Coronary Collateral Function in Patients Without Occlusive Coronary Artery Disease

By Robert E. Goldstein, M.D., Lawrence L. Michaelis, M.D., Andrew G. Morrow, M.D., and Stephen E. Epstein, M.D.

SUMMARY

Little is known of the functional capacity of coronary collaterals in humans without occlusive coronary artery disease. We, therefore, measured peripheral coronary pressure (PCP) and retrograde flow (RF) from coronary arteries at aortic valve replacement in seven patients without occlusive coronary artery disease. Using a T-connection interposed in left (LCA) and right (RCA) coronary perfusion lines, data were obtained during brief proximal occlusion of each line. PCP was expressed as a fraction of perfusion pressure (PP), and collateral resistance (CR) was calculated as PP/RF. Median values were as follows:

<table>
<thead>
<tr>
<th></th>
<th>RF (ml/min)</th>
<th>CR (mm Hg/ml/min)</th>
<th>PCP (mm Hg)</th>
<th>PCP/PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCA</td>
<td>2.4</td>
<td>48</td>
<td>15</td>
<td>0.19</td>
</tr>
<tr>
<td>RCA</td>
<td>1.7</td>
<td>64</td>
<td>16</td>
<td>0.24</td>
</tr>
</tbody>
</table>

In contrast, previous studies of well-collateralized distal segments of diseased coronary arteries revealed mean RF 15.7, CR 5.1 and PCP/PP 0.50. Under the conditions of study, all vessels interconnecting the non-diseased RCA and LCA delivered flow and pressure less readily than collaterals to a single distal segment of a diseased coronary artery. Thus, collaterals in patients without diseased coronary arteries have an extremely limited capacity to transmit either flow or pressure. The absolute values of RF were small relative to the muscle mass perfused by each coronary artery, suggesting that perfusion of only one coronary artery in man during operation may not provide substantial perfusion for large portions of myocardium. Comparison of performance of collaterals supplying atherosclerotic and nonatherosclerotic coronary arteries indicates that proximal occlusion may be an important factor stimulating enhancement of collateral function. Moreover, the nitroglycerin-induced improvement in collateral function seen in patients with chronic occlusive coronary disease was not demonstrable in patients without coronary occlusion. Thus, coronary collaterals may acquire nitroglycerin responsiveness as a result of changes induced by chronic coronary occlusion.

Additional Indexing Words:
Peripheral coronary pressure
Aortic valve disease
Retrograde flow
Nitroglycerin
Aortic valve replacement

SEVERAL STUDIES have examined the function of coronary collateral channels in patients with chronic occlusive coronary artery disease.\(^1\)\(^-\)\(^4\)

Much less information is available, however, concerning the importance of coronary collaterals in patients without occlusive coronary disease. Anatomic investigation has shown that collateral vessels in normal human hearts are very small when compared either with normal coronary arteries or with collateral vessels of patients with occlusive coronary disease.\(^6\)\(^-\)\(^7\)

The frequent occurrence of myocardial infarction following acute coronary obstruction (e.g., coronary embolization) in patients without underlying chronic occlusive coronary disease also suggests that coronary collateral channels in these individuals have very little functional capacity. Nevertheless, perfusion of one coronary artery, at the time of routine aortotomy, can yield obvious backbleeding from the nonperfused coronary ostium. Indeed, this observation might suggest that coronary collateral function during aortotomy is so ample that perfusion of only one coronary artery may provide substantial blood flow to the bed of the other, nonperfused, coronary artery.

To elucidate the extent of coronary collateral function in patients without occlusive coronary artery disease, measurements reflecting collateral function were made in nonatherosclerotic patients with aortic valve disease at the time of operative replacement of the aortic valve.

Methods

Coronary collateral function frequently has been assessed by measuring back pressure (subsequently termed...
CORONARY COLLATERAL FUNCTION IN MAN

Peripheral coronary pressure or PCP) in the distal portion of an occluded coronary artery, and retrograde flow issuing when this distal arterial segment is vented to atmospheric pressure. In the present study, PCP and retrograde flow were measured in seven patients by manipulating the coronary perfusion apparatus routinely employed during aortic valve replacement.

Anesthesia was achieved using varying combinations of nitrous oxide, halothane, penthane, and morphine sulfate. Cardiopulmonary bypass was established, systemic hypothermia (30°C) instituted, and the left ventricle drained through the apex. When this was accomplished ventricular fibrillation developed spontaneously in all but one patient (J. S.). The aortic root was opened and a perfusion cannula introduced into each coronary ostium. After approximately five minutes of coronary perfusion, flow in one coronary perfusion line was temporarily arrested by clamping.

Using T-connections previously interposed in each perfusion line, PCP was measured in that portion of the nonperfused system distal to the occluding clamp; these connectors also permitted pressure measurement in the perfused artery (fig. 1). Pressures were recorded using two saline-filled Statham P23Db pressure transducers with zero reference set at the midplane of the right atrium. Phasic changes in perfusion pressure were eliminated by an electronic averaging circuit. After PCP attained stable values (20–30 sec), the nonperfused system was vented to atmospheric pressure at the level of the right atrial midplane and retrograde flow issuing from the nonperfused artery was collected for 30 seconds to one minute. In eight duplicate collections from two patients the first flow rate differed from the second by an average of −2.1% ± 6.1 (standard error). After completion of retrograde flow collection, the occluding clamp was released and the occluded system perfused for approximately two minutes in an antegrade fashion. The occluding clamp was then applied to the opposite, previously unperfused perfusion line, and PCP and retrograde flow from this opposite line were recorded in the manner just described. This technique permitted an assessment of the ability of left coronary perfusion to sustain pressure and flow to the right coronary artery and the ability of right coronary perfusion to sustain pressure and flow transmission to the left coronary artery. Assessments of collateral function were related to the pressure perfusing the opposite vessel. The order in which occlusions were performed was randomized.

Following release of the second occlusion, and after a brief recovery period, nitroglycerin, 100 μg/min, in sterile saline, was infused into the right atria of six of the seven study subjects. After two to four minutes, physiologic effects of nitroglycerin were observed uniformly: systemic perfusion pressure fell an average of 10 mm Hg (range 7–14 mm Hg). While nitroglycerin infusion continued, PCP and retrograde flow measurements in each perfusion system were repeated according to the protocol outlined above. The order in which perfusion lines were occluded prior to nitroglycerin was preserved in these repeat determinations during nitroglycerin infusion.

Throughout the course of study frequent measurements were made of antegrade flow in perfused coronary arteries using rotameters that were interposed in each coronary perfusion line. The rotameters were calibrated with human blood at 30°C with an hematocrit the same as present at the time of study. The accuracy of the rotameter measurements was estimated to be ±10%.

In accordance with routine practice, a Mayo balloon-tip cannula was used to perfuse the right coronary artery, and a special Teflon cannula with a rubber O-ring at its tip was used to perfuse the left coronary artery. Blood for coronary perfusion was supplied from a side arm in the arterial line of the heart-lung machine. Blood flowed from the T-connections to the cannulae through approximately three feet of Teflon tubing. (This permitted the surgeons to proceed with operative repair without interruption throughout the study.) During antegrade perfusion, however, resistances in the tubing and cannulae were sufficient to create substantial (20–50 mm Hg) pressure gradients between the pressure transducers and the coronary ostia. Therefore, immediately after discontinuation of cardiopulmonary bypass and removal of cannulae from coronary arteries, pressure gradient from transducer to open end of the cannula was measured for each observed rate of coronary perfusion. These measurements were then subtracted from recorded pressures to yield corrected values of coronary perfusion pressure. It should be emphasized that a significant pressure gradient between pressure transducer and coronary ostium existed only during rapid flow in the coronary perfusion line. Hence, no correction was applied to PCP, a quantity measured when flow between pressure transducer and coronary ostium was arrested. Similarly, retrograde flows observed in this study were so small that they would not be expected to create a pressure difference.

Figure 1

Diagram of the heart (left anterior oblique projection) showing arrangements for coronary perfusion and data collection. In the left panel, the left coronary artery and its branches (cross-hatching) are perfused; a T-connection interposed in the perfusion line to the left coronary permits measurement of perfusion pressure (PP). The perfusion line to the right coronary artery (unshaded) is occluded by a clamp. A T-connection in the perfusion line to the right coronary distal to the clamp allows measurement of back pressure (peripheral coronary pressure or PCP). Alternatively, the right coronary artery can be vented to atmospheric pressure via the T-connection and the resultant retrograde flow (RF) can be collected for measurement. The direction of blood flow in the perfusion lines during retrograde flow collection is indicated by arrows. In the right panel, the right coronary artery (cross-hatching) is perfused while the perfusion line to the left coronary artery (unshaded) is clamped. Under these circumstances the functions of the two T-connections are interchanged.

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between coronary ostium and pressure transducer in excess of 3 mm Hg.

Patients were selected for study if they were to have prosthetic replacement of only the aortic valve, and if they had no clinical or angiographic evidence of coronary atherosclerosis or other complicating disease. Of the patients initially selected, four were excluded at the time of operation because perfusion cannulae could not be introduced into both coronary ostia.

The data obtained from patients without occlusive coronary disease were compared to similar data from patients with coronary atherosclerosis who did not have aortic valve disease. A detailed account of the methods used in this latter group has already been published. In brief, PCP and retrograde flow measurements were made at the time of saphenous vein bypass graft implantation. After its distal attachment to coronary artery, but prior to its proximal attachment to aorta, the vein graft served as a conduit to the distal portion of the diseased coronary artery while antegrade flow in the coronary was temporarily arrested. The data so obtained were compared with the appearance of coronary collaterals to the vessel under study on the preoperative coronary angiogram. The methods used in studying atherosclerotic patients differed importantly from those used in the present study. Thus, the arterial segments drained by the saphenous vein cannula in the atherosclerotic patients were necessarily smaller than the arterial systems drained by the coronary ostial cannula in patients with aortic valve disease. Also, the hypothermia used in aortic valve patients (30°C) was somewhat deeper than that used in patients having saphenous vein bypass grafts (32–36°C). Nevertheless, the data from atherosclerotic patients are presented in order to put into perspective the data from patients without occlusive disease.

Results

Clinical data concerning the study subjects are given in table 1. Of the seven subjects, there were six men and one woman. Their ages ranged from 23 to 51 years. Five had pure aortic regurgitation, one had pure aortic stenosis, and one had mixed aortic stenosis and regurgitation. Except for one patient (M. N.) who had a mitral commissurotomy following aortic valve replacement, all patients were free of complicating valvular or myocardial disease. Five patients had normal coronary arteriograms. Coronary arteriography was not performed in two patients, aged 23 and 36 years, who had no clinical evidence of coronary artery disease. At the time of study, blood gas determinations revealed normal arterial pH and moderately elevated arterial PO₂ (range 175–325 mm Hg) in all patients.

PCP in patients without occlusive coronary disease (fig. 2, left, and table 2) was quite low, ranging from 6.6 to 21 mm Hg (median 15). Values measured in the left coronary perfusion system (LCA) were generally similar to values in the right system (RCA) in the same

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years) and sex</th>
<th>Disease</th>
<th>Symptoms</th>
<th>Coronary angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.D.</td>
<td>23 M</td>
<td>RHD-AR</td>
<td>DOE</td>
<td>Not done</td>
</tr>
<tr>
<td>O.L.</td>
<td>38 M</td>
<td>RHD-AR</td>
<td>DOE, PND</td>
<td>Normal, RD</td>
</tr>
<tr>
<td>N.K.</td>
<td>38 M</td>
<td>RHD-AR</td>
<td>DOE</td>
<td>Not done</td>
</tr>
<tr>
<td>M.N.</td>
<td>38 M</td>
<td>RHD-AR,</td>
<td>AP, PND</td>
<td>Normal, RD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mild MS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.S.</td>
<td>51 F</td>
<td>CHD-AS</td>
<td>AP, DOE</td>
<td>Normal, NA</td>
</tr>
<tr>
<td>L.M.</td>
<td>50 M</td>
<td>CHD-AS, AR</td>
<td>AP</td>
<td>Normal, RD</td>
</tr>
<tr>
<td>M.P.</td>
<td>36 M</td>
<td>RHD-AR</td>
<td>DOE</td>
<td>Normal, RD</td>
</tr>
</tbody>
</table>

Abbreviations: M = male; F = female; RHD = rheumatic; CHD = congenital; AR = aortic regurgitation; AS = aortic stenosis; MS = mitral stenosis; DOE = dyspnea on exertion; PND = paroxysmal nocturnal dyspnea; AP = angina pectoris; RD = right coronary artery dominant; NA = dominance data not available.

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### Table 2

**Intraoperative Results**

<table>
<thead>
<tr>
<th>Patient and CIL occluded</th>
<th>PCP (mm Hg)</th>
<th>PCP/PP ratio</th>
<th>RF (ml/min)</th>
<th>CCR (mm Hg/ml/min)</th>
<th>PP (mm Hg)</th>
<th>CF (ml/min)</th>
<th>% change CCR after TNG</th>
<th>% change PCP/PP after TNG</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.D. LCA</td>
<td>14.0</td>
<td>0.25</td>
<td>6.8</td>
<td>8.1</td>
<td>55</td>
<td>165</td>
<td>+ 1.2</td>
<td>− 8</td>
</tr>
<tr>
<td>RCA</td>
<td>18.0</td>
<td>0.35</td>
<td>6.0</td>
<td>8.7</td>
<td>32</td>
<td>104</td>
<td>− 1.2</td>
<td>0</td>
</tr>
<tr>
<td>O.L. LCA</td>
<td>6.6</td>
<td>—</td>
<td>11.0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>RCA</td>
<td>9.8</td>
<td>—</td>
<td>4.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>N.K. LCA*</td>
<td>15.1</td>
<td>0.29</td>
<td>1.2</td>
<td>53.0</td>
<td>53</td>
<td>170</td>
<td>+ 36.0</td>
<td>− 7</td>
</tr>
<tr>
<td>RCA*</td>
<td>16.4</td>
<td>0.32</td>
<td>5.6</td>
<td>9.5</td>
<td>53</td>
<td>140</td>
<td>− 2.1</td>
<td>− 16</td>
</tr>
<tr>
<td>M.N. LCA*</td>
<td>15.0</td>
<td>0.16</td>
<td>14.4</td>
<td>6.9</td>
<td>96</td>
<td>220</td>
<td>− 44.0</td>
<td>+ 50</td>
</tr>
<tr>
<td>RCA*</td>
<td>15.4</td>
<td>0.34</td>
<td>2.4</td>
<td>19.4</td>
<td>46</td>
<td>140</td>
<td>+ 49.0</td>
<td>+ 15</td>
</tr>
<tr>
<td>J.S. LCA</td>
<td>14.7</td>
<td>0.08</td>
<td>0.6</td>
<td>330.0</td>
<td>182</td>
<td>250</td>
<td>− 34.0</td>
<td>+ 12</td>
</tr>
<tr>
<td>RCA</td>
<td>21.0</td>
<td>0.09</td>
<td>0.75</td>
<td>241.0</td>
<td>181</td>
<td>182</td>
<td>− 70.0</td>
<td>+ 111</td>
</tr>
<tr>
<td>L.M. LCA</td>
<td>10.6</td>
<td>0.16</td>
<td>0.15</td>
<td>435.0</td>
<td>65</td>
<td>240</td>
<td>+ 305.0</td>
<td>− 19</td>
</tr>
<tr>
<td>RCA</td>
<td>11.5</td>
<td>0.13</td>
<td>0.05</td>
<td>1400.0</td>
<td>67</td>
<td>216</td>
<td>ΔRF = 0†</td>
<td>+ 19</td>
</tr>
<tr>
<td>M.P. LCA</td>
<td>17.5</td>
<td>0.21</td>
<td>3.6</td>
<td>23.0</td>
<td>84</td>
<td>260</td>
<td>+ 79.0</td>
<td>− 33</td>
</tr>
<tr>
<td>RCA</td>
<td>17.0</td>
<td>0.16</td>
<td>1.0</td>
<td>109.0</td>
<td>109</td>
<td>150</td>
<td>− 48.0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Range (median)</strong></td>
<td><strong>6.6 – 17.5</strong></td>
<td><strong>0.08 – 0.29</strong></td>
<td><strong>0.15 – 14.4</strong></td>
<td><strong>6.9 – 435</strong></td>
<td><strong>53 – 182</strong></td>
<td><strong>165 – 260</strong></td>
<td><strong>− 44 – +305</strong></td>
<td><strong>− 33 – +50</strong></td>
</tr>
<tr>
<td><strong>RCA</strong></td>
<td><strong>9.8 – 21.0</strong></td>
<td><strong>0.09 – 0.35</strong></td>
<td><strong>0.5 – 6.0</strong></td>
<td><strong>8.7 – 1400</strong></td>
<td><strong>46 – 181</strong></td>
<td><strong>104 – 216</strong></td>
<td><strong>− 70 – +49†</strong></td>
<td><strong>− 16 – +111</strong></td>
</tr>
</tbody>
</table>

Abbreviations: CPL = coronary perfusion line; PCP = peripheral coronary pressure; PP = perfusion pressure (i.e., pressure in the perfused coronary artery); RF = retrograde flow; CCR = calculated collateral resistance (= PP/RF); CF = antegrade flow when coronary artery receives perfusion; TNG = nitroglycerin.

*Values are mean of two replicate determinations.
†No detectable retrograde flow was present after nitroglycerin administration to L.M.
patient. PCP measurements in atherosclerotic patients are shown for two subgroups (fig. 2): those with no collaterals visible on preoperative angiogram (small collateral group) and those with one or more large collaterals on angiogram (large collateral group). PCP in the large collateral group ranged from 19 to 50 mm Hg. Even when adjusted for differences in perfusion pressure (fig. 2, right), PCP values in patients without occlusive coronary disease more closely approximated results in atherosclerotic patients with the poorest grade of collateral development.

Retrograde flow (fig. 3, table 2) in those patients without occlusive coronary disease ranged from 0.05 to 14.4 ml/min. Values in the LCA and RCA of the same patient often showed considerable disparity. There was no consistent tendency, however, for retrograde flow to be higher from one particular coronary system. In contrast to findings in aortic valve patients, retrograde flow in six of twelve atherosclerotic patients with large collaterals was greater than 15 ml/min. Often retrograde flow in patients without occlusive disease approximated values observed in atherosclerotic patients with the poorest grade of collateral development. Thus, both retrograde flow and PCP data suggest that intraproductive collateral function in study subjects without occlusive coronary disease is very limited.

Comparisons of retrograde flow and antegrade flow in the same vessel are shown in figure 4. Except in one subject (M. N.), perfusion pressures responsible for retrograde flow and antegrade flow for each particular vessel were similar. It is uncertain how much blood flow is required to sustain the myocardium under the conditions present at the time of study. However, even if all retrograde flow were redirected to pass through capillary channels, it is clear that this flow would represent only a very small fraction of the tissue perfusion achieved by antegrade flow at comparable perfusion pressures.

To compensate, at least partially, for the influence of differing perfusion pressures among the study subjects, coronary collateral resistance was calculated as the ratio of perfusion pressure to retrograde flow (fig. 5, table 2). Although collateral resistance measurements sometimes differed considerably when calculated using retrograde flow data from the LCA and RCA of the same patient, there was no consistent

Figure 3

Intraoperative retrograde flow data are shown for aortic valve patients without occlusive coronary disease (solid circles) and for patients with occlusion due to coronary atherosclerosis (open circles). Abbreviations are explained in the legend of figure 1. In general, retrograde flows from the larger arterial systems studied in patients with no CAD were much less than retrograde flows from distal arterial segments of CAD patients with large collaterals on angiogram. They often approached the low values found in CAD patients with small collaterals.

Figure 4

Comparison of retrograde flow and antegrade flow in the same coronary artery of aortic valve patients without occlusive coronary disease. Retrograde flow measurements were made with coronary perfusion line clamped; antegrade flow measurements were made with the same perfusion line unclamped. Retrograde flow was consistently a minute fraction of antegrade flow in the same vessel. Since perfusion pressure in the two coronary perfusion lines was similar when they were unclamped (except in the case of M. N., denoted by an asterisk) the great disparity of flow reflects the fact that collateral resistances to retrograde flow are far in excess of capillary resistances to antegrade flow.
tendency for either LCA or RCA measurements to yield higher values. Even in the small group of patients studied, calculated collateral resistance varied widely, ranging from 6.9 to 1400 mm Hg/ml/min (median 38). However, data from patients without coronary occlusive disease were generally closer to values from atherosclerotic patients with the poorest degree of collateral development (range 28–440, median 64) than to values from atherosclerotic patients with one or more large collaterals (range 1.6–16.4, median 2.9). The high collateral resistance in patients without occlusive disease, like the low values for PCP and retrograde flow, is indicative of very limited coronary collateral function.

In patients with coronary atherosclerosis, parenteral nitroglycerin generally reduced collateral resistance, implying a nitroglycerin-induced facilitation of coronary collateral blood flow (fig. 6, left). This tendency was equally evident in patients with large collaterals and in patients with no visible collaterals on preoperative coronary angiograms. In contrast, no consistent beneficial action on coronary collateral resistance was observed after a physiologically effective dose of nitroglycerin was administered to patients without coronary occlusive disease (fig. 6, left, table 2). Only one of this latter group (J. S.) had a decrease in collateral resistance calculated from retrograde flow to both LCA and RCA. In addition to decreased collateral resistance after nitroglycerin, atherosclerotic patients also tended to have higher values of PCP after nitroglycerin (fig. 6, right), a change consistent with a drug-induced improvement in coronary collateral function. Although the scatter of results and the relatively small number of patients tested preclude firm conclusions, the tendency for nitroglycerin to raise PCP appeared to be somewhat less in patients without occlusive disease (fig. 6, right, table 2). Thus, the PCP data tend to corroborate the more clear-cut resistance data indicating that nitroglycerin responsiveness is less in patients without coronary occlusive disease than in patients with atherosclerotic coronary occlusion.

Discussion

By measuring PCP and retrograde flow we have obtained quantitative evidence indicating that patients with aortic valve disease who do not have
occlusive coronary lesions have very poor intraoperative coronary collateral function. Thus, in the large arterial systems evaluated in this study, PCP was less than 20 mm Hg in 13 of 14 determinations (fig. 2) and retrograde flow was under 7 ml/min in 12 of 14 instances (fig. 3). Under the conditions of study, all vessels interconnecting the nondiseased right and left coronary arteries generally delivered flow and pressure less readily than optimally developed collaterals to a single distal segment of a diseased coronary artery (figs. 2, 3 and 5). The intraoperative function of collaterals in patients without occlusive disease corresponded closely with the function of the most poorly developed collaterals observed in patients with chronic coronary occlusion.

The significance of the data must be circumscribed by the conditions present at the time of study. Ventricular fibrillation, myocardial hypothermia (30°C), left ventricular evacuation, and the anesthetic agents and other drugs may produce metabolic and physical changes that significantly alter coronary collateral function. Furthermore, aortic valve disease with its accompanying left ventricular hypertrophy and (in most cases) left ventricular enlargement may also modify coronary collateral function. Hence, our results may not apply to hearts that are normal in every respect. An additional selection factor was introduced by the requirement that both left and right coronary ostia permit the insertion of perfusion cannulae.

Despite these potential limitations, it is noteworthy that the data are consistent with anatomic5-7 and clinical results indicating poor coronary collateral function in the absence of occlusive coronary disease. Angiographic8 and histologic9 studies have shown that human coronary collateral vessels enlarge and mature in response to chronic coronary occlusive disease. The correlation of angiographically severe coronary occlusive disease and coronary collateral development is well documented.8-11 Although results in aortic valve patients and in atherosclerotic patients may not be fully comparable, our findings suggest that these anatomic changes are accompanied by a substantial improvement in the functional capacity of coronary collateral vessels. Such functional improvement already has been demonstrated when experimental animals are subjected to chronic coronary occlusion. Thus, proximal coronary occlusion in man (as well as in experimental animals) may be an important factor stimulating enhancement of coronary collateral function. In this regard it is interesting to note that collateral function was uniformly poor in those three aortic valve patients (M. N., J. S., L. M.) with typical angina pectoris. Thus, in these three patients, ischemia per se (without associated occlusive coronary lesions) was apparently not a potent stimulus for collateralization.

Our data indicate that the nitroglycerin-induced reduction in calculated collateral resistance usually demonstrable in patients with chronic coronary obstruction1 was not consistently elicited in patients lacking chronic obstructive coronary disease (fig. 6). This absence of nitroglycerin responsiveness was not simply due to low baseline levels of collateral function since nitroglycerin responsiveness was present in those atherosclerotic patients with coronary collateral function as low as that seen in patients without occlusive coronary disease. Although poor responsiveness of coronary collaterals to nitroglycerin in patients without occlusive disease may reflect procedural differences (e.g., somewhat deeper hypothermia in aortic valve patients than in atherosclerotic patients), it also is possible that facilitation of collateral flow by nitroglycerin may be a unique pharmacologic feature of chronic obstructive coronary disease. In the presence of chronic coronary occlusion, coronary collaterals become much larger and acquire a much thicker muscle layer.6 Also, new bridging collaterals develop to join proximal and distal portions of the same diseased artery. Such anatomic differences may form the basis for enhanced nitroglycerin responsiveness in collaterals of patients with coronary occlusive disease. The hypothesis that collaterals to occluded coronary arteries exhibit unique responsiveness to nitroglycerin is substantiated by the work of Fam and McGregor,18 who found that nitroglycerin improved coronary collateral function in dogs with chronically ligated coronary arteries but not in dogs with normal coronary arteries. Moreover, studies in patients with coronary artery disease indicated that the greatest degrees of improvement in collateral function following nitroglycerin (drug-induced reduction in collateral resistance in excess of 30%) were found exclusively in individuals with ischemic symptoms for over six months.1 Although none of these data are wholly conclusive, they suggest that with the onset of coronary occlusive disease coronary collaterals change from a state in which nitroglycerin responsiveness is absent and functional capacity generally quite limited to a state in which nitroglycerin responsiveness is usually present, and, in some individuals, functional capacity is greatly increased.

As indicated previously, it is possible that the data presented are not generally applicable to all individuals without coronary occlusive disease. Nevertheless, our data clearly relate to coronary collateral function at the time of aortic valve replacement. It is doubtful that individuals with substantially better coronary collateral function were eliminated by our exclusion of aortic valve patients who had normal...
coronary arteriograms but who could not accommodate perfusion cannulae in both coronary ostia. Thus, we conclude that perfusion of only a single coronary artery during aortic valve replacement is likely to yield very low pressures and flows in the nonperfused coronary artery, even when tissue perfusion is maximized by occlusion of the nonperfused coronary ostium. The amount of intraoperative perfusion necessary to sustain myocardial function is uncertain. Nevertheless, absolute values of retrograde flow were particularly small relative to the mass of muscle supplied by each coronary artery, suggesting that intraoperative perfusion of only one coronary artery may not provide substantial perfusion to large portions of myocardium. Thus, when only a single coronary artery is perfused, it is appropriate (at least in nonatherosclerotic patients) to consider measures, such as myocardial cooling, that will act to preserve the potentially ischemic regions normally supplied by the nonperfused coronary artery.

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