Coronary Collateral Function During Exercise

CALVIN ENG, M.D., RANDOLPH E. PATTERSON, M.D., STEVEN F. HOROWITZ, M.D.,
DORIS A. HALGASH, R.N., AUGUSTO D. PICHARD, M.D., JAY MIDWALL, M.D.,
MICHAEL V. HERMAN, M.D., AND RICHARD GORLIN, M.D.

SUMMARY A totally occluded coronary vessel subtending a noninfarcted, entirely collateral-dependent myocardial region (NIECDMR) provides an opportunity to assess collateral perfusion during exercise stress. Collateral function was determined by analysis of exercise thallium-201 myocardial perfusion images from 31 patients who had at least one NIECDMR (total 41 NIECDMRs) documented during catheterization. Twenty-two of 41 NIECDMRs manifested exercise-induced perfusion defects and 19 were normally perfused. The exercise-negative NIECDMRs were further categorized: Group 1 NIECDMRs (n = 13) were associated with defects in other myocardial regions supplied by diseased vessels and were considered negative relative to other jeopardized regions; group 2 NIECDMRs (n = 6) were not associated with exercise-induced defects in other myocardial regions, which suggests that collateral perfusion was adequate during maximal exercise. Regions supplied by a diseased left anterior descending coronary artery manifested exercise defects regardless of collaterals, possibly because these regions were larger and required more perfusion. Angiographic indexes of collateral function did not clearly predict exercise results.

THE FUNCTIONAL ROLE of human coronary collaterals has been the subject of intense interest since their recognition in pathologic studies and coronary arteriography.1 Coronary arteriography shows the ability of coronary collaterals to provide adequate perfusion and preserve function at rest by demonstrating totally occluded coronary vessels without historical, electrocardiographic, or ventriculographic evidence of myocardial infarction.2-4 These noninfarcted, entirely collateral-dependent myocardial regions (NIECDMRs) — encountered in 28–50% of all total occlusions — present a unique opportunity to assess the capabilities of the human collateral circulation to provide perfusion during exercise. However, an exercise study must be able to correlate coronary lesions with their respective regionally perfused myocardium. Exercise electrocardiography has been used to assess collateral function, but does not provide the regional specificity required to evaluate collateral function during exercise, particularly in patients with multivessel coronary disease.5 Exercise myocardial perfusion imaging (MPI), which has a high regional specificity,6-8 allows coronary anatomy to be more confidently correlated with regional myocardial perfusion during exercise.

In this study, we used regional analysis of exercise MPI to assess the ability of coronary collaterals to perfuse NIECDMRs.

Methods

Patients

One hundred eighty-four patients were referred to Mount Sinai Hospital during the years 1977–1979 for cardiac catheterization, an exercise ECG and thallium-201 MPI. Thirty-one consecutive patients who had at least one totally occluded coronary vessel that did not result in myocardial infarction were selected for the study.

Cardiac Catheterization

All patients underwent cardiac catheterization by the Sones or Judkins technique. Coronary cineangiography and left ventriculography were performed at a filming rate of 30 or 60 frames/sec. Two angiographers reviewed the angiograms independently. The severity of the coronary lesions was assessed by the percentage of luminal diameter narrowing compared with the normal adjacent luminal diameter. A vessel was considered totally occluded if no dye traversed the obstruction in the antegrade pathway. The location (proximal, middle or distal) of the most severe lesion in each major vessel was noted. Left ventriculography was routinely performed in the right anterior oblique projection, and in the left anterior oblique projection if disease of the left circumflex artery (LCx) was present. End-diastolic and end-systolic images of the left ventricle were traced, and the regional pattern of ventricular contraction was analyzed using methods previously described.9

Exercise Testing

Exercise testing was performed within 2 weeks of catheterization. A 12-lead ECG (standard Bruce multistage protocol) was recorded during exercise thallium-201 MPI. The heart rate and blood pressure were recorded at 1–2-minute intervals during exercise, and the exercise-limiting symptom was noted.

Twelve-lead ECGs were recorded before (baseline) and at 1-minute intervals during and after exercise until the ECG reverted to baseline. The exercise ECG was considered positive if there was ≥ 1 mm of horizontal or downsloping or ≥ 2 mm of upsloping ST-segment depression for more than 0.08 second after the J point; equivocal if there was 1 mm of upsloping ST depression for more than 0.08 second after the J point; and uninterpretable if the patient was taking digitalis or if a conduction abnormality was present on the ECG.

From the Division of Cardiology, Department of Medicine, Mount Sinai Medical Center, New York, New York.
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For correspondence: Calvin Eng, M.D., Cardiovascular Research Laboratories, Albert Einstein College of Medicine, Forchheimer 715, 1300 Morris Park Avenue, Bronx, New York 10461.
Thallium-201, 1.5–2.0 mCi, was injected intravenously at or near the peak of treadmill exercise, and the patient continued to exercise for at least 1 minute. Within 10 minutes after termination of exercise, imaging was performed with an Ohio Nuclear Series 120 camera in 45° left anterior oblique, anterior and left lateral views (exercise image). The patients were imaged again in all three views 3–4 hours later (delayed rest or redistribution image), as previously described.10 The patient studies were recalled from a computer and recorded on transparency film in both unprocessed and contrast-enhanced forms. Images were read by two independent observers; interobserver agreement was 90%. Differences were resolved by consensus. Coronary lesions were related to myocardial regions on MPI using the analysis of Lenaers et al.6 and Rigo et al.7 The apical region in the anterior and lateral views was excluded from analysis because it does not correlate with a particular coronary vessel.7 For a left-dominant coronary system, the inferior region on MPI was considered as supplied by the LCx. An MPI region was considered nonischemic during exercise if all corresponding segments to that region were judged to have no perfusion deficit.

Noninfarcted, Entirely Collateral-dependent Myocardium
For the exercise study, 41 totally occluded vessels that did not result in myocardial infarction were identified in 31 patients. Infarction was considered absent when no significant Q waves were present on the ECG and the regional ventricular contraction pattern and the delayed rest MPI in the corresponding myocardial distribution were normal. Thus, these NIECDMRs were protected by collateral perfusion from ischemia and infarction, at least in the resting state. All 41 NIECDMRs had normal delayed rest MPI in their respective MPI regions; the regional response to maximal exercise was used to assess collateral perfusion during exercise.

Angiographic Indices of Collateral Flow
Angiographically, all 41 occluded vessels subtending NIECDMRs demonstrated the presence of collateral perfusion by the delayed appearance of dye in the distal portion of the occluded vessel. We tested five common angiographic indexes of collateral function for their ability to predict exercise regional MPI results of the NIECDMR: Visualized vs nonvisualized connecting channel present; jeopardized (> 50% stenosis of the vessel giving off the visualized connecting collateral channel) vs nonjeopardized collateral; intracoronary vs intercoronary collateral; the size or diameter of the vessel distal to the 100% occlusion corrected for magnification by comparison with the width of the catheter tip; and time of appearance of angiographic dye defined as the time (msec) for the portion of the vessel distal to the 100% occlusion to opacify after injection of contrast dye. The number of film frames after the initiation of injection to the first frame demonstrating opacification of dye distal to the obstruction was denoted the dye appearance time.11 Each measurement was performed three times to document reproducibility. In vessels that received collateral contribution from two sources, the earliest dye appearance time was used.

Spatial Sensitivity of MPI to Detect Regional Pathology
Because of possible technical or geometric factors inherent in MPI, ischemia may not be detected with equal sensitivity in all regions of the myocardium. To assess the spatial sensitivity of MPI, regional analysis of MPI was performed in a separate group of 53 patients (selected from the original 184 patients) who had a documented myocardial infarction (significant Q waves on the ECG, and regional ventricular akinesis or dyskinesis).

Statistics
The data were analyzed using the unpaired t test and 2 × 2 chi-square analysis. Summary data are presented as mean ± sd.

Results
Clinical and Angiographic Data
The anatomic and exercise results in the 31 patients in the exercise study are summarized in table 1. There were 26 males and five females, mean age 52 ± 7.6 years. Four patients had one-vessel disease, 11 patients had two-vessel disease, and 16 patients had three-vessel disease. Patients 6, 10, 17 and 25 had infarcted regions, which were not analyzed. All patients had at least one totally occluded coronary vessel without resulting electrocardiographic, ventriculographic, or scintigraphic evidence of myocardial infarction in the corresponding myocardial segment. Ten patients had two NIECDMRs, yielding a total of 41 NIECDMRs for our exercise study. The regional MPIs were all normal at rest except in the four infarcted regions, in which perfusion defects were present at rest and during exercise. In two patients who had a nondominant right coronary artery (RCA), the LCx was correlated with the results in both lateral and inferior MPI regions.

Regional MPI Analysis of NIECDMR Response to Exercise
During exercise, 22 of 41 NIECDMRs (54%) had new perfusion deficits and 19 (46%) remained normal. Thirteen of these 19 exercise-normal NIECDMRs were in patients who had new perfusion defects in myocardial regions perfused by another diseased vessel. The remaining six NIECDMRs were in patients who did not have exercise-induced perfusion defects in any MPI region during maximal exercise. These six negative NIECDMRs (in four patients) were associated with a maximal exercise test (> 85% of the predicted maximal heart rate achieved). Thus, all 31 patients achieved a level of exercise that was adequate to produce a new perfusion deficit or achieved at least 85% of the maximal predicted heart rate.
<table>
<thead>
<tr>
<th>Pt</th>
<th>Sex</th>
<th>(years)</th>
<th>RCA</th>
<th>LAD</th>
<th>LCx</th>
<th>Exercise ECG</th>
<th>% predicted HR achieved</th>
<th>Exercise symptoms</th>
<th>Maximal HR x SBP</th>
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<td>72</td>
<td>CP</td>
<td>15,870</td>
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</table>

Arteries subtending noninfarcted, entirely collateral-dependent myocardial regions are underlined.

*Myocardial infarction (region excluded from analysis).

†Nondominant right coronary artery.

§Group 1 exercise-negative NIECDMR.

Group 2 exercise-negative NIECDMR.

Abbreviations: RCA = right coronary artery; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; U = uninterpretable; E = equivocal; NR = not recorded; HR = heart rate; SBP = systolic blood pressure; CP = chest pain; F = fatigue; SOB = shortness of breath; H = hypotension; (+) = exercise-induced perfusion defect on myocardial perfusion imaging; (-) = normal perfusion on exercise myocardial perfusion imaging; + = positive exercise ECG; − = negative exercise ECG; NIECDMR = noninfarcted entirely collateral-dependent myocardial region.
TABLE 2.  Location of Noninfarcted, Entirely Collateral-dependent Myocardial Regions and Myocardial Perfusion Imaging: Results of Exercise

<table>
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<tr>
<th>Occluded vessel corresponding to NIECDMR</th>
<th>Exercise MPI results</th>
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<tr>
<td></td>
<td>Positive</td>
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<td>RCA (n = 16)</td>
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<tr>
<td>LAD (n = 15)</td>
<td>12</td>
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<tr>
<td>LCx (n = 10)</td>
<td>4</td>
</tr>
<tr>
<td>Total (n = 41)</td>
<td>22</td>
</tr>
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</table>

LAD vs RCA, p < 0.025.
LAD vs LCx, p < 0.05.
LAD vs RCA and LCx, p < 0.02.
Abbreviations: See table 1.

Regional Differences in Collateral Perfusion of NIECDMRs in Response to Exercise

The regional exercise MPI results categorized to the occluded coronary artery subtending the corresponding NIECDMR are summarized in table 2. Fifteen of 41 NIECDMRs were located in the myocardial distribution of an occluded left anterior descending coronary artery (LAD), 16 in the distribution of an occluded dominant RCA, and 10 in the distribution of an occluded LCx artery. LAD NIECDMRs were significantly more likely to manifest perfusion deficits during exercise than those in the RCA (p < 0.025), those in the LCx (p < 0.05), or those in the LCx and RCA combined (p < 0.025). Classification of obstruction as proximal, middle or distal (table 3) did not predict exercise results of the NIECDMRs. However, most of the occlusions were proximal.

Exercise-negative NIECDMRs

Nineteen NIECDMRs did not manifest perfusion defects during exercise. Thirteen of the 19 exercise-negative NIECDMRs (group 1, table 1) were in patients who had new perfusion defects in other myocardial regions during exercise. Thus, we can only infer that group I exercise-negative NIECDMRs were negative relative to other jeopardized regions. The group I NIECDMRs might not have remained negative if perfusion deficits and probable ischemia in other regions, presumably, had not caused termination of the exercise. However, seven of 13 group I exercise-negative NIECDMRs were negative relative to less severe angiographic coronary lesions. Six of 19 exercise-negative NIECDMRs (group 2) were in patients 9, 10, 25 and 27, who did not have exercise-induced perfusion deficits anywhere on exercise MPI despite achieving greater than 85% of maximal predicted heart rate. Although all six exercise-negative NIECDMRs in group 2 were associated with a positive exercise ECG, four were in three patients who did not have chest pain during exercise. In addition, the heart rate–systolic pressure product in patients with group 2 NIECDMRs was significantly higher than that in patients with group 1 NIECDMRs (26,120 ± 2486 vs 20,126 ± 6538, p < 0.03).

Spatial Sensitivity of MPI

From the overall group of 184 patients, regions with documented pathology (myocardial infarction) were selected to test the ability of MPI to detect abnormalities located in various myocardial regions (table 4). Fifty-three patients were identified (57 myocardial infarctions). Thirty of 33 infarcts (91%) in the anterior or septal regions (due to LAD disease) were detected by MPI. Thirteen of 15 (87%) infarcts located in the inferior region (due to dominant RCA disease) were detected by MPI. Eight of nine infarcts (89%) located in the lateral region (due to LCx disease) were detected by MPI. There were no differences in the ability of MPI to detect documented pathology in the various myocardial regions. The overall sensitivity of MPI in detecting myocardial infarction was 89% (51 of 57). This is consistent with previous findings.12

Angiographic Indexes of Collateral Function

Five angiographic indexes of collateral function were measured for each of the 41 NIECDMRs (table 5). These angiographic indexes were tested for their ability to predict the functional exercise results of the NIECDMRs. Visualization of collateral connecting channels did not predict functional results. Among the 27 visualized collateral connecting channels, classification of collaterals in terms of jeopardized, nonjeopardized, intercoronary and intracoronary did not correlate with or predict the functional results. The magnification-corrected diameter of the vessel distal to the total occlusion as described by Levin2 was also unable to predict true collateral function. Only the

TABLE 3.  Exercise Results of Noninfarcted, Entirely Collateral-dependent Myocardial Regions According to Location of Complete Obstruction

<table>
<thead>
<tr>
<th>100% coronary lesion</th>
<th>Positive regional MPI (n = 22)</th>
<th>Negative regional MPI (n = 19)</th>
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<tr>
<td></td>
<td>Proximal</td>
<td>Middle</td>
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<tr>
<td>RCA (n = 16)</td>
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<td>1</td>
</tr>
<tr>
<td>LAD (n = 15)</td>
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<td>3</td>
</tr>
<tr>
<td>LCx (n = 10)</td>
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<td>2</td>
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<tr>
<td>Total</td>
<td>14</td>
<td>6</td>
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Proximal, middle and distal indicate the location of occlusion. Abbreviation: MPI = myocardial perfusion imaging. See table 1 for other abbreviations.

TABLE 4.  Spatial Sensitivity of Myocardial Perfusion Imaging in Detecting Documented Pathology

<table>
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<th>Coronary lesion (infarct location)</th>
<th>Detected by MPI</th>
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<tr>
<td>RCA (inferior)</td>
<td>13/15 (87%)</td>
</tr>
<tr>
<td>LAD (septum, anterior)</td>
<td>30/33 (91%)</td>
</tr>
<tr>
<td>LCx (lateral)</td>
<td>8/9 (89%)</td>
</tr>
<tr>
<td>Overall sensitivity</td>
<td>51/57 (89%)</td>
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Abbreviation: MPI = myocardial perfusion imaging. See table 1 for other abbreviations.
TABLE 5.  Angiographic Indexes of Collateral Function

<table>
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<th>Regional exercise MPI results</th>
<th>(+) NIECDMR</th>
<th>(-) NIECDMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 22)</td>
<td>(n = 19)</td>
<td></td>
</tr>
</tbody>
</table>

1. Visualized vs nonvisualized collaterals:
   - Visualized (n = 27): 13 vs 14
   - Nonvisualized (n = 14): 9 vs 5
   \( p = \text{NS} \)

2. Jeopardized vs nonjeopardized collateral (for visualized collaterals only, n = 27):
   - Jeopardized (n = 11): 5 vs 6
   - Nonjeopardized (n = 16): 8 vs 8
   \( p = \text{NS} \)

3. Intercoronary vs intracoronary collateral:
   - Intercoronary (n = 20): 10 vs 10
   - Intracoronary (n = 7): 3 vs 4
   \( p = \text{NS} \)

4. Diameter of vessel distal to occlusion (distal runoff):
   - (+) NIECDMR (n = 22): 1.53 ± 0.42 mm
   - (-) NIECDMR (n = 19): 1.50 ± 0.25 mm
   \( p = \text{NS} \)

5. Angiographic dye appearance time:
   - (+) NIECDMR (n = 22): 1641 ± 545 msec
   \( p < 0.025 \)
   - (-) NIECDMR (n = 19): 1233 ± 445 msec

Abbreviation: NIECDMR = noninfarcted, entirely collateral-dependent myocardial region; (+) = exercise positive; (-) = exercise negative.

angiographic dye appearance time predicted functional collateral results. Shorter dye appearance times were associated with collaterals that provided normal perfusion of the NIECDMRs during exercise. The mean dye appearance time for the exercise-positive NIECDMRs was 1641 ± 545 msec, compared with 1233 ± 445 msec for the exercise-negative NIECDMRs (\( p < 0.025 \)).

Discussion

The controversy over the functional significance of human coronary collaterals is based on data obtained by angiography and pathology, which can only assess for their presence or absence at one point in time. From experimental studies of the collateral circulation, the time course of coronary occlusion is likely to be the prime determinant of whether collaterals can prevent infarction and death.\(^\text{13}\) Full development of collateral pathways requires a gradual occlusion. Schaper\(^\text{14}\) showed that coronary collateral vessels enlarge by an active growth process. Gradual coronary occlusions achieved in dogs by ameroid constrictors have resulted in complete occlusion of the vessel, with a success rate of up to 70%, without histologic evidence of infarction. This method of gradual occlusion also promotes development of coronary collaterals in pigs, which have minimal collateral perfusion and high mortality rates with acute occlusion.\(^\text{14}\)

The human analog to these experimental studies is a totally occluded coronary artery without evidence of myocardial infarction. In man, although the process of atherosclerosis may be relatively gradual, factors such as coronary spasm,\(^\text{15, 16}\) thrombosis\(^\text{17-19}\) and acute hemorrhage into a plaque can result in abrupt occlusion of atherosclerotic vessels, which might otherwise progress to complete occlusion at a slower rate. Thus, if these factors play a major role in the majority of myocardial infarctions,\(^\text{17}\) the resulting infarction does not truly reflect the potential collateral perfusion and subsequent results that might have occurred with more gradual occlusion. Two large angiographic studies in man indicate that the incidence of totally occluded coronary arteries without ventriculographic evidence of myocardial infarction is impressively high. Levin\(^\text{2}\) reported that 46 of 166 totally occluded vessels (28%) did not result in infarction. Hamby et al.\(^\text{3}\) reported that 138 of 465 totally occluded vessels (30%) did not result in infarction. These investigators could not assess for the time course of coronary occlusion, but Rösch and Rahimtoola\(^\text{4}\) studied 77 patients for the progression of coronary disease and found that nine of 18 coronary lesions (50%) that progressed to complete occlusion did not result in infarction. The mean follow-up period between angiographic studies was 29 months. Other investigators concerned with the progression of coronary lesions have noted progression to total occlusion but did not evaluate the effect on the myocardium. In a pathologic study, Baroldi\(^\text{5}\) demonstrated that 44% of patients with one or more occlusions did not have histologic evidence of myocardial necrosis; however, inferences from pathologic studies may be limited.

Totally occluded vessels subtending NIECDMRs permit the study of the adequacy of collateral perfusion during exercise. Gregg and Patterson\(^\text{6}\) suggested that patients with a total coronary occlusion without myocardial infarction and without disease of other vessels might be the optimal subset of patients in which to study human coronary collaterals during exercise. However, they suggested that these patients may be asymptomatic and would not generally consult a physician and would not ultimately be referred for studies. All 31 of our patients were referred for cardiac catheterization, and four had one-vessel disease and total occlusions subtending NIECDMRs. These four had
exercise-induced perfusion defects in the collateral-dependent regions.

Collateral Responses to Exercise

Previous studies of collateral function during exercise have used exercise electrocardiography. The inability of the exercise ECG to localize the lesion causing ischemia renders this test unsuitable for the study of collaterals in multivessel coronary disease. One cannot assume that the most severe angiographic coronary lesion is the source of the exercise ischemia. Indeed, seven of our 31 patients had perfusion deficits during exercise in regions corresponding to diseased vessels that did not contain the most severe angiographic lesions. The high sensitivity and regional specificity of MPI permit a better correlation of angiographically determined pathoanatomy with functional regional responses during exercise. Rigo et al. used exercise MPI to study coronary collateral function during exercise. However, interpretation of their results is difficult because a majority of the regions analyzed were infarcted. Nevertheless, the study suggested a role of coronary collaterals in providing relative protection from stress-induced ischemia.

Twenty-two of 41 NIECDMRs (54%) manifested perfusion deficits during exercise; MPI demonstrated uniform perfusion in 19 NIECDMRs (46%) during exercise. The high percentage of exercise-negative NIECDMRs suggested that collateral perfusion has a functional role during exercise. Thirteen of the 19 exercise-negative NIECDMRs were in patients who had exercise-induced defects in other myocardial regions, and were thus negative relative to other jeopardized regions simultaneously present. They might have become positive if perfusion deficits or ischemia in other regions had not, presumably, terminated exercise. However, six of the 19 exercise-negative NIECDMRs (group 2) were in patients who did not have exercise-induced perfusion deficits in any myocardial region. These group 2 NIECDMRs might have received adequate collateral perfusion during maximal exercise. Although all these group 2 exercise-negative NIECDMRs were associated with a positive exercise ECG, the achieved work load (rate-pressure product) for these patients was significantly higher than that of patients who had NIECDMRs associated with new perfusion defects during exercise. In addition, four of the six group 2 NIECDMRs were associated with fatigue rather than chest pain as the exercise-limiting symptom. Thus, although the presence of ischemia during exercise in group 2 NIECDMRs was unclear, the distinctly higher level of exercise achieved in this group suggests that uniform global malperfusion and inappropriate timing of thallium injection as causes of false-negative exercise MPI are less likely. Experimental studies of fully developed chronic collaterals in dogs have shown that protection from ischemia during exercise ranges from minimal to complete.

Regional Nature of Collateral Protection

Collateral perfusion during exercise appeared to be adequate in the inferior and lateral myocardial regions. LAD disease, when present, was invariably the source of exercise perfusion deficits regardless of whether collaterals were present. The possibility that MPI preferentially detected anterior or septal perfusion defects due to spatial or technical factors inherent in the technique is not likely, as MPI detected documented pathology in all myocardial regions with similar sensitivity. These data are consistent with other studies demonstrating the high sensitivity of MPI in detecting the fixed perfusion defect of infarction regardless of location. MPI detection of infarction may differ from detection of ischemic perfusion. In patients with multivessel disease, however, the possibility that several myocardial regions were simultaneously ischemic but only one region manifested a perfusion defect on exercise MPI should theoretically result in significant hemodynamic alterations during exercise. Only one of our patients had hypotension during exercise.

The inability of collaterals to provide adequate perfusion during exercise in the LAD myocardial distribution may be due either to intrinsic differences between LAD collaterals and RCA or LCx collaterals or to the larger myocardial mass supplied by the LAD artery in man. The latter is the more likely explanation because pathologic, hemodynamic and enzymatic estimations of infarct size and prognostic studies indicate that the LAD perfuses the greater portion of the left ventricular myocardium in man. The regional response to exercise is dependent on the myocardial perfusion and on the size of the myocardium at risk to which perfusion must be distributed. Regional myocardial blood flow normalized to the mass of the perfused myocardium is a variable used extensively in experimental and clinical studies. Thus, myocardial perfusion imaging provides information about the presence of coronary disease and probably gives a gross assessment of the relative regional myocardial perfusion normalized to the mass of the region. We did not attempt to quantify the size of NIECDMRs, as angiographic determinations of the size of perfused regions are only approximations and the technetium-labeled albumin technique is appropriate only when antegrade flow is present. The size of the risk region assessed in terms of proximal, middle, or distal occlusion of the vessel did not predict the exercise NIECDMR response, probably because of the preponderance of proximal lesions in this series.

Angiographic Features That Predict Collateral Function

The reliance on coronary angiography as the standard to assess collateral function is a major source of the controversy over collateral function. Collateral function is heavily dependent on adequate development of collateral pathways before occlusion; even then, only exercise studies can assess their capabilities. In addition, methods of analysis used in the past are probably inappropriate:

(1) Inclusion of myocardial infarctions in the analysis of collateral function is affected by healing and scarring, which could affect the caliber and nature of the collaterals visualized angiographically. Experimental myocardial infarctions after acute coronary oc-
clusions suggest inadequate prior collateral protection. Yet, these same pathways would likely provide protection from infarction if more gradual occlusion had occurred.

(2) Analysis of collaterals in vessels that are not completely occluded cannot separate the contributions of the antegrade and collateral flow. In addition, less severe coronary stenosis may not promote full collateral development.

(3) Analysis of collateral function by exercise ECG in the presence of multivessel disease is limited because the exercise ECG does not accurately localize the source of ischemia.

(4) The assumption that angiographic indexes of collateral function should predict true collateral responses is not supported by our results (table 5), which indicate that several common angiographic indexes of collateral function did not predict true functional exercise responses as measured by the adequacy of collateral perfusion on exercise MPI. Only the angiographic dye appearance time predicted functional results; shorter angiographic dye appearance times correlated with collaterals that provided normal perfusion during exercise. However, this index varied widely and is probably not a reliable index for individual cases. In addition, none of the collateral indexes assess the mass of the jeopardized myocardium, which may be a major determinant of the ultimate regional response during exercise.

We conclude that coronary collaterals, in general, may provide relatively adequate perfusion to the inferior and lateral regions of the myocardium subtended by the RCA and LCx. Disease of the LAD is more likely to result in exercise-induced deficits regardless of collateral perfusion, probably due to the larger mass of myocardium requiring indirect sources of perfusion. Angiographic indexes of collateral function are not useful for predicting the collateral response to exercise. The high incidence of coronary lesions that progress to complete occlusion without resulting infarction suggests that coronary collaterals can play a major adjunctive role in medical therapy aimed at preventing coronary spasm and acute thrombosis. Collaterals that develop fully may provide adequate perfusion to prevent infarction and exercise-induced ischemia. In addition, therapy that has direct effects on collateral conductance would also be beneficial. These modalities provide an important rationale for the medical management of coronary artery disease. The time course required for adequate collateral development in man needs further definition. This may be derived from studies of the time course of the progression of coronary lesions to complete obstruction and the effects of the total occlusion on the underlying myocardium.

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Significance of the Angiographic Morphology of Localized Coronary Stenoses: Histopathologic Correlations

DAVID C. LEVIN, M.D., AND JOHN T. FALLON, M.D., PH.D.

SUMMARY Postmortem coronary angiographic morphology was correlated with histologic sections of 73 localized subtotal coronary artery stenoses (50-99% reduction of luminal diameter) to determine whether complicated or uncomplicated atherosclerotic lesions could be detected angiographically. Lesions were divided into two types, according to angiographic morphology: Type I stenoses had smooth borders, an hourglass configuration, and no intraluminal lucencies; type II stenoses had irregular borders or intraluminal lucencies. Histologic sections were also divided into two types: “Uncomplicated” stenoses had fatty or fibrous plaques with intact intimal surfaces and no superimposed thrombus; “complicated” stenoses manifested plaque rupture, plaque hemorrhage, superimposed partially occluding thrombus, or recanalized thrombus.

Among 35 lesions with type I angiographic morphology, four (11.4%) were complicated lesions histologically. Among the 38 stenoses showing type II angiographic morphology, 30 (78.9%) were complicated lesions. Postmortem angiography thus had a sensitivity of 88% and specificity of 79% for detecting complicated stenoses on the basis of irregular borders or intraluminal lucencies.

Pathologic studies have shown that acute occlusive thrombosis of a coronary artery is usually associated with complicated atherosclerotic stenoses. Thus, complicated lesions represent a greater risk factor for acute myocardial infarction or sudden death than do uncomplicated lesions. This study suggests that coronary stenoses characterized angiographically by irregular borders or intraluminal lucencies are probably the clinically more dangerous “complicated” type.

IN REVIEWING and interpreting coronary angiograms, it is customary for the angiographer to describe a focal lesion only in terms of the percent luminal diameter or area narrowing it produces. This practice is uniformly adhered to both in published series and in the dictation, coding and scoring of individual angiographic reports. Virtually no attempt has been made to characterize the morphology of coronary lesions by their arteriographic appearance.

Atherosclerotic coronary artery narrowing is a complex and dynamic process. According to Roberts,1 these lesions can be classified into fatty, fibrous and complicated types. Complicated lesions are often characterized by superimposed thrombosis or ulceration and are most commonly associated with acute myocardial infarction (MI). Friedman2 has pointed out that hemorrhage or acute thrombosis in recanalized coronary artery thrombi is also frequently associated with acute MI. Other pathologic studies have confirmed the fact that atherosclerotic plaques complicated by rupture, ulceration, subintimal hemorrhage, and partially occluding or recanalized thrombi are more dangerous than uncomplicated fatty or fibrous coronary lesions in that they are more likely to become acutely occluded and precipitate MI.3,2

Because complicated atherosclerotic plaques are more dangerous, it would be of great value if the angiographer could identify them in patients undergoing coronary arteriography. This study represents an initial attempt to predict the presence of complicated atheromatous lesions on the basis of angiographic morphology.
Coronary collateral function during exercise.
C Eng, R E Patterson, S F Horowitz, D A Halgash, A D Pichard, J Midwall, M V Herman and R Gorlin

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