

Role of Coronary Spasm for a Positive Noninvasive Stress Test Result in Angina Pectoris Patients Without Hemodynamically Significant Coronary Artery Disease

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ABSTRACT: *Background:* A positive noninvasive stress test result is often considered as a false-positive indicator of coronary artery disease (CAD) when coronary angiography reveals no hemodynamically significant CAD. *Methods:* From January 2001 through December 2004, 5474 patients scheduled to undergo exercise electrocardiogram (ECG) [exercise ECG without imaging or exercise ECG with thallium-201 (201Tl) single photon emission tomography (SPECT)] or dipyridamole 201Tl tomography at our outpatient clinic because of chest oppressive sensation were included in this prospective study. Coronary angiography was performed when a noninvasive test result was positive for ischemia or when ischemic chest pain was suspected. Intracoronary methylergonovine testing was performed when spastic angina was suspected and coronary angiography showed no hemodynamically significant CAD. *Results:* Noninvasive stress testing was positive in 113 (67%) patients with coronary spasm. Of the 53 pa-

tients who had positive exercise ECG (exercise ECG with or without imaging), ST depression was found in 50 patients and ST elevation in 3 patients. Multivessel spasm was found in 6 (15%), 6 (15%), and 7 (21%) of the patients with a positive result on exercise ECG without imaging, exercise ECG with 201Tl SPECT, and dipyridamole 201Tl SPECT, respectively. There was no significant difference in the results of noninvasive stress testing and the number of vessels with coronary spasm (1-vessel spasm versus multivessel spasm) among these 3 noninvasive stress testing groups. *Conclusion:* Intracoronary ergonovine testing induced coronary spasm in over 50% of patients who had suspected ischemic chest pain, a positive noninvasive stress test, and no hemodynamically significant CAD. **KEY INDEXING TERMS:** Coronary spasm; Exercise-testing; Thallium-201 tomography. [*Am J Med Sci* 2008;335(5):354-362.]

Transient reduction of myocardial blood flow resulting from coronary spasm is the pathogenic mechanism responsible for attacks in patients with coronary spastic angina.^{1,2} The diagnosis of coronary spasm, however, is usually made based on the finding of the transient electrocardiographic ST changes or by the positive results on invasive provocation testing. Patients with coronary spastic angina, how-

ever, may present with chest pain, which is atypical for myocardial ischemia, thus preventing an early and accurate diagnosis and adequate treatment. Because of the persistent nature of symptoms, some patients with atypical chest pain may be treated empirically or evaluated angiographically because of suspicion of fixed coronary stenosis. Data are very limited on the diagnostic value of the noninvasive modalities of treadmill exercise electrocardiogram, exercise thallium-201 (201Tl) single photon emission tomography (SPECT), or dipyridamole 201Tl SPECT in patients with coronary spastic angina.³⁻⁶ Because a positive noninvasive stress test in patients without hemodynamically significant coronary artery disease (CAD) is recognized as a false-positive indicator of CAD, it is important to identify the underlying factors responsible for the positive noninvasive stress test result, as the accurate diagnosis and appropriate treatment vary accordingly. The purpose of this study was to assess the relation of coronary spasm to noninvasive stress test results

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Table 1. Clinical Characteristic of Patients without Clinically Significant CAD Who Had a Positive Intracoronary Ergonovine Test

Variables	All (n = 169)	Noninvasive Stress Test		P ^a
		Positive (n = 113)	Negative (n = 56)	
Age (yr)	59 ± 12	60 ± 11	58 ± 13	0.301
Men	116 (69)	81 (72)	35 (63)	0.226
BMI (kg/m ²)	26 ± 4	26 ± 3	25 ± 4	0.087
Current smoker	74 (44)	46 (41)	28 (50)	0.252
Diabetes mellitus	31 (18)	20 (18)	11 (20)	0.759
Hypertension	65 (39)	38 (34)	27 (48)	0.067
Hypercholesterolemia	32 (19)	25 (22)	7 (13)	0.133
Total cholesterol (mg/dL)	205 ± 40	206 ± 42	204 ± 36	0.850
Spasm-provoked coronary artery				0.981
Right	121 (57.6)	79 (57)	42 (59)	
Left anterior descending	62 (29.5)	42 (30)	20 (28)	
Left circumflex	27 (12.9)	18 (13)	9 (13)	
No. spastic coronary arteries				0.860
1	139 (82)	93 (82)	46 (82)	
2	20 (12)	14 (13)	6 (11)	
3	10 (6)	6 (5)	4 (7)	
Left ventricular ejection fraction (%)	67 ± 8	66 ± 8	70 ± 8	0.007

Data are presented as mean ± SD or number of patients (percentage).

^a Statistical differences between positive and negative noninvasive stress test results.

in angina pectoris patients without hemodynamically significant CAD.

Methods

Patients

We prospectively studied patients who underwent treadmill exercise electrocardiogram (ECG) or 201Tl SPECT or both to investigate the cause of oppressive chest sensation at our outpatient clinic from January 2001 through December 2004. If a positive stress test (either exercise ECG or 201Tl SPECT) or ischemic chest pain was suspected despite a negative stress test result, coronary angiography was advised to identify whether the underlying pathology involved fixed coronary stenosis or coronary spasm. The study inclusion criteria were a positive result on intracoronary ergonovine testing. Exclusion criteria were as follows: (1) negative result on intracoronary ergonovine testing; (2) prior myocardial infarction as determined by medical history, available hospital records and the finding of Q-waves ≥40 milliseconds on serial electrocardiograms. Written informed consent was obtained from all patients before enrollment.

Clinical Data

The clinical records were reviewed, and data were collected on cardiac risk factors, including cigarette smoking habits, diabetes mellitus, hypercholesterolemia, and hypertension (Table 1). A patient who smoked >10 cigarettes/d within 3 weeks before cardiac catheterization was classified as a current smoker. Diabetes mellitus was defined as the requirement for dietary treatment or the medical therapy. Hypercholesterolemia was defined as a serum total cholesterol level >240 mg/dL or the use of statin medication. Hypertension was defined as the use of antihypertensive medication or a blood pressure >140/90 mm Hg.

Noninvasive Stress Testing

Treadmill Exercise ECG. If the patient did not undergo exercise 201Tl SPECT, the treadmill exercise ECG was performed in the afternoon. If the patient underwent exercise 201Tl SPECT, the treadmill exercise ECG was performed in the morning (9:00 AM–10:00 PM). Exercise testing was performed after the patients had fasted for ≥4 hours. Before the exercise testing, beta-blocking and rate-lowering calcium-blocking agents were

discontinued for 48 hours, and nitrate agents were discontinued for ≥4 hours. The exercise stress testing was carried out according to the modified Bruce protocol. Two 3-minute warm-up stages (1.7 mph and 0% grade and 1.7 mph and 5% grade) were performed before the standard Bruce protocol, which started at 1.7 mph and 10% grade. Signals from a 12-lead ECG were displayed continuously for observation and recorded at regular intervals and when chest pain occurred during the exercise or in the recovery phase.

An exercise test result was considered positive if either of the following two criteria were met: (1) horizontal or downsloping ST depression of ≥1 mm below the PR isoelectric line or ≥1 mm further if there was baseline depression with a duration of ≥0.08 seconds; or (2) ST elevation of ≥0.1 mV compared with the resting tracing with a duration of ≥0.04 seconds after the J point in 2 of the inferior or lateral leads or ≥0.2 mV in ≥2 contiguous precordial leads. Three consecutive complexes meeting one of these criteria were required for a test to be accepted as positive. Angina pectoris was defined as the development of exertional or post-exertional chest discomfort that was relieved with rest or sublingual nitrates. The duration of chest pain and heart rate changes were recorded. Blood pressure was monitored by indirect sphygmomanometry at 1-minute intervals during the test and recovery phase. Exercise end points included physical exhaustion, claudication, angina pectoris, dyspnea, ST depression ≥2 mm, ST elevation ≥1 mm, sustained ventricular tachycardia, and exertional hypotension (≥10 mm Hg decrease in systolic blood pressure).

201Tl SPECT. In patients who underwent exercise 201Tl SPECT, 3 millicuries (111 MBq) of thallous chloride was administered intravenously approximately 1 minute before stopping exercise. The exercise ECG was recorded before stopping exercise. Thallium tomographic imaging was performed immediately after stopping exercise and 4 hours later. If patients could not do the physical exercise, 201Tl SPECT was performed using intravenous dipyridamole infusion at the dose of 0.142 mg/kg/min for 4 minutes. Thallium tomographic imaging was performed starting at 4 minutes after dipyridamole infusion and again 4 hours later.

Vertical short-axis and long-axis tomograms were reconstructed from the raw scintigraphic data, and 4 consecutive slices of each view were selected for interpretation. A positive test was defined as the finding of reversible perfusion defects. The location

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