Coronary Collateral Circulation and Myocardial Blood Flow Reserve

By Suzanne B. Knoebel, M.D., Paul L. McHenry, M.D., John F. Phillips, M.D., and Ferrel J. Pauletto, M.D.

SUMMARY
This study was undertaken to assess the effect of collateral circulation on myocardial blood flow (MBF) reserve (ability to increase myocardial blood flow with a stress that increases myocardial oxygen requirements). One hundred patients had MBF measured at rest and after isoproterenol. After classification by anatomic severity of coronary artery disease (CAI), the groups were further compared by presence or absence of collateral vessels, and whether the collaterals were intercoronary or bridge collaterals. Forty patients (group A) had no coronary artery disease demonstrated by cineangiography. The increase in MBF with isoproterenol for this group was 87% (P < 0.001). Fifteen patients (group B) had CAI of 175 or greater. These patients increased MBF 73% on infusion of isoproterenol, an insignificant difference from group A. Forty-five patients (group C) had CAI of 175 or less when an index of 300 represents no occlusive disease. Those with intercoronary collateral vessels (group C1, 2) were unable to increase MBF to the same extent as patients in groups A and B did. There was no difference between this group and those without collateral vessels and the same severity of disease. Fifteen patients with CAI of 175 or less (group C3, 4) had bridge collaterals and were able to increase MBF to a greater extent than those with no collaterals or with intercoronary collateral vessels. This same group of patients, in a parallel observation, showed less S-T-segment depression on treadmill exercise than patients with intercoronary collateral vessels.

The data suggest that intercoronary collateral vessels contribute insignificantly, statistically, to myocardial blood flow reserve. Bridge collaterals, however, do seem to contribute in selected patients.

Additional Indexing Words:
Isoproterenol
Rubidium
Coronary blood flow
Coincidence counting

The functional significance of the coronary collateral circulation has received increasing attention with the advent of arteriographic technics and with surgical efforts to increase myocardial blood supply. It has been shown that intercoronary collateral vessels are not protective in the sense that their presence or absence apparently does not alter significantly the incidence of angina, myocardial infarction, and hemodynamic or ventriculographic abnormalities.1-3 On the other hand, the suggestion has been made that collateral vessels are responsible for the normal electrocardiogram seen in patients with coronary artery disease.4 The presence of

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84 Circulation, Volume XLVI, July 1972
collaterals has been shown to correlate with the severity of coronary obstructive disease in that collaterals have not been demonstrated cinearteriographically in patients without coronary artery disease or in those with less than 50% reduction in lumen.

To examine the effect of collateral circulation on myocardial blood flow reserve, or the ability to increase myocardial blood flow with a stress designed to increase myocardial oxygen requirements, patients, after classification by anatomic severity of coronary artery disease, were divided into groups depending on the type of collateral vessels. Myocardial blood flow was measured with a coincidence counting system and single bolus of $^8$RbCl at rest and during isoproterenol stress. Parallel observations were made on treadmill exercise performance.

**Methods**

In 100 patients undergoing selective coronary cinearteriographic studies for the diagnosis or evaluation of coronary arteriosclerotic occlusive disease, the myocardial blood flow was determined while they were at rest and during isoproterenol infusion just prior to arteriographic study. All patients with a normal resting electrocardiogram had been tested on the treadmill a day or two before the blood flow and arteriographic studies.

The exercise-induced changes in the depression and slope of the S-T segment were quantitated with a digital computer. The quantitated S-T-segment changes were expressed in terms of an S-T index giving the equal weight to the slope and the depression of the S-T segment. The larger the S-T index the greater the degree of segmental S-T depression.

Criteria for an abnormal computer-quantitated S-T-segment index are (1) if S-T depression of 1.0 mm or greater and (2) the sum of S-T depression in millimeters and S-T slope in millivolts per second of zero or less. An example of a normal response would be:

S-T depression = −1.5 mm
S-T slope = +2.5 mv/sec
Sum of −1.5 and +2.5 = +1.0 S-T index

An example of an abnormal response would be:

S-T depression = −2.5 mm
S-T slope = +1.5 mv/sec
Sum of −2.5 and +1.5 = −1.0 S-T index

Only patients with normal resting electrocardiograms could be so quantitated.

All studies were performed in the morning with the patients in a fasting state and without sedation. Measurements were made in the supine position.

Blood pressure was measured via an indwelling polyethylene catheter, introduced percutaneously into the right brachial artery, connected to a Statham P23-D strain-gauge transducer, and recorded on a Sanborn recorder (model 150). The mean arterial pressure was obtained by electrical integration. Heart rate was measured from a simultaneously recorded electrocardiogram. The cardiac output was determined by using $^8$RbCl as the indicator. A previous comparison of cardiac outputs measured by $^8$RbCl and indocyanine green (Cardio-Green) in dogs resulted in a correlation coefficient of 0.9178.

Myocardial blood flow (MBF) in ml/min/total heart was calculated by the formula:

$$MBF = q(t) \int_0^\infty Ao(t) \, dt$$

where $q(t)$ is the myocardial uptake of $^8$RbCl as measured by the coincidence counting system and

$$\int_0^\infty Ao(t) \, dt$$

represents the concentration of the isotope in arterial blood during the first circulation, determined by extrapolation after recirculation begins. The experimental and theoretic background for this technic has been previously described. Reproducibility of this measurement of myocardial blood flow has been demonstrated ($P < 0.005$).

After the resting measurements, isoproterenol infusion was begun (3 to 5 $\mu$g/min), and the second measurements were made either when angina was induced or when the infusion had been given for 2 minutes at a control rate. This relatively brief but rapid rate of infusion was chosen so that those patients experiencing chest pain necessitating discontinuance of the infusion would not receive significantly less isoproterenol than other patients.

After completion of the myocardial blood flow and hemodynamic measurements, selective coronary cinearteriography was performed by the percutaneous femoral approach with appropriate preshaped catheters. Multiple oblique views were obtained after administration of methylglucamine diatrizoate (Renographin 76 contrast media). Injections were made before and after a sublingual dose of nitroglycerin. Recording was with 35-mm double-X film developed in Ethol-90. A Phillips 6-inch image intensifier was utilized with 100-mm lens at 64 frames/sec.

*Circulation, Volume XLVI, July 1972*
Only patients whose cineangiograms were of good quality in multiple projections of all three major coronary vessels were included in this study. Classification of the coronary arterial lesions was done as follows: Each of the three major coronary vessels (right, left anterior descending, and circumflex) was given a rating of 100. The number of vessels which remained open was estimated in increments of 25%. If the left main coronary artery was diseased, the percentage of occlusion was subtracted from a rating of 200. In the case of branch stenosis, the degree of occlusion was estimated according to the technic of Rowe and associates.\textsuperscript{12} That is, if for example the anterior descending branch bifurcated giving off a branch which was estimated to be 50% of the size of the parent vessel and if this vessel were 50% occluded, the occlusion was equivalent to a 25% occlusion of the anterior descending coronary artery. A final coronary artery index was then based on the estimated percentage of lumen of all three vessels remaining open (300 equalling no occlusive disease).

Collateral vessels were classified as follows: type 0, no collaterals; type 1, collaterals present by indirect evidence, i.e., collaterals were inferred from delayed visualization of an arterial segment distal to a complete or nearly complete occlusion with injection into a heterolateral artery; type 2, collaterals present by visible anastomoses between the artery producing collateral flow and the recipient vessel; type 3, intersegmental (bridge) anastomoses forming a bypass network; and type 4, intersegmental (bridge) anastomoses formed by a vessel the approximate size of the occluded vessel. Type 3 and 4 collaterals were demonstrated by injection in the same artery proximal to the site of occlusion. The cinearteriograms were interpreted independently by three observers without knowledge of the physiologic data. When observer disagreement was found, the films were reviewed and appropriate agreement was reached.

The myocardial blood flow and the cardiac output responses were then compared with the coronary artery index: group A having no demonstrable coronary disease; group B, a coronary artery index of 175 or greater; and group C, an index of 175 or less. An index of 175 was a natural dividing point, as 15 of 16 patients with this index had a myocardial blood flow response to isoproterenol which fell within the range of patients without coronary artery disease. The data were analyzed as the difference of group means of paired data. After this first division, further breakdown was by groups of patients with collateral vessels: group B\textsubscript{1,2} (coronary artery indices of 175 or greater and collaterals of type 1 or 2); group C\textsubscript{1,2} (coronary indices of 175 or less and collateral vessels of type 1 and 2); group C\textsubscript{3,4} (coronary artery indices of 175 or less and collaterals of type 3 or 4); and groups B\textsubscript{0} and C\textsubscript{0} (with the respective cardiac indices of 175 or more and 175 or less but without collateral vessels). The myocardial blood flow, cardiac output, percentage of cardiac output which was myocardial blood flow, and the amount of S-T-segment depression on treadmill test for these groups were compared by using the standard comparison of differences between independent group means.

\textbf{Results}

\textbf{Group A}

Of the 100 patients studied, 40 (group A) had no coronary artery disease demonstrated cineangiographically and, therefore, had coronary artery indices of 300. No collateral vessels were visualized. The average increase in myocardial blood flow over resting value (average, 239 ml/min ± 82) was 189 ml/min or 87% ± 43 (P < 0.001). The average resting cardiac output was 5.5 liters/min with an increase to 8.7 liters/min with isoproterenol (P < 0.001), or 60%. The resting myocardial blood flow equalled 4.4% of the cardiac output. With isoproterenol the myocardial blood flow was 5.0% of the cardiac output. The difference between the myocardial blood flow expressed as percentage of cardiac output at rest and with isoproterenol was significant at the (P < 0.001) level. The data for group A are presented in table 1.

\textbf{Group B}

Group B included 15 patients with coronary artery indices of 175 to 250. These patients were able to increase myocardial blood flow to within the range of normal (42 to 144%), the average increase being 180 ml/min, or 73% ± 29 above resting values (P < 0.001). Nine patients in this group had collateral vessels of types 1 to 3, and six had no collaterals visualized. The average resting cardiac output for the group was 5.1 liters/ min, increasing an average of 3.6 liters/min, or 73% ± 29 with isoproterenol (P < 0.001). Resting and isoproterenol myocardial blood flow equalled 4.3 and 4.8% of the cardiac output, respectively. The significance of this difference was P < 0.02. There was no difference in any

\textit{Circulation, Volume XLVI, July 1972}
of the resting or isoproterenol data for patients with collateral vessels and those without them. This group was, therefore, handled as a homogeneous group from this point forward. The data for this group are presented in Table 2.
Myocardial Blood Flow (MBF) and Cardiac Output (CO) Response during Rest (R) and Isoproterenol Infusion (I) in Patients with Coronary Artery Indices (CAI) of 175 or Greater (Group B)

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<th>Age (yr)</th>
<th>Sex</th>
<th>MBF (ml/min/total heart)</th>
<th>CO (liters/min)</th>
<th>MBF (%Δ)</th>
<th>CO (% of CO)</th>
<th>CAI*</th>
<th>Collaterals†</th>
<th>S-T index*</th>
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Average 49  
220  400  +73  5.1  8.7  +73  4.3  4.8  -1.7  

sd  
+43  +88  +29  +0.9  +1.7  +29  +0.8  +1.0  ±0.95  

P  
<0.001  <0.001  <0.001  

*See text for derivation.  
†Collaterals by type (numbers) and direction of flow (for example, L-R signifies left-to-right flow).  
‡Abnormal baseline ECG.

Group C

Group C included 45 patients with coronary artery indices of 175 or less. Thirty-eight (84%) of these patients had collateral vessels. Twenty-three of these 38 patients (group C1, 2) had collaterals of type 1 or 2 (table 3). The average increase in myocardial blood flow with isoproterenol for this group was 5% ± 16. The change was not significant (P > 0.1). Average resting cardiac output was 5.6 liters/min ± 1.6 for the group. This increased an average of 39% ± 30 with isoproterenol to 7.5 liters/min (P < 0.001). Average myocardial blood flow was 4.5% of the CO at rest and 3.6% with isoproterenol (P < 0.001).

Fifteen patients (group C3, 4) had type 3 or 4 collaterals. The average increase in myocardial blood flow for this group with isoproterenol was 42% ± 22 (P < 0.001). Resting myocardial blood flow was 211 ml/min ± 64. Resting cardiac output was 4.7 liters/min ± 1.1 as an average for the group. This increased with isoproterenol to an average of 6.6 liters/min ± 1.3 for an average increase of 43% (P < 0.001). Percent of cardiac output which was myocardial blood flow was 4.5 at rest and 4.4 with isoproterenol, an insignificant change. The data for group C3, 4 are shown in table 4.

Seven patients without collaterals (group C0) had an average resting myocardial blood flow of 202 ml/min ± 48. This increased insignificantly (P > 0.1) with isoproterenol to an average of 225 ml/min ± 75 or 10%. Resting cardiac output (4.9 liters/min ± 0.8 average) increased to an average of 7.0 liters/min ± 1.8 (P < 0.01) with isoproterenol. This was an increase of 42% (P < 0.01). The percentage of cardiac output which was myocardial blood flow was 4.2 at rest and 3.4 with isoproterenol (P < 0.01) (table 5).

Comparison of Groups

The groups were then compared as to the significance of the differences in values of myocardial blood flow, cardiac output, the percentage of the cardiac output which was
Table 3
Myocardial Blood Flow (MBF), Cardiac Output (CO), and MBF as Percentage of CO at Rest (R) and with Isoproterenol (I) in Patients with Coronary Artery Indices (CAI) of 175 or Less and Type 1 or 2 Collaterals

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<th>Sex</th>
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<th>MBF (%Δ)</th>
<th>CO (dl/min)</th>
<th>CO (%Δ)</th>
<th>MBF (% of CO)</th>
<th>CAI*</th>
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<tr>
<td>SD</td>
<td></td>
<td>90</td>
<td>±112</td>
<td>±16</td>
<td>±2.1</td>
<td>±30</td>
<td>±1.0</td>
<td>±1.3</td>
<td>±0.51</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>NS</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*See text for derivation.
†Collaterals by type (numbers) and direction of flow.
‡Abnormal baseline ECG.

myocardial blood flow at rest and with infusion of isoproterenol. The grouped data are summarized in table 6. There were no significant differences between group A and group B in the flow and output parameters, either at rest or with isoproterenol, nor were there significant differences between any of the groups in resting myocardial blood flow, cardiac output, or percentage of the cardiac output which was myocardial blood flow.

The differences in myocardial blood flow and cardiac output in response to isoproterenol between group A patients and all patients in group C were significant at the P < 0.001 level; the latter group were unable to increase myocardial blood flow or cardiac output to the same degree as group A patients. There was also a significant difference (P < 0.001) between group C1,2 and group C3,4. Group C3,4 increased myocardial blood flow on isoproterenol infusion an average of 42% as compared with an average of 5% for group C1,2. There was no difference between the two groups, however, in the response of cardiac output to the drug. There were no differences of significance in any values between groups C1,2 and C0.

Relative to the percentage of cardiac output which was myocardial blood flow, there were significant differences (P < 0.001) in group
Table 4
Myocardial Blood Flow (MBF), Cardiac Output (CO), and MBF as Percent of CO at Rest (R) and with Isoproterenol (I) in Patients with Coronary Artery Indices (CAI) of 175 or Less and Type 3 or 4 Collaterals

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Sex</th>
<th>MBF (ml/min/total heart)</th>
<th>CO (liter/min)</th>
<th>CO (%A)</th>
<th>MBF (% of CO)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>T</td>
<td>R</td>
<td>T</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>163</td>
<td>255</td>
<td>+56</td>
<td>3.4</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>205</td>
<td>296</td>
<td>+43</td>
<td>5.6</td>
</tr>
<tr>
<td>60</td>
<td>M</td>
<td>332</td>
<td>450</td>
<td>+35</td>
<td>5.6</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>306</td>
<td>340</td>
<td>+11</td>
<td>5.9</td>
</tr>
<tr>
<td>54</td>
<td>M</td>
<td>222</td>
<td>351</td>
<td>+58</td>
<td>4.0</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>251</td>
<td>258</td>
<td>+3</td>
<td>4.1</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>167</td>
<td>205</td>
<td>+22</td>
<td>3.4</td>
</tr>
<tr>
<td>36</td>
<td>M</td>
<td>237</td>
<td>445</td>
<td>+87</td>
<td>5.8</td>
</tr>
<tr>
<td>62</td>
<td>M</td>
<td>138</td>
<td>217</td>
<td>+57</td>
<td>4.1</td>
</tr>
<tr>
<td>41</td>
<td>M</td>
<td>188</td>
<td>322</td>
<td>+71</td>
<td>3.9</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>253</td>
<td>364</td>
<td>+43</td>
<td>6.1</td>
</tr>
<tr>
<td>56</td>
<td>M</td>
<td>111</td>
<td>141</td>
<td>+27</td>
<td>4.7</td>
</tr>
<tr>
<td>44</td>
<td>M</td>
<td>193</td>
<td>267</td>
<td>+38</td>
<td>4.5</td>
</tr>
<tr>
<td>67</td>
<td>M</td>
<td>138</td>
<td>211</td>
<td>+52</td>
<td>3.4</td>
</tr>
<tr>
<td>46</td>
<td>M</td>
<td>267</td>
<td>346</td>
<td>+30</td>
<td>6.9</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>211</td>
<td>298</td>
<td>+42</td>
<td>4.7</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>±64</td>
<td>±88</td>
<td>±22</td>
<td>±1.1</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: LAD = left anterior descending coronary artery; LC = left circumflex coronary artery.
*See text for derivation.
†Collaterals by type (numbers) and direction of flow (for example, L-R signifies left-to-right flow).
‡Abnormal baseline ECG.

A, group C1,2, and C6, the latter two groups having a smaller percentage of the cardiac output as myocardial blood flow with isoproterenol than the normal group (group A). There were no significant differences between group A and group C3,4.

The treadmill comparisons showed a significantly lower S-T index in group C3,4 than in group C1,2 (P < 0.001). The difference between group C6 and group C1,2 could not be determined as there were too few patients with no collaterals and normal resting electrocardiograms in the C6 group. There was no difference, however, between group B and group C1,2.

In summary, the group comparisons showed (1) no significant difference in resting values between any of the groups, (2) a significant difference in myocardial blood flow and cardiac output response to isoproterenol between patients without coronary artery disease (group A) or with coronary artery indices of 175 or greater (group B) and those patients with coronary artery indices of 175 or less (group C). In addition, within group C, those patients with intracoronary or bridge collaterals (group C3,4) were significantly different from those without collaterals (group C6) or intercoronary collaterals (group C1,2) in the myocardial blood flow response to isoproterenol, in degree of S-T segment depression with treadmill exercise, and in the percentage of cardiac output that was myocardial blood flow. This group (group

Circulation, Volume XLVI, July 1972
Table 5
Myocardial Blood Flow (MBF), Cardiac Output (CO), and MBF as Percentage of CO at Rest (R) and with Isoproterenol (I) in Patients with Coronary Artery Indices (CAI) of 175 or Less and No Collaterals

<table>
<thead>
<tr>
<th>Groups</th>
<th>MBF (ml/min/total heart)</th>
<th>CAI*</th>
<th>Collaterals†</th>
<th>S-T index*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (CAI = 300)</td>
<td>239 ± 82</td>
<td>86.7 ± 43.0</td>
<td>5.6 ± 1.3</td>
<td>60 ± 30</td>
</tr>
<tr>
<td>N = 40</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B (CAI = 175-250)</td>
<td>218 ± 43</td>
<td>72.9 ± 29.0</td>
<td>5.1 ± 0.95</td>
<td>73 ± 29</td>
</tr>
<tr>
<td>N = 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C (CAI = 50-175)</td>
<td>246 ± 91</td>
<td>4.7 ± 16.3</td>
<td>5.6 ± 1.7</td>
<td>39.3 ± 29.8</td>
</tr>
<tr>
<td>C_{1,2} (with collaterals type 1 and 2)</td>
<td>211 ± 64</td>
<td>42.2 ± 22.3</td>
<td>4.8 ± 1.1</td>
<td>42.2 ± 21.2</td>
</tr>
<tr>
<td>N = 23</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_{3,4} (with collaterals type 3 and 4)</td>
<td>211 ± 64</td>
<td>10.4 ± 15.5</td>
<td>4.9 ± 0.8</td>
<td>41.6 ± 15.6</td>
</tr>
<tr>
<td>N = 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_0 (without collaterals)</td>
<td>202 ± 48</td>
<td>30.0 ± 15.5</td>
<td>4.9 ± 0.8</td>
<td>41.6 ± 15.6</td>
</tr>
<tr>
<td>N = 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CAI = coronary artery index; see text for derivation; A = no coronary artery disease; B = coronary artery index 175 or greater; C_{1,2} = coronary artery index 175 or less, type 1 or 2 collaterals; C_{3,4} = coronary artery index 175 or less, type 3 or 4 collaterals; C_0 = coronary artery index 175 or less, no collaterals.

C_{3,4} was also a significantly older age group. There was no significant difference between any of the other groups in age.

Discussion

While it is difficult to compare the data on myocardial blood flow measured by the coincidence technic (which gives values in ml/min/total area of myocardium seen by the counters) with that secured by other technics giving results in ml/min/100 g of left ventricle, there are some general areas of agreement. If one extrapolates the data from the nitrous oxide technic which gives average values for flow of 70 to 88 ml/min/100 g to a 300-g heart, our average value for patients without coronary artery disease of 239 ml/min/total heart is appropriate.8,15 In addition, it has been stated that
the coronary blood flow is approximately 4% of
the cardiac output in a normal subject at
rest.\textsuperscript{16} Our data agree completely with those
figures. Somewhat higher percentages have
been reported, however.\textsuperscript{13} The literature does
not allow further correlations of the percent-
age of cardiac output that is myocardial blood
flow with exercise or stress intervention, as the
data for cardiac output are usually reported in
terms of cardiac index.

Our data support those previously reported
from this laboratory\textsuperscript{11} indicating that coronary
artery stenosis of more than one vessel
restricts myocardial blood flow reserve, or, the
ability to increase nutrient myocardial blood
flow on stress which increases myocardial
oxygen requirement. They also indicate that
collateral anastomoses, in general, do not
affect myocardial blood flow reserve. Intra-
coronary (bridge) anastomoses, however,
had statistically greater effect than did inter-
coronary collateral vessels. While for the
entire group with intracoronary anastomoses,
myocardial blood flow reserve did not reach
levels found in patients without coronary
artery disease, selected patients were able to
respond normally.

Whether or not the ability to augment
myocardial blood flow to normal ranges noted
in these few patients with large intracoronary
anastomoses increased their exercise tolerance
or raised the angina threshold was of interest.
Our data do demonstrate that less S-T-segment
depression occurred with treadmill exercise in
these patients as a group than in patients with
similar anatomic disease but without such
large anastomoses. No difference was evident,
however, in angina threshold or exercise
tolerance. These patients could not perform
more strenuous exercise or for a longer
duration than the other patients. No further
conclusions can be drawn from these parallel
observations as isoproterenol and exercise are
not necessarily similar interventions. It is
interesting, however, that this group (group
C\textsubscript{a,4}) was significantly older than the other
patients studied. It is also of interest that 12 of
the 15 patients had normal resting electrocar-
diograms, a much higher percentage than
among those patients with no collateral ves-
sels or intersegmental collaterals.

The exact reason why patients with signifi-
cant coronary artery occlusive disease were
unable to increase myocardial blood flow to
levels reached in normal individuals remains
to be elucidated. As has been suggested,\textsuperscript{17} it
may be that maximal vasodilation exists distal
to occlusive lesions. It would seem, however,
that if maximal vasodilation already existed, it
would not be possible to increase myocardial
blood flow over basal levels. Furthermore, it
has been demonstrated that most individuals
with coronary occlusive disease are capable of
increased myocardial flow over basal lev-
els\textsuperscript{12,18} up to the point of coronary insuffi-
cency. In addition, if maximal dilation existed,
nutrient coronary flow could only be increased
by an increase in perfusion pressure or a
decrease in extravascular resistance. There
was no consistent decline in mean arterial
blood pressure in this study to account for the
inability to increase myocardial blood flow.
Also, a more complete analysis of the relation-
ship of flow to pressure in 50 patients has
previously been done and no relationship
could be shown.\textsuperscript{19} As isoproterenol has been
demonstrated to increase contractility\textsuperscript{20} which
would, presumably, increase extravascular
compression, it is possible that this could
result in a decreased flow reserve although the
extravascular resistance factor in the control of
coronary flow is still in question\textsuperscript{21} and is
impossible to separate in the human subject.
Using the same reasoning, however, if inter-
coronary collateral vessels are intramural,
perhaps isoproterenol would have a "throttling
effect" on this type of collateral flow and no
effect on epicardial bridge collaterals.

Whether or not the inability of patients
with a restricted myocardial blood flow
reserve to increase cardiac output to the same
level as that achieved in normal patients
accounts for the decreased reserve, or, is a
secondary manifestation due to poor myocar-
dial contractility because of inadequate nutri-
tional flow has been a continuing problem.
When flow was analyzed as a percentage of
cardiac output, however, flow did not increase

\textit{Circulation, Volume XLVI, July 1972}
proportionately in those patients with significant coronary artery disease whereas it did in patients without coronary artery disease. This is an interesting consideration and may suggest that the deficit in coronary artery disease is primary and not merely reflective of depressed myocardial function. This would be expected if autoregulatory mechanisms are preserved.

The technic for measuring myocardial blood flow in this study has certain technical advantages, primarily that nutritionally unperfused areas affect the total myocardial blood flow measurement by adding a zero value to the myocardial count of isotope. Because the coincidence technic is basically a clearance technic, however, it is subject to the criticism of clearance technics raised by Moir, namely, that while certain clearance technics give an accurate estimate of directional changes in myocardial blood flow, systematic understatement of flows may be observed at high flow rates. Therefore, clearance technics have been stated to be inaccurate for quantitative measurement. It is not clear, however, that quantitation of flow, although ideally desirable, is an absolute necessity when studying myocardial blood flow reserve or the effect of various interventions on flow. Accuracy of results in terms of directional change is critical. We have not found it necessary to invoke absolute quantitation, the flow characteristics of an abnormal coronary circulation in response to an applied stress having been analyzed as the difference in group means and as correlated with another determination, i.e., severity of occlusive disease. Directional change in flow might be influenced if ventricular volume increased significantly so that a smaller percentage of myocardium was seen by the counters. This is highly unlikely with isoproterenol, however.

Of greater importance when methodologic differences are considered, is the recognition that the coincidence technic as applied in this study measures nutrient myocardial flow and not necessarily total coronary flow. This problem has been discussed by Cowan and associates, and in experimental data given in an earlier report by the same group of investigators. It is important when comparing results from different groups to recognize what the measurements represent and to appreciate that coronary blood flow and nutritional flow are not necessarily synonymous. We have used the term myocardial blood flow to represent nutritional flow and have avoided the term coronary blood flow. It has been pointed out that with isoproterenol there is an almost proportionate increase in total and nutritional flow.

The question has been asked whether the ischemic myocardium might behave differently toward rubidium than the normal myocardium. If so, could such differences relating to isotopic exchange affect comparisons of myocardial blood flow determined by this method. Moir's studies indicated that $^{86}$Rb clearance most closely approximated metered coronary flow rates when the flow rates were sufficiently low to produce electrocardiographic and hemodynamic evidence of myocardial hypoxia. He concluded that the cellular transport mechanisms for $^{86}$Rb were nonlimiting even in the presence of metabolic abnormalities.

Another consideration in interpreting the results of this study should be the means of grading the occlusive disease and establishing a coronary artery index. We looked at this problem by estimating the amount of myocardium potentially perfused by any one artery in each individual patient and then compared these data with the myocardial blood reserve. There was no difference in the myocardial blood reserve data when compared with the data derived from the use of the arbitrary index described in this paper. We have recognized, however, from treadmill studies, that isolated right coronary and circumflex artery lesions may be less demonstrable by physiologic studies. Oversimplified as the grading system is, our experience has been that it introduces less subjectivity than other methods we have tried. Perhaps the variability in the coronary circulation balances any overweighting or underweighting in this arbitrary index.
References


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Coronary Collateral Circulation and Myocardial Blood Flow Reserve
SUZANNE B. KNOEBEL, PAUL L. MCHENRY, JOHN F. PHILLIPS and FEBREL J. PAULETTO

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