

Evidence of Abnormal Vasodilator Reserve in Coronary Spasm

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Although reduction of coronary flow reserve (CFR) is a common consequence of significant coronary stenoses, recent observations suggest that it may also be abnormal in other clinical settings such as myocardial hypertrophy or syndrome X in the absence of stenoses.^{1,2} This report shows that the CFR may also be abnormal in patients with normal coronary arteries and vasospasm.

A 60-year-old man was referred for cardiac catheterization because of increasingly frequent episodes of chest pain occurring mainly at rest but also with exertion. He had a history of mild systemic hypertension and esophagitis due to gastroesophageal reflux. A treadmill test performed shortly after the onset of his symptoms 3 years earlier was negative at a pressure rate product of 264×10^2 mm Hg \times beats/min. Medications included propranolol 120 mg/day, topical nitrates 20 mg/day, hydrochlorothiazide 50 mg/day and cimetidine 400 mg/day. The blood pressure was 150/85 mm Hg and the heart rate was 56 beats/min. The remainder of the examination was entirely normal as was the electrocardiogram at rest, the chest roentgenogram and an M-mode echocardiogram. No evidence for left ventricular hypertrophy was present. A repeat treadmill exercise test was stopped after 7 minutes of the standard Bruce protocol because of fatigue. The pressure-rate product achieved was 224×10^2 mm Hg \times beats/min. The patient had no chest pain, but there was 2 mm of horizontal ST depression in leads V₄, V₅ and V₆, and concomitant thallium-201 scintigraphy revealed a reversible anteroseptal perfusion defect. All medications were withheld the night before catheterization. Left ventriculography and coronary arteriography were performed using the

Judkins technique. The left ventriculogram showed normal segmental wall motion. Selective right and left coronary cineangiography revealed a left dominant system without obstructive lesions. Ergonovine maleate, 0.2 mg, produced total obstruction of the left anterior descending artery (LAD), a 60% narrowing in the proximal circumflex artery, and diffuse circumflex narrowing in association with angina and ST-segment elevation in lead V₄ (Fig. 1). These changes subsided rapidly after nitroglycerin was given.

Digital coronary arteriography of the left coronary artery was performed before the ergonovine challenge in a manner described previously.³ Color-coded contrast-medium-appearance pictures were generated at baseline and during contrast-induced hyperemia. With this technique, regional blood flow estimates are inversely proportional to the appearance time of contrast and directly proportional to the intensity of contrast in the myocardial bed. Regional CFR is then calculated as the hyperemic-to-baseline regional blood flow estimate. The contrast intensity ratio (15.92/14.52) and appearance time ratio (1.71/1.85) resulted in a CFR of 1.02 (Fig. 2). For the circumflex bed, the contrast intensity ratio (23.81/13.82) and appearance time ratio (1.87/2.02) resulted in a CFR of 1.86. Both values were abnormally low before ergonovine administration when no focal spasm or diffuse narrowing of the coronary arteries was present. In this laboratory, patients with normal coronary arteries and normal exercise tests have CFR values greater than 1.95.

Exercise-induced ischemia has been noted in 24% of patients with spastic angina and normal coronary arteries.⁴ Coronary arterial spasm and reduced coro-

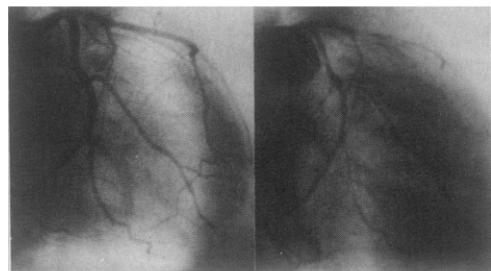


FIGURE 1. Left coronary arteriogram in the right anterior oblique projection. The baseline coronary arteriogram (*left*) is normal. After ergonovine maleate 0.2 mg (*right*), areas of total and subtotal obstruction are seen in the left anterior descending artery, and a 60% stenosis with diffuse narrowing develops in the circumflex system. At this time, the patient had angina and ST-segment elevation.

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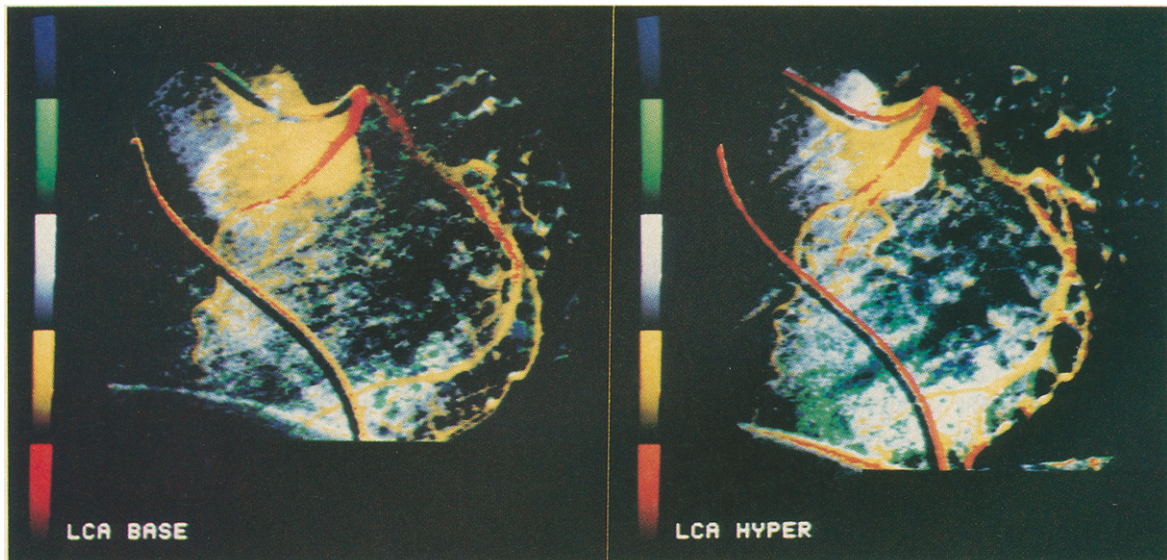


FIGURE 2. Contrast-medium-appearance pictures of the left coronary artery (LCA) in the left anterior oblique projection at baseline (BASE) (*left*) and during hyperemia (HYPER) (*right*). Regions of interest in the left anterior descending and circumflex perfusion beds are computer analyzed to provide the average arrival time and contrast intensity. **Red** indicates progression of contrast in 1 cardiac cycle after injection; **yellow**, 2 cycles; **white**, 3 cycles; **green**, 4 cycles; and **blue**, 5 cycles. Coronary flow reserve is absent in the left anterior descending bed, whereas contrast appears earlier and image intensity is higher in the circumflex distribution during hyperemia, indicating some preservation of vasodilator reserve in this bed.

nary flow during exercise, with concomitant ST-segment changes, have been documented and are believed to be the mechanisms of ischemia during exercise in this group of patients.⁵ In our patient, however, the association of an abnormal CFR and exercise-induced ischemia in the distribution of the artery showing the most severe spasm suggests a different mechanism. The occurrence of ischemia in the LAD distribution may be explained by the inability of LAD flow to increase in the face of increased metabolic demand. Because exercise-induced ischemia was associated with ST-segment depression rather than with ST-segment elevation, as observed during the ergonovine challenge, this latter mechanism may have been the most relevant in this patient, although some milder degree of coronary spasm causing ST depression during exercise cannot be excluded.

Reduced CFR in patients with normal arteriographic findings has been documented in cases of syndrome X and myocardial hypertrophy.^{1,2} The present report shows that CFR of vessels subject to coronary spasm may also be abnormal in the absence of coronary stenoses or concurrent spasm. The reduction of the hyperemic response in the distribution of a spastic vessel may be related to persistent abnormalities of

vasomotor tone,² successive transient episodes of ischemia⁶ or degrees of diffuse atherosclerosis that may be undetected by coronary arteriography.⁴ This case demonstrates that patients with a proved propensity for coronary spasm may also have abnormalities of CFR in the absence of focal spasm. This reduction in hyperemic response may be an alternative or concomitant mechanism in the genesis of exercise-induced ischemia in this patient subgroup.

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