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Does the Combination with Handgrip Increase the Sensitivity of Dipyridamole-Echocardiography Test?

E. PICANO, M.D., F. LATTANZI, M.D., M. MASINI, M.D., A. DISTANTE, M.D., A. L'ABBATE, M.D.

C.N.R. Institute of Clinical Physiology, University of Pisa, Pisa, Italy

Summary: The aim of this study was to assess the possibility of increasing the sensitivity of dipyridamole-echocardiography testing (DET:2-D echo monitoring during dipyridamole infusion) by combining this procedure with handgrip testing. Dipyridamole-handgrip test (DHT) was therefore performed in 24 patients with rest/effort angina, negative DET, and negative handgrip-echo (without dipyridamole pretreatment). DHT consisted of 4.5 min of sustained 25% maximum grip strength, started 4 min after the end of dipyridamole infusion (0.56 mg/kg for 4 min). Interpretable studies were obtained in all patients. Of the 24 patients tested (10 without and 14 with significant coronary artery disease, CAD), only one CAD patient had a positive DHT, which indicates an increased sensitivity of 7% versus DET alone. In conclusion, DHT is feasible in all patients and—if compared to DET—has the same specificity. However, in spite of the theoretical premises, it provides only a modest step up in sensitivity.

Key words: coronary heart disease, handgrip exercise, dipyridamole test, angina pectoris

Introduction

In previous studies we showed that dipyridamole-echocardiography testing (DET: two-dimensional echocardiographic and 12-lead ECG monitoring during dipyridamole infusion at a dosage of 0.56 mg/kg over 4 min) may offer useful information in patients with angina pectoris (Picano *et al.*, 1985, 1986, in press a, b). In comparison with exercise stress test (EST), DET has some advantages, since:

It is more specific (being grounded on a mechanical rather than electrical marker of ischemia)
It locates with accuracy the site of apparent ischemia, differently from exercise-induced ST-segment depression
It may unmask the elusive entity of "electrocardiographically silent" myocardial ischemia (that is, anginal patients with either nondiagnostic or negative EST (Picano *et al.*, 1986)
It evaluates the coronary reserve, eliminating the uncertainties of variable coronary tone, which modulates the response to EST (Picano *et al.*, in press a,b)

An important limitation of DET is a lower sensitivity than EST (56 vs. 62% in a group of 66 patients with effort angina pectoris) (Picano *et al.*, 1985); (62 vs. 80% in 62 patients with angina at rest), (Picano *et al.*, in press b). It has been proposed that the sensitivity of thallium-201 (^{201}Tl) dipyridamole scintigraphy might be augmented by the combination of isometric exercise (handgrip) (Brown *et al.*, 1981). This may not be necessarily true for DET, since this latter test requires myocardial ischemia as a diagnostic end-point, while thallium-201 dipyridamole does not (Gould, 1978; Gould *et al.*, 1978).

The aim of the present study was therefore to assess whether the sensitivity of DET might be increased by combination with handgrip.

Materials and Methods

Selection of Patients

Twenty-four patients with angina at rest and/or on effort were enrolled in the study. All patients had performed a DET, which was negative for ischemia (no transient asynergy of contraction developed after the dipyridamole infusion). On the following day, all patients performed a handgrip–echo test, and one hour later, a dipyridamole–handgrip test (DHT).

Dr. Eugenio Picano is recipient of the A.R.MED. research fellowship for ultrasonic diagnosis of atherosclerosis.

Address for reprints:

Eugenio Picano, M.D.
Istituto di Fisiologia Clinica del CNR
Via P. Savi 8
56100 Pisa, Italy

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Handgrip-Echo Test

Each patient performed 4.5 min of sustained isometric handgrip exercise at 25% of a predetermined maximum grip strength. Twelve-lead ECG tracings and blood pressure, by a cuff sphygmomanometer, were recorded every minute. Two-dimensional echocardiographic monitoring was continuously performed during the test (Mitamura *et al.*, 1981). After this effort the patient was allowed to rest and hemodynamic parameters quickly returned to control values.

Dipyridamole-Handgrip Test

DHT was carried out performing a handgrip (with the same modalities previously described) 4 min after the end of the dipyridamole infusion (at the usual dose of 0.56/mg kg over 4 min). Twelve-lead ECG and blood pressure, by cuff sphygmomanometer, were taken every minute.

Echocardiographic Examination and Data Analysis

For all these tests (DET, handgrip, DHT), the detection of a new asynergy of contraction was taken as the only criterion of positivity. Two-dimensional echocardiograms were continuously recorded during each of the described tests. A commercially available wide-angle phased-array imaging system (Hewlett Packard Model 77020, 3.5 and 5.0 MHz transducers) was used. In the baseline studies all standard echocardiographic views (parasternal and subxyphoid long and short axis, apical four chamber and two chamber) were obtained when possible.

During the test any new area of abnormal wall motion was identified on multiple views by rapidly moving the ultrasound transducer through various positions. Having established an optimal position for the observation of abnormal wall motion, the transducer was held stationary throughout the remainder of the study and the recovery period.

The videotapes were analyzed by two independent observers. When there was disagreement about the result (positivity vs. negativity), a third observer reviewed the study and the subsequent majority judgment was binding. None of the three observers has access to angiographic findings before their interpretation. Segmental anatomy and wall motion were assessed in a qualitative manner as previously reported (Distante *et al.*, 1984). The wall motion was graded as: hyperkinetic, normal, hypokinetic, akinetic, and dyskinetic.

Hemodynamic differences after handgrip-echo and DHT were tested for significance by the Student's paired *t*-test.

Angiographic Study

All patients underwent selective coronary arteriography, using either the Judkins or the Sones technique. Multiple views of each vessel were filmed. A vessel was considered to have significant obstruction if its diameter was narrowed by 70% or more.

Results

Of the 24 patients, 10 had absent and 14 had significant coronary artery disease: 8 had single-, 6 had double-, no one had triple-vessel disease.

Interpretable echocardiograms were obtained in all patients from both handgrip-echo test and DHT.

No patient had a positive handgrip-echo test (and neither angina nor ECG changes). Only one patient had a positive DHT (this patient had septal akinesia; coronary angiography showed 90% left anterior descending artery disease): this means an increase in sensitivity of 1/14, that is 7% versus DET alone. This patient had also mild chest pain and diagnositic (>0.15 mV) ST-segment depression, more obvious in lead V_4, during DHT. Anginal pain was elicited by DHT in another 2 patients (1 had significant coronary artery disease), while diagnostic ST-segment depression occurred in one other patient with significant coronary artery disease. Hemodynamic findings after handgrip-echo and DHT are reported in Table 1. No complications of any kind occurred after DHT.

Discussion

DHT slightly increases the sensitivity of DET alone, with no loss in feasibility and specificity (which remained 100%), and no apparent increase in risk.

From a theoretical point of view, handgrip could provoke ischemia—when superimposed on dipyridamole infusion—through at least two different mechanisms: an increase in myocardial oxygen demand or a decrease in supply (Brown *et al.*, 1984b). As previously shown by Brown *et al.*, (1981), dipyridamole does not block the hemodynamic response of handgrip. The *peak* rate-pressure product (an established index of cardiac work (Gobel *et al.*, 1978) achieved after DHT was significantly higher than after DET alone. As far as the blood supply, it has been documented that dipyridamole causes a slight to mild reduction in coronary arterial vasomotor tone, but it does not prevent the coronary constrictor effects of handgrip (Brown *et al.*, 1981). In the presence of increased flow, the handgrip-induced increase in epicardial coronary stenoses might detrimentally potentiate the increase in dynamic coronary stenosis (Brown *et al.*, 1984a). In fact, for any given degree of stenosis, increasing rates of flow (as those induced by dipyridamole) markedly raise the transtenotic gradient present in resting conditions. Finally, the increase in left ventricular end-diastolic pressure induced by handgrip might reduce perfusion (by increasing extravascular resistances) and increase the oxygen demand (increasing the wall stress).

TABLE I Hemodynamic findings

	Basal	HG	DIP	DIP+HG
Patients without CAD (n=10)				
Heart rate (beats/min)	72±6	90±12[a]	88±22[a]	98±19[a]
Systolic pressure (mmHg)	137±14	179±16[b]	131±18[a]	165±33[b]
Diastolic pressure (mmHg)	85±11	101±8[a]	82±10	100±15[a]
RPP (×1/100) (beats/min×mmHg)	99±16	162±26[b]	117±45	171±42[b]
Patients with CAD (n=14)				
Heart rate (beats/min)	69±5	87±6[b]	81±10[b]	98±14[b]
Systolic pressure (mmHg)	135±18	181±20[b]	126±15[a]	175±16[b]
Diastolic pressure (mmHg)	82±12	98±11[a]	79±10	95±15[a]
RPP (×1/100) (beats/min×mmHg)	95±18	162±31[b]	105±23	172±37[b]

[a] = $p<0.05$.
[b] = $p<0.01$.
Abbreviations: CAD=coronary artery disease; DIP=dipyridamole test; HG=handgrip test; RPP=rate pressure product.

Nevertheless, the ischemic effects of such combined action was modest: we had only 1 DHT-positive patient out of the 14 tested patients with coronary artery disease. To explain this rather disappointing result, it must be considered that the increased aortic pressure—induced by handgrip—might well balance the increased severity of the stenosis, ultimately even enhancing the poststenotic perfusion pressure. As a consequence, myocardial regions relatively underperfused may result, which are not necessarily ischemic. This fact can potentiate the diagnostic sensitivity of thallium-201 dipyridamole test, whose positivity is based on the detection of differences of *perfusion* but whose *diagnostic* end-point is not myocardial ischemia (Brown *et al.*, 1984a; Gould *et al.*, 1978). On the contrary, DET sensitivity is only slightly increased by the association of handgrip, since this test—being grounded on a mechanical marker—does require myocardial ischemia to be positive.

In conclusion, DHT is feasible in all patients and—if compared to DET alone—has the same specificity. However, in spite of the theoretical premises, it provides only a modest step up in sensitivity. Other, more effective ways to increase the sensitivity of the test are needed (Picano *et al.*, 1985b).

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