both in patients with angina on effort ($r=.93$, $p<0.01$) and at rest ($r=.92$, $p<0.01$). In conclusion, DET has a very high short-term reproducibility regarding the presence and timing of asynergy.

Key words: dipyridamole, echocardiography, reproducibility

Introduction

Intravenous dipyridamole combined with echocardiographic monitoring has been proposed as a useful tool for the diagnosis of coronary artery disease, either with a low, 0.56 mg/kg over 4 min,[1] or high, 0.84 mg/kg over 10 min,[2] dose of dipyridamole. However, extensive data on short-term reproducibility of dipyridamole effects are still lacking; this parameter represents a key feature for any provocative test of potential clinical use for the diagnosis of coronary artery disease. The aim of this study was to evaluate the short-term reproducibility of dipyridamole-echocardiography test (DET) in patients with angina either at rest or on effort.

Materials and Methods

Patient Selection

A total of 87 patients referred to our center for evaluation of anginal pain were enrolled in the study. Of the 87 patients, 36 had angina at rest and 51 on effort. All performed two DETs on consecutive days.

Dipyridamole-Echocardiography Test

Patients were instructed to fast for at least 3 hours before each test, and to avoid coffee, tea, and cola drinks; all were off medications.

Two-dimensional echocardiographic and 12-lead electrocardiographic monitoring were performed in combination with dipyridamole infusion:[2] 0.56 mg/kg over 4 minutes followed by a 4-min interval and then 0.28 mg/kg over 2 min. The cumulative dose was 0.84 mg/kg over 10 min.

Aminophylline (240 mg), which promptly reverses the effects of dipyridamole, was ready at hand. During the procedure, the blood pressure and the electrocardiogram were recorded each minute. Two-dimensional echocardiograms were recorded continuously during and up to 20 minutes after dipyridamole administration. A commercially available wide-angle phased-array imaging system (Hewlett Packard Mod. 77020, 3.5 and 5.0 MHz transducers) was used.

Segmental anatomy and wall motion were assessed in a qualitative manner as previously reported.[1] Wall motion was graded as hyperkinetic, normal, hypokinetic, akinetic, or dyskinetic.

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Positivity of the test was linked to detection of a transient asynergy of contraction that was absent or of lesser degree in the baseline examination. For every patient, each DET was evaluated by consensus decision of 2 observers unaware of the result of the other test.

Data Analysis

Three parameters of reproducibility, all clinically relevant to the presence and grading of ischemic response after dipyridamole,[3] were analyzed: (1) presence of asynergy (that is, positivity versus negativity) in positive patients was further considered; (2) dose of dipyridamole necessary to induce ischemia (low dose versus high dose); (3) timing of onset of the asynergy (the moment, from the beginning of the test, when the asynergy was first detected). Statistical correlation between the results of the two tests (taking into account the time of onset of the asynergy) was made using linear regression analysis.

Results

Irrespective of whether angina was induced by effort or occurred at rest, all 60 patients with a positive DET had a positive repeat test, and the 27 negative DETs were also negative on the following day. Of the 60 patients with positive DET, 41 were positive with the low dose test, and 19 with the high dose test. All 41 patients with low dose positivity had a repeat positive low dose test; similarly, all 19 patients with high dose positivity had a repeat positive high dose test. The timing of the asynergy, the parameter hypothetically more susceptible to variation, due to the qualitative type of assessment, was also significantly similar between the two tests, both in patients with angina on effort ($r=.93$, $p<0.01$; Fig. 1) or at rest ($r=.92$, $p<0.01$; Fig. 2).

Discussion

Our data suggest that repeated dipyridamole infusions produce fairly constant effects—at least when taking into account the left ventricular mechanics monitored by echocardiography. The high DET reproducibility is, in contrast with the reported short-term variability of exercise stress test findings, more pronounced in patients with angina at rest,[4,5] but present also in patients with angina on effort.[5,6] Dipyridamole infusion does not suffer from the variables coming into play during exercise stress testing, such as modulation of coronary tone elicited by effort, training effects, physical conditioning, motivation, and cardiovascular efficiency.

Reproducibility of DET was excellent even in the 36 patients with angina at rest. This is in agreement with clinical[8] and experimental[10,11] data documenting that dipyridamole does not induce coronary vasoconstriction, whereas in this subset of patients with angina at rest, functional factors heavily modulate the response to the exercise stress test.

One potential mechanism of variable threshold effort angina might theoretically affect DET results also. It was hypothesized that subtle vasoconstrictor influences playing on the large coronary arteries episodically caused clinically significant alterations in coronary vascular resistance. Such alterations in coronary tone, although not necessarily producing such profound coronary vasoconstriction that angina at rest would be precipitated, could be severe enough to interfere with the normal augmentation in flow that occurs with exercise.[12] Similarly, after dipyridamole, flow-related changes in resistance might be significantly influenced by changes in stenosis geometry, finally affecting the positivity of the test or the timing of onset of asynergy. From the practical point of view, this mechanism seems to play a minor role and did not substantially affect the reproducibility of DET results.

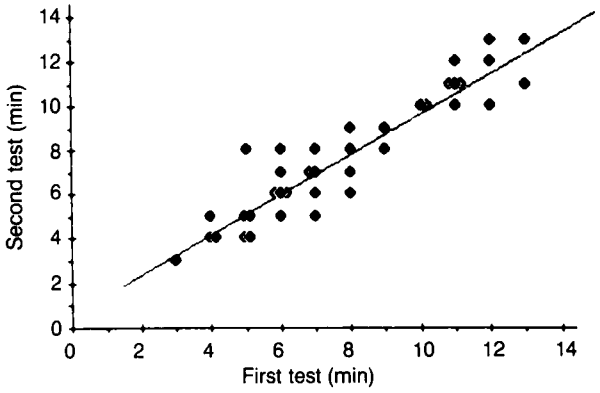

FIG. 1 Graph depicting the correlation between the onset of the asynergy in the first and in the second test, in the 38 patients with angina on effort and positive DET. Values are rounded off to the nearest minute. r=.93.

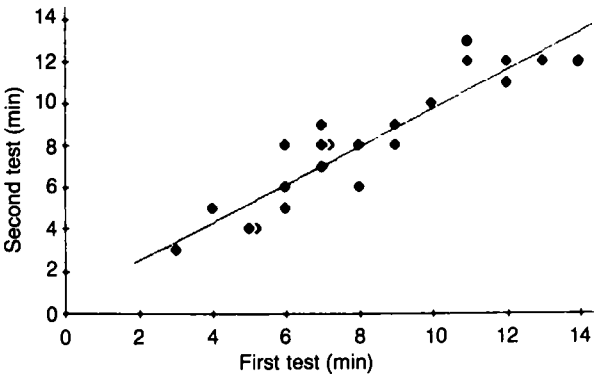

FIG. 2 Graph depicting the correlation between the onset of the asynergy in the first and in the second test, in the 22 patients with angina at rest and positive DET. Values are rounded off to the nearest minute. r=.92.

Conclusion

In conclusion, DET has a very high short-term reproducibility regarding presence, dose of dipyridamole needed to induce ischemia, and timing of asynergy. The lack of substantial variability of DET findings in patients with angina at rest, gives further clinical evidence that functional factors have no importance in the pathogenesis of dipyridamole-induced ischemia.

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