Relation Between Coronary “Steal” and Contractile Function at Rest in Collateral-Dependent Myocardium of Humans With Ischemic Heart Disease

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Background—We tested the hypothesis that rest asynergy in collateral-dependent myocardium correlates with coronary steal.

Methods and Results—PET with [13]N ammonia measured myocardial blood flow and flow reserve in 15 patients with symptomatic chronic ischemic heart disease. Coronary angiography assessed stenosis severity and collateral blood supply. Echocardiography or contrast ventriculography evaluated regional wall motion. Collateral-dependent segments with normal flow at rest and supplied by coronary vessels having ≤50% diameter stenosis were studied. Steal was defined as a decline in myocardial blood flow with adenosine ≥0.15 mL · min⁻¹ · g⁻¹ versus rest. Blood flow at rest in asynergic, collateral-dependent segments with steal (1.15±0.35 mL · min⁻¹ · g⁻¹) exceeded that of asynergic segments without steal (0.81±0.24) and those with normal contraction (0.77±0.18). Although the flow reserve ratio of segments with normal contraction (1.8±0.8) exceeded that of asynergic ones with (0.6±0.1) or without (1.3±0.4) steal, overlap was great. Correlation between basal contraction and flow reserve ratio in collateral-dependent myocardium was significant but weak (r=0.45, P<0.001). However, segments demonstrating “steal” with adenosine manifested asynergy in 22 of 23 collateral-dependent segments versus 24 of 39 nonsteal segments (χ²=7.10, P<0.01).

Conclusions—Although myocardial flow reserve in collateral-dependent segments with normal contraction exceeded that of asynergic segments, overlap was great. However, in patients with angina or congestive heart failure, left ventricular segments demonstrating steal with adenosine almost always exhibit asynergy at rest. Thus, coronary steal may play an important role in the pathogenesis of chronic contractile impairment at rest, whereas simple reduction of flow reserve may be less important in selected patients. (Circulation. 1999;99:2510-2516.)

Key Words: myocardium ■ blood flow ■ ischemia ■ heart diseases ■ collateral circulation

Few quantitative data are available concerning flow reserve in collateral-dependent myocardium and its relation to basal myocardial contraction in humans with ischemic heart disease.1,2 Although coronary collaterals have been shown to limit the size of acute myocardial infarction,3 their ability to protect against stress-induced ischemia is uncertain. The question is important not only from the perspective of acute, demand-induced ischemia but also with regard to the longer-term issue of repetitive bouts of ischemia leading to chronic contractile dysfunction.2,4 Coronary “steal” is potentially very important in this regard but has not been addressed in previous human studies. The purpose of the present investigation, therefore, was to test the hypothesis that regional asynergy at rest in collateral-dependent myocardium correlates with coronary steal. To test this hypothesis, we studied a carefully defined set of collateral-dependent myocardial segments characterized by normal resting blood flow and a coronary feed vessel having ≤50% diameter stenosis.

Methods

Patient Population

After approval was obtained from the Human Studies Committees of the Massachusetts General Hospital, 15 patients were recruited and gave written informed consent between August 1, 1994, and May 30, 1996. Exclusion criteria included unstable angina, uncontrolled left ventricular failure or atrial fibrillation, severe hypertension, recent (within 1 month of PET study) myocardial infarction, severe chronic obstructive pulmonary disease, and inability to lie supine for a sufficient time to allow data acquisition. β-Blocker drugs were withheld for 48 hours before the study. Patients were selected for the study because of symptomatic angina (n=9) or left ventricular failure (n=6) severe enough to merit coronary revascularization and resting asynergic collateral-dependent segments with normal resting perfusion.

PET Imaging

PET imaging was performed on a Scanditronix PC4096 whole-body tomograph.5–7 The ECG and arterial pressure (Dynamap) were...
monitored continuously. At baseline, ~25 mCi of [13N]ammonia was administered intravenously over 30 seconds, with dynamic imaging begun just before injection. After image acquisition, radioactivity was allowed to decay for ~30 minutes, at which time the count rate seen by the scanner was sufficiently low to be overwhelmed by the subsequent dose. Next, 2 minutes after an infusion of adenosine at 140 µg · kg⁻¹ · min⁻¹ × 5 minutes IV had been started, dynamic data acquisition was begun, and several seconds later, ~25 mCi of [13N]ammonia was administered. Images were acquired as described above.

Attenuation-corrected [13N]ammonia images were reconstructed with a filtered back-projection algorithm. Scans using the last 6 minutes of data were summed, and a region of interest was placed over the left ventricular cavity. The region of interest was used to generate the arterial input function for the 2-compartment, 3-parameter tracer kinetic model used to compute K₁.⁵,⁸ No correction was used for partial volume effect or recirculation of labeled ammonia metabolites.⁹ A computer program developed at our institution used the dynamic 9-minute data set to generate parametric (K₁) images for determination of myocardial blood flow.¹⁰

**PET Image Analysis**

Only myocardial segments having (1) rest blood flow ≥0.6 mL · min⁻¹ · g⁻¹, (2) a feed coronary vessel with ≤50% stenosis, and (3) location in the mid or distal third of the left ventricle were analyzed. Criterion 1 excluded infarct segments; criterion 2 excluded moderate/severe, discrete, focal stenosis as a cause of impaired flow reserve; and criterion 3 ensured the best possible correspondence between PET measurements and coronary angiography.

Segments in the distribution of a coronary vessel supplying collaterals that met the above criteria also were analyzed. Conductance was computed as the ratio of myocardial blood flow to mean arterial pressure (mL · min⁻¹ · g⁻¹ · mm Hg⁻¹ · 1000). Mean arterial pressure was computed as diastolic pressure plus 0.5 x pulse pressure. A decline in blood flow with adenosine ≥0.15 mL · min⁻¹ · g⁻¹ versus baseline defined “steal” in the collateral-dependent or supply regions.

**Echocardiography**

Two-dimensional echocardiography was performed with a 2.5-MHz transducer and commercially available scanner.⁶ Short-axis rings at base and mid left ventricular levels were divided into 8 sections, each of which corresponded to those of the PET scan. By echocardiographic convention, the ring at the distal third of the left ventricle was divided into 4 sections (septum, anterior, lateral, and inferior) and matched by interpolation to appropriate PET segments for the distal third of the left ventricle.⁶ Echocardiograms were performed 24 to 48 hours after the PET study in all cases except 1, which was done 4 months later without interval change in the patient’s condition. Regional contraction in 4 patients without echocardiograms was assessed by contrast ventriculograms performed between 8 and 45 days (average, 22 days) after the PET study.

**Coronary Arteriography**

Coronary arteriography was performed by the Judkins technique. Cine films were reviewed by a single observer who was unaware of PET and echo data. Coronary stenoses were measured by the hand-caliper technique.¹¹ Coronary collaterals were graded by eye as follows: grade 1, collaterals visualized but failure to opacify recipient vessel; grade 2, recipient vessel partially opacified; and grade 3, recipient vessel fully opacified.

**Statistical Analysis**

All data are expressed as mean±SD. Group mean values of hemodynamics and blood flow parameters were compared by ANOVA and post hoc multiple-comparison test (Fisher’s Protected Least Significant Difference test; StatView V4.0, Abacus Concepts). Paired and unpaired t tests also were used for comparison of myocardial blood flow at rest versus adenosine within a segment type (paired test) and across segment types (unpaired).

### Results

**Patient Population**

Fifteen patients (12 men and 3 women) 67±8 years old (range, 50 to 81 years) were studied. Prior myocardial infarction was present in 8 patients. Triple-vessel coronary artery disease (≥70% lumen diameter reduction) was present in 1 patient, double-vessel disease in 10, and single-vessel disease in 4. Medications used are listed in Table 1. Treadmill exercise testing for clinical purposes was performed in 5 of 7 patients later found by PET examination to have steal and revealed moderate (n=2) or severe (n=3) ischemia in thalium or sestamibi images.

Eleven normal volunteers (6 men, 5 women 45±12 years old) had PET studies of myocardial blood flow at rest and with adenosine according to the same protocol as outlined above. Data from 9 of the control subjects have been reported previously.⁶

**Hemodynamics During PET**

In patients, baseline pulse was 70±13 bpm, systolic pressure 131±16 mm Hg, and rate-pressure product 9128±2050 mm Hg/min. Pulse increased significantly (76±15 bpm; P<0.01), systolic pressure declined (123±20 mm Hg; P<0.05), and rate-pressure product (9332±2144) was unchanged with adenosine. Patients with and without steal are shown separately in Table 2. Only patients without steal had a significant decline in arterial pressure with adenosine.

In control subjects, baseline pulse was 64±9 bpm, systolic pressure 130±19 mm Hg, and rate-pressure product 8351±1708 mm Hg/min. In response to adenosine, pulse increased significantly (98±31 bpm; P<0.01), systolic pressure was unchanged (128±17 mm Hg; P=NS), and rate-pressure product increased (12 664±4920; P<0.01).

**Regional Myocardial Blood Flow**

All collateral-dependent segments were in the distribution of an occluded coronary artery. Collateral vessels appeared in all cases to originate from the epicardial portion of the donor...
vessel and not from intramyocardial arterioles. Myocardial blood flow and conductance for collateral-dependent (n=62, 15 patients) and supply (n=47, 13 patients) segments, without regard to regional contraction or coronary steal status, are shown in Table 3.

Rest blood flow (0.95±0.23 mL·min⁻¹·g⁻¹) and conductance (8.37±1.88 mL·min⁻¹·g⁻¹·mm Hg⁻¹×1000) in control subjects did not differ from those of patients. Normal volunteers increased blood flow substantially with adenosine (3.21±0.72 mL·min⁻¹·g⁻¹; P<0.001 versus rest). Myocardial flow reserve ratio of control subjects (3.6±1.3) and maximal conductance (29.85±10.42 mL·min⁻¹·g⁻¹·mm Hg⁻¹×1000) both exceeded (P<0.001) those of collateral-dependent and donating zones of patients (Table 3).

### Basal Contraction Versus Rest Myocardial Blood Flow and Flow Reserve

#### Collateral-Dependent Segments

Normally contracting segments had rest blood flow (mL·min⁻¹·g⁻¹) (0.77±0.18) similar to that of segments having asynergy without steal (0.81±0.24) but less than that of asynergic segments with steal (1.15±0.35, P<0.0001; Table 4). Conductance (mL·min⁻¹·g⁻¹·mm Hg⁻¹×1000) at rest of asynergic segments with steal (10.43±4.52) was elevated (P<0.05) versus normal (6.86±1.54), but not that of asynergic segments without steal (8.04±1.93; Table 5). Maximal blood flow with adenosine (1.38±0.61) and flow reserve ratio (1.8±0.8) of normal segments exceeded (both P<0.001) that of segments with asynergy with (0.74±0.29 and 0.6±0.1, respectively) and without (1.02±0.33 and 1.3±0.4, respectively; Table 4) steal. Similarly, maximal conductance was greater in normal segments (13.03±5.52) than in those with asynergy with (7.13±2.38; P<0.0001) and borderline greater without (10.65±3.30; P=0.06) steal. The decline in myocardial blood flow with adenosine in asynergic segments with steal was 36±14% versus rest and by definition was highly significant (P<0.0001).

Although mean values of flow reserve ratio, maximal myocardial blood flow, and conductance differed significantly, substantial overlap occurred across contraction groups (Figure, top) and only weak, albeit statistically significant, correlations between each of these parameters and regional contraction at rest (Table 6). Indeed, of 16 segments having normal contraction at rest, only 3 had normal maximal flow response to adenosine. In contrast, 22 of 23 segments exhibiting steal with adenosine had asynergy at rest, and only 1 contracted normally (z=-2.97; P=0.01). Collateral grade was modestly lower and percent stenosis of feed vessels somewhat greater for segments with normal contraction than that of asynergic segments (Table 7).

#### Collateral Supply Segments

Normally contracting segments had basal blood flow (0.85±0.24) similar (both P=NS) to that of segments with asynergy (1.09±0.57) or without (0.97±0.34) steal. Conductance at rest was modestly lower in normal segments than in those with asynergy and steal (Table 5). Maximal myocardial blood flow (2.02±0.87) and flow reserve ratio (2.4±0.9) of normally contracting segments exceeded (both P<0.01) those of asynergic segments with (0.72±0.50 and 0.6±0.1, respectively) or without (1.31±0.58 and 1.4±0.5, respectively) steal. Similarly, maximal conductance of normally contracting segments (19.59±6.92) (Table 5) exceeded that of asynergic segments with (7.08±4.07) or without (12.92±4.91) steal. Maximal conductance of normally contracting segments in collateral supply myocardium also exceeded (P<0.01) that of collateral-dependent segments. The decline in myocardial blood flow with adenosine in asynergic segments with steal was 38±12% versus rest and by definition was highly significant (P<0.0001). Finally, there was substantial overlap between flow reserve ratio, maximal

### TABLE 3. Myocardial Blood Flow

<table>
<thead>
<tr>
<th>Zone</th>
<th>Qrsₐ</th>
<th>Qado</th>
<th>Qado/Qrsₐ</th>
<th>Grsₐ</th>
<th>Gado</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collateral dependent</td>
<td>0.94±0.34</td>
<td>1.01±0.46</td>
<td>1.2±0.7</td>
<td>8.92±2.99</td>
<td>9.94±4.30</td>
</tr>
<tr>
<td>Collateral supply</td>
<td>0.97±0.38</td>
<td>1.36±0.73†</td>
<td>1.5±0.9³</td>
<td>9.17±3.13</td>
<td>13.29±6.94†</td>
</tr>
</tbody>
</table>

Qrsₐ indicates rest myocardial blood flow; Qado, adenosine myocardial blood flow; Grsₐ, rest myocardial conductance; and Gado, adenosine myocardial conductance. Values for blood flow are mL·min⁻¹·g⁻¹; for conductance, mL·min⁻¹·g⁻¹·mm Hg⁻¹×1000. Data shown are for all segments regardless of contraction or “steal” status.

*P=0.05 vs collateral dependent; †P<0.001 vs Qrsₐ; ‡P<0.01 vs Grsₐ.
myocardial blood flow, and conductance with adenosine on the one hand and myocardial contraction at rest in collateral supply regions on the other (Table 6, Figure, bottom).

**Discussion**

**Principal Findings**

This study tested the hypothesis that regional contractile abnormalities at rest in collateral-dependent myocardium correlate with coronary steal. We demonstrated that myocardial flow reserve is considerably impaired in collateral-dependent and to a lesser extent in collateral-supply myocardium. The degree of impairment in \( \approx 33\% \) (23 of 62) of collateral-dependent segments was sufficient to result in coronary steal with adenosine. Segments susceptible to steal, in accordance with the proposed hypothesis, had asynergy at rest in 22 of 23 cases (96%). Because only myocardial regions with normal resting blood flow were included in this analysis, prior myocardial infarction is an unlikely cause of rest asynergy.

Abnormal myocardial flow reserve, maximal myocardial blood flow, and conductance demonstrated in collateral-dependent and supply myocardium probably reflect a combination of factors. In collateral-dependent myocardium, impedance to flow in the collateral vessels and the expected

**TABLE 4. Myocardial Blood Flow**

<table>
<thead>
<tr>
<th>Basal Contraction</th>
<th>Q_{st}</th>
<th>Q_{sb}</th>
<th>Q_{sb}/Q_{st}</th>
<th>Segments, n</th>
<th>Patients, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collateral-dependent zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0.77±0.18</td>
<td>1.38±0.61( \dagger)§</td>
<td>1.8±0.8§</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>1.15±0.35( \dagger)</td>
<td>0.74±0.24*</td>
<td>0.6±0.1</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>0.81±0.24</td>
<td>1.02±0.33( \dagger)</td>
<td>1.3±0.4</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Collateral-supply zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0.85±0.24</td>
<td>2.02±0.80( \dagger)</td>
<td>2.4±0.9( \dagger)</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>1.09±0.54</td>
<td>0.72±0.50*</td>
<td>0.6±0.1</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>0.97±0.34</td>
<td>1.31±0.58( \dagger)</td>
<td>1.4±0.5( \dagger)</td>
<td>22</td>
<td>8</td>
</tr>
</tbody>
</table>

Asynergy indicates hypokinesis or akinesis. Abbreviations as in previous tables. Note, two segments with normal contraction, one collateral dependent and one collateral supply, had steal with adenosine and thus are not included in group mean data. Values are mL·min \(^{-1} \)·g \(^{-1} \)·mm Hg \(^{-1} \)·1000, mean±SD.

\*\( P<0.0001 \) vs rest.
\( \dagger\)\( P<0.005 \) vs rest.
\( \ddagger\)\( P<0.0001 \) vs normal and asynergy, nonsteal.
\( \S\)\( P<0.0001 \) vs asynergy, steal and \( P<0.01 \) vs asynergy, nonsteal.
\( ||\)\( P<0.05 \) vs asynergy, steal.
\( \dagger\)\( P<0.001 \) vs asynergy, steal and nonsteal.
\#\( P<0.005 \) vs asynergy, steal.

**TABLE 5. Myocardial Conductance**

<table>
<thead>
<tr>
<th>Basal Contraction</th>
<th>G_{st}</th>
<th>G_{sb}</th>
<th>Segments, n</th>
<th>Patients, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collateral-dependent zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6.86±1.54</td>
<td>13.03±5.52( \dagger)</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>11.03±3.20( \dagger)</td>
<td>7.13±2.38( \dagger)</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>8.04±1.93</td>
<td>10.65±3.30( \dagger)</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Collateral-supply zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>7.87±2.10(</td>
<td>19.59±6.92( \dagger)</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>10.43±4.52</td>
<td>7.08±4.07( \dagger)</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>9.12±2.54</td>
<td>12.92±4.91( \dagger)</td>
<td>22</td>
<td>8</td>
</tr>
</tbody>
</table>

Asynergy indicates hypokinesis or akinesis. Abbreviations as in previous tables. Note, two segments with normal contraction, one collateral dependent and one collateral supply, had steal with adenosine and thus are not included in group mean data. Values are mL·min \(^{-1} \)·g \(^{-1} \)·mm Hg \(^{-1} \)·1000, mean±SD.

\( \dagger\)\( P<0.0001 \) vs rest.
\( \dagger\)\( P<0.005 \) vs rest.
\( \ddagger\)\( P<0.0001 \) vs normal and asynergy, nonsteal.
\( \S\)\( P<0.0001 \) vs normal and \( P<0.001 \) vs asynergy, nonsteal.
\( ||\)\( P<0.05 \) vs asynergy, steal.
pressure drop proximal to collateral origin in the conduit artery will both contribute to reduced conductance in the collateral-dependent bed during coronary dilation with adenosine. Furthermore, in the presence of diffuse atherosclerosis or even mild focal stenosis of the supply vessel, pressure loss in the conduit portion of the supply artery may be even greater and result in steal. Under such conditions and in the presence of either diffuse atherosclerosis or even mild focal stenosis, impedance to flow in the conduit supply artery may be increased substantially and could contribute importantly to reduced maximal blood flow and conductance in the collateral supply bed.

Steal in collateral-supply myocardium occurred simultaneously with steal in collateral-dependent myocardium in 5 of 7 patients in whom steal developed. Because the mechanism of steal involves the combination of pressure drop at the origin of collaterals and enhanced flow as a result of lower overall resistance in collateral supply myocardium, the simultaneous decline in myocardial blood flow in both territories argues against the standard model in such cases. Although collapse of a stenotic lesion as a result of adenosine-induced vasodilation could account for simultaneous decline in flow in both collateral-dependent and supply myocardium, diffuse atherosclerosis of the supply artery, which may cause substantial flow impendence, appears more likely, because collapse generally occurs only with severe stenoses, which were excluded in these patients.

Literature Review and Clinical Implications

A previous study indicated that normally contracting, collateral-dependent segments had normal flow reserve with dipyridamole (n=3 patients), whereas similar segments with impaired basal contraction had impaired flow reserve (n=8 patients), but coronary steal was not considered. The present study indicates that basal contraction may be well preserved despite substantial impairment of flow reserve in collateral-dependent myocardium (Figure, top) but is impaired in the presence of myocardial steal.

Impaired flow reserve in collateral-dependent and supply myocardium of humans with ischemic heart disease has been reported, although flow reserve ratio was reduced somewhat more in the present study. The reason for this primarily reflects a difference in the level of basal myocardial blood flow, which was reduced in previous reports but normal in the present one. Because segments in the present study were selected for normal resting blood flow, the question of reduced resting flow with persistent vasodilator reserve is not relevant. It is noteworthy, however, that in collateral-dependent myocardium in the present study, some vasodilator reserve persisted in segments with normal contraction and may have contributed to its maintenance, because the increment in myocardial blood flow required to meet the demands of maximal dobutamine stress is not large. Finally, although coronary steal is frequently associated with collateral-dependent status, data from the present study indicate that

### TABLE 6. Correlation Matrix: Segment Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>r</th>
<th>r²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent stenosis</td>
<td>−0.30</td>
<td>0.09</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Collateral grade</td>
<td>0.38</td>
<td>0.14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Q̇_ad</td>
<td>0.27</td>
<td>0.07</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_rst</td>
<td>−0.33</td>
<td>0.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_all</td>
<td>−0.45</td>
<td>0.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q̇_ad</td>
<td>0.33</td>
<td>0.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_all</td>
<td>−0.31</td>
<td>0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Percent stenosis</td>
<td>−0.51</td>
<td>0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Collateral grade</td>
<td>0.34</td>
<td>0.12</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Q̇_ad</td>
<td>0.14</td>
<td>0.02</td>
<td>NS</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_rst</td>
<td>−0.36</td>
<td>0.13</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_all</td>
<td>−0.47</td>
<td>0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q̇_ad</td>
<td>0.13</td>
<td>0.02</td>
<td>NS</td>
</tr>
<tr>
<td>Q̇_ad/Q̇_all</td>
<td>−0.38</td>
<td>0.14</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Abbreviations as in previous tables. Percent stenosis and collateral grade refer to the collateral supply artery.
only a minority of collateral-dependent segments with normal resting blood flow will have steal with coronary vasodilation (23 of 62; 37%) and that many collateral-dependent segments, especially those without steal, have normal basal contraction (15 of 62; 23%).

The question of steal induced by exogenous adenosine and susceptibility to steal under clinical conditions also requires discussion. Exercise stress in the face of normal myocardial perfusion is a less potent stimulus to coronary vasodilation than exogenous adenosine in the dose used in the present study.\(^7\) However, under conditions of restricted coronary inflow, interstitial fluid adenosine may increase as much as 10-fold (from 0.1 to 1.0 \(\mu\)mol/L) as a result of stress-induced myocardial ischemia\(^{23,24}\) and thereby achieve levels comparable to those observed with exogenous administration. Furthermore, the adenosine dose-response relationship is very steep, with an \(\text{ED}_{50}\) estimated at 0.15 \(\mu\)mol/L.\(^{25}\) Thus, small increments in interstitial adenosine have rather large effects in terms of arteriolar dilation\(^{26}\) and thus would favor conditions for intraregional steal.\(^{20}\) A previous study from our laboratory\(^7\) also demonstrated that segments prone to steal with adenosine are likely to have steal with dobutamine, a pharmacological stress much more similar to exercise. Accordingly, it is possible that segments exhibiting steal with exogenous adenosine are vulnerable to steal under clinical conditions.

The selection of patients in this small study as having angina or heart failure may have specifically selected those with the combination of just enough collaterals and diffuse coronary artery disease that would maintain resting perfusion but cause steal with daily activity in association with myocardial stunning and resting left ventricular dysfunction. However, other patients without angina or heart failure may have steal after adenosine or dipyridamole without steal or ischemia occurring with daily activities, because clinically and in previous reports of quantitative myocardial steal by PET,\(^{26}\) left ventricular dysfunction is not a prominent aspect of the population studied. Our study, considered with previous reports, indicates a spectrum of collateral effects ranging from preventing infarction but causing myocardial stunning and resting asynergy to prevention of any ischemia.

### Study Limitations

The finite spatial resolution of the PET scanner is the principal limitation, but partial-volume effect seems unlikely, because there was no correlation between regional wall motion and rest blood flow (Table 4). If endocardial scar were present and contributed importantly to lowering rest blood flow, segments with asynergy on average would have lower, not higher, flows than normally contracting segments.

The potential reversibility of resting contraction abnormalities after revascularization was not evaluated. Because accurate prediction of return of contractile function after coronary revascularization remains problematic,\(^{27}\) the use of clinical criteria to exclude a substantial degree of scar in segments with rest asynergy may be unreliable. However, to the extent that such criteria are useful, it has been shown\(^{28}\) that segments with improved contraction after revascularization had higher levels of rest blood flow (0.84 ± 0.27) than those without (0.60 ± 0.26). Rest blood flow in collateral-dependent myocardium in the present study (0.94 ± 0.34) compares favorably with that in segments that improved in the earlier report.\(^{28}\)

### Summary

Maximal blood flow generally is substantially impaired in collateral-dependent myocardium, although less so in segments with normal basal contraction. Collateral supply myocardium also has reduction of maximal blood flow, albeit less marked than that of collateral-dependent myocardium. The cause of impaired maximal blood flow appears to be multifactorial, with hydraulic, conduit-vessel factors playing an important role, although microvascular dysfunction may contribute.

Simple reduction of flow reserve per se is a poor predictor of rest asynergy and suggests that some other factor(s) must

---

**TABLE 7. Coronary Anatomy**

<table>
<thead>
<tr>
<th>Basal Contraction</th>
<th>Collateral Grade</th>
<th>Percent Stenosis</th>
<th>Segments, n</th>
<th>Patients, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collateral-dependent zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>2.3±0.6*</td>
<td>45±8†</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>2.7±0.5</td>
<td>29±20</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>2.5±0.5</td>
<td>23±22</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Collateral-supply zone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1.7±0.9‡</td>
<td>43±9§</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Asynergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steal</td>
<td>2.6±0.5</td>
<td>38±15</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Nonsteal</td>
<td>2.3±0.6</td>
<td>26±21</td>
<td>22</td>
<td>8</td>
</tr>
</tbody>
</table>

Note: Two segments with normal contraction, one collateral dependent and one collateral supply, had steal with adenosine and thus are not included in group mean data. Percent stenosis and collateral grade refer to the collateral supply artery. Values are mean±SD.

\*\(P<0.01\) vs asynergy, steal.

†\(P<0.001\) vs asynergy, nonsteal and \(P<0.05\) vs asynergy, steal.

‡\(P<0.001\) vs asynergy, steal and \(P<0.05\) vs asynergy, nonsteal.

§\(P<0.01\) vs asynergy, nonsteal.
be involved. Because segments susceptible to steal with adenosine are most likely to have asynergy at rest, the data suggest that ischemia required to produce rest asynergy must be severe or repetitive, as may occur with myocardial steal.

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Relation Between Coronary "Steal" and Contractile Function at Rest in Collateral-Dependent Myocardium of Humans With Ischemic Heart Disease
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