Collateral conductance changes during a brief coronary occlusion in awake dogs

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ABSTRACT Function of the coronary collateral circulation during the course of a single abrupt coronary occlusion was evaluated in awake dogs instrumented over the long term. Studies were performed approximately 2 weeks after collateral development had been stimulated in the dogs by partial stenosis of the proximal left circumflex coronary artery. The pressure drop from the central aorta to the distal circumflex coronary artery was measured continuously. Under control conditions and at 30 sec and 4 min of a single abrupt complete circumflex occlusion, myocardial blood flow was determined by a radioactive microsphere technique. Coronary collateral conductance was calculated as mean collateral blood flow divided by the mean drop in pressure. The following was noted in dogs that developed collateral vessels: during the coronary occlusion, mean distal circumflex coronary pressure increased from $42 \pm 9$ to $49 \pm 10$ mm Hg ($p \leq .01$); mean collateral flow increased from $0.78 \pm 0.30$ to $0.84 \pm 0.33$ ml/min/g ($p \leq .05$); the endocardial/epicardial flow ratio increased from $0.77 \pm 0.36$ to $1.04 \pm 0.25$ ($p \leq .01$); and the coronary collateral conductance increased significantly from $0.017 \pm 0.017$ to $0.021 \pm 0.021$ (ml/min/g)/mm Hg ($p \leq .005$). These data suggest that during a brief occlusion of a major coronary artery, immature coronary collateral channels do not reach maximal function immediately after the occlusion. Rather, coronary collateral conductance increases with time and may be associated with improved transmural perfusion of the myocardium.


Significant areas of viable myocardium often are dependent on coronary collateral channels for blood supply when advanced occlusive coronary artery disease is present. During periods of coronary spasm or acute occlusion of a major coronary artery, the degree of myocardial ischemia that develops is dependent on the availability of coronary collateral channels and the rate at which these channels begin to function. A native and usually marginally functional collateral circulation exists in both dogs and humans. Collateral channels develop rapidly after an appropriate stimulus in dogs, but do not become as functional as native arteries until approximately 6 months; thus, during development they are characterized as immature. Studies in which Khouri et al. observed coronary pressure in dogs suggested that previously well-formed collateral channels may open gradually.

Greenfield et al. observed in patients undergoing coronary artery bypass surgery that reactive hyperemia was present after an acute 10 sec interruption of flow in the vein graft. However, reactive hyperemia largely disappeared if the occlusion was maintained for up to 1 min. This observation suggests that existing collateral channels may not fully open immediately after an acute interruption of antegrade blood flow but may begin to function over several minutes. Brazzamano et al. observed in dogs that when immature collaterals were present, repeated coronary artery occlusions of 5 min duration augmented collateral flow above that during the initial coronary occlusion.

The purpose of the present study was to determine the rapidity with which immature coronary collateral channels begin to function during a brief occlusion of a major coronary artery. An awake animal preparation was used in which coronary collateral development had been stimulated by the placement of a partial stenosis on the left circumflex coronary artery. In this preparation a region of myocardium was perfused by both the partially stenosed circumflex coronary artery and from immature but developing coronary collateral channels. The change of the pressure drop across the
collateral network as well as transmural myocardial flow was determined during a brief interruption in circumflex coronary flow. These measurements allowed an estimation of the time course of the changes in conductance across the collateral network independent from conductance changes occurring in the distal myocardial circulation. These observations have not been made previously and are important to the understanding of the physiology of the coronary collateral circulation.

Methods

Thirty-eight mongrel dogs of both sexes weighing from 30 to 40 kg were instrumented and studied. They were free of signs of ill health and were suited in temperament to the laboratory environment.

Surgical preparation. Surgical anesthesia was induced with sodium thiopental (30 to 40 mg/kg iv). A left thoracotomy was performed via the fourth intercostal space under sterile conditions. Small supplemental doses of sodium thiopental were given throughout the operative procedure as required. The heart was suspended in a pericardial cradle. Heparin-filled polyvinylchloride catheters (3.0 mm outside diameter [OD]) were introduced into the arch of the aorta via the internal mammary artery, into the left ventricle through the apex, and into the left atrium via the atrial appendage. The catheters were secured with purse-string sutures. The left circumflex coronary artery was dissected free from its origin proximal to the first large marginal branch. A pneumatic coronary artery occluder, constructed in our laboratory, was placed on the circumflex coronary artery. In 25 of the 38 dogs, an electromagnetic flow probe (Howell Instruments, Inc.) was placed just proximal to the occluder. Since results of the study are based on the condition that zero antegrade coronary flow was maintained during coronary occlusion, the flow probe was used specifically to verify zero flow at that time. A specially constructed Teflon sleeve 4 mm in length was placed proximal to the occluder and the electromagnetic flow probe. The internal diameter of the Teflon sleeve was chosen to produce an approximate 85% reduction in the luminal area of the coronary artery.

A Teflon coronary pressure catheter that could be inserted into the coronary artery was constructed in our laboratory. This catheter was designed as a modification of the method described by Gould.4 The catheter was 1.00 mm OD, 0.80 mm inside diameter (ID) in the first 2 cm of length, and 1.25 mm OD, 1.00 mm ID in the remaining 4 cm of length. The distal end was tapered to aid with insertion. Three polyvinylchloride rings 1 mm in length and of 1.25 mm ID were placed on the distal end of the pressure catheter to prevent movement of sutures used in securing the catheter to the myocardium. Figure 1 shows the phasic coronary pressure tracings. The frequency response of the coronary catheter system and other pressure catheters were evaluated with use of a pop test.5 The natural frequency was approximately 11 cycles/sec with a damping coefficient of 0.4 for the coronary pressure catheter system. The natural frequency of the aortic and left ventricular catheters was approximately 60 cycles/sec with a damping coefficient of 0.3.

Gould4 has evaluated the degree of difference expected between a downstream as compared with a sidearm coronary pressure determination and found that this difference was approximately 1 to 2 mm Hg. This should have been consistent throughout our study and therefore should have had a negligible effect on the observed data. The lengths of the coronary, aortic, and left ventricular catheters were 25 to 30 cm. The distances

**FIGURE 1.** Typical examples of pressure and flow tracings from a group 1 dog. Coronary pressure was measured in the distal circumflex coronary artery. Coronary blood flow was measured in the circumflex coronary artery proximal to the coronary pressure catheter. Note the fidelity of the coronary pressure tracings. A, Control, resting conditions. B, Thirty seconds after the onset of an abrupt circumflex occlusion. C, Four minutes into the same circumflex occlusion.

from the distal end of coronary and aortic catheters to the orifice of the left coronary artery were similar. The catheter was inserted into the coronary artery with the aid of a metal needle stylet. A needle puncture was made through the arterial wall with the needle stylet and the Teflon catheter was advanced into the left circumflex coronary artery facing downstream just distal to the balloon occluder. The inner stylet was removed and the Teflon catheter was connected to a 20 cm length of clear polyvinylchloride tubing, 1.5 mm OD, 1.25 mm ID. The Teflon pressure catheter was secured to the fascia and the connective tissue surrounding the coronary artery with a 4-0 silk suture. Since no arteriotomy had been performed, there was no bleeding at the site of insertion. The distal end of the coronary catheter was secured to the myocardium.

The catheters, balloon snare occluder, and electromagnetic flow probe leads were tunneled dorsally and exteriorized individually at the base of the neck. The coronary pressure catheter was fitted with a rubberized heparin well. The heparin well was secured to the skin with a purse-string suture. The coronary catheter then could be flushed percutaneously via a needle puncture through the rubber membrane. The dogs were treated with antibiotics for 7 days. The coronary pressure catheter was flushed daily for 5 days with 1000 units of heparin, and then every 2 days until the time of study. Postmortem evaluation indicated that the coronary pressure catheter obstructed the left circumflex vessel by 10% to 20%. This measurement was obtained in five dogs by planimetry of a cross-sectional area of the barium-filled circumflex vessel, which contained the coronary pressure catheter.

Study protocol. All animals were brought to the laboratory approximately 7 to 14 days after the surgical procedure and were evaluated to be sure that they were fully recovered, afebrile, had normal hematocrits, and had resting pulse rates less than 90 beats/min. They were premedicated with 10 mg im morphine for analgesic purposes at least 1 hr before the study. Aortic, atrial, left ventricular, and coronary pressure catheters were connected to Statham P23Db pressure transducers and adjusted to the same zero pressure reference at the midstest level. The transducers were calibrated equally by simultaneous standardization with a mercury column. Coronary flow was measured with a Howell electromagnetic flowmeter. Before the study, flowmeter calibrations were performed in vitro by col-
lecting measured amounts of normal saline through the probes within a known amount of time; both high and low flow rates were measured to test linearity. The coronary probe calibrations remained within ±4% throughout the series of experiments. In this report coronary flow refers to antegrade blood flow through the left circumflex coronary artery.

Lead II of the electrocardiogram was monitored. Hemodynamic data were recorded both on a Hewlett-Packard direct-writing oscillograph (model 7700), and an FM magnetic tape recorder (model 3520B). After the instrumentation was connected, hemodynamic data were monitored continuously to ensure that steady-state conditions had been obtained. After recording of control pressure and myocardial flow measurements a single coronary occlusion lasting approximately 5 min was performed in all dogs. Regional myocardial blood flow determinations were made at 30 sec and then again at 4 min during this single coronary occlusion. The occluder was released and the animals were allowed to recover. Blood flow was measured by injection of carbonized radioactive microspheres 9 ± 1 μm in diameter, labeled with one of seven gamma-emitting nuclides (125I, 141Ce, 51Cr, 99mTc, 35S, 113I, 103Pd, or 85Sr; New England Nuclear). The microsphere method, tissue counting, and flow calculations used in our laboratory have been described previously by others.6,7

At the end of the study all animals were killed with a lethal dose of sodium thiomylal followed by potassium chloride. Each heart was removed and the circumflex artery was cannulated at the orifice. Methylene blue dye was injected into the proximal circumflex coronary artery during an occlusion of the balloon occluder to verify the completeness of the coronary occlusion in the 13 dogs without flow probes. The heart was then placed in buffered formalin. The left ventricle was sectioned into four transverse rings and six anatomic regions as described previously.7 Each region was divided into four transmural layers, epicardium (layer 1) to endocardium (layer 4), each 0.5 to 2 g of myocardial tissue. If myocardial infarction or fibrosis exceeded 15% of the surface in any one of the four transmural myocardial layers, or if fibrosis was found in more than one layer, the data from the animal were rejected. In five dogs these changes were observed in the collateral-dependent myocardium and therefore the data were excluded from the analysis.

For purposes of this study, the collateral-dependent region was defined as the region of most severe ischemia as determined by radioactive microsphere measurements and was most often the posterior papillary muscle. The anterior region was defined as the control, noncollateral-dependent region.

Data analysis. Collateral coronary conductance was calculated as the mean myocardial blood flow in the collateral-dependent area divided by mean aortic pressure minus mean circumflex coronary arterial pressure. The systolic, diastolic, and mean aortic-circumflex pressure gradients were not significantly different. Thus, the mean gradient was used in the calculation of conductance. Distal coronary conductance was calculated as mean myocardial blood flow in the collateral-dependent area divided by mean coronary pressure minus left ventricular end-diastolic pressure.

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\text{Collateral coronary conductance} = \frac{\text{Mean collateral blood flow}}{\text{Mean aortic - mean circumflex pressure}}
\]

\[
\text{Distal coronary conductance} = \frac{\text{Mean collateral blood flow}}{\text{Mean circumflex - left ventricular end-diastolic pressure}}
\]

The nonparametric Wilcoxon two-sample signed-rank test was used for statistical comparisons within each group. Comparisons between groups were done with Student’s t test for unpaired data. Linear regression analysis was used to evaluate trends and relationships between parameters. All data presented are expressed as mean ± SD.

Results

Studies were performed in 38 dogs. Data from 14 dogs were excluded from the analysis: five dogs were excluded because of the development of significant myocardial fibrosis and nine dogs were excluded because of technical difficulties. The 24 dogs in which complete studies were performed were separated into two groups according to their circumflex coronary pressure 30 sec after circumflex coronary occlusion at the time of study. Group I consisted of 16 dogs with evidence of collateral development at the time of study and circumflex diastolic pressure greater than 17 mm Hg at 30 sec. This value represents 1 SD above the mean of the diastolic coronary pressure observed in five dogs in which distal coronary pressure during occlusion was measured at the time of the initial surgical instrumentation. This pressure is similar to pressures observed by Khouri et al.,4 who studied awake dogs before collateralization. Group II consisted of eight dogs without evidence of collateral development and circumflex diastolic pressures of less than 17 mm Hg at 30 sec.

The hemodynamic and myocardial blood flow data for both groups are summarized in table 1. During control resting conditions in group I dogs the myocardial blood flow was 0.83 ± 0.34 ml/min/g in the collateral-dependent posterior papillary region and 0.82 ± 0.36 ml/min/g in the noncollateral-dependent anterior region. The transmural blood flow was distributed so that endocardial/epicardial blood flow ratios were 1.13 ± 0.19 and 1.39 ± 0.24, respectively. In group II dogs under control resting conditions, similar myocardial blood flows and distributions were observed in collateral- and in noncollateral-dependent areas.

Thirty seconds after the onset of a complete circumflex occlusion in group I dogs, mean circumflex coronary pressure was 42 ± 9 mm Hg. At 4 min, mean circumflex coronary pressure had increased significantly to 49 ± 10 mm Hg (p ≤ .01). The minimal coronary pressure was usually reached within the first 15 sec. The subsequent increase in pressure was gradual over the course of the duration of occlusion. No significant changes occurred in heart rate or aortic or left ventricular pressure. From 30 sec to 4 min after onset of circumflex occlusion mean myocardial flow in the collateral-dependent region increased slightly from
### Hemodynamic data

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<th>Pressure (mm Hg)</th>
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<td>Heart rate</td>
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<td>(beats/min)</td>
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<td>Group I (n = 16)</td>
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<td>Circumflex occlusion</td>
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<td>79 ± 8</td>
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<td>Group II (n = 8)</td>
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<td>Circumflex occlusion</td>
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<td>30 sec</td>
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<td>76 ± 10</td>
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Values are mean ± SD.

*p ≤ .05 comparing the observations made at 30 sec and at 4 min during the same circumflex occlusion; *p ≤ .05 comparing observations at 30 sec and 4 min with control.

0.78 ± 0.30 to 0.84 ± 0.33 ml/min/g (p ≤ .05). The transmural blood flow distribution improved, resulting in a significant increase in mean endocardial/epicardial flow ratio from 0.77 ± 0.36 to 1.04 ± 0.25 (p ≤ .01). No significant changes were observed in myocardial flow or in the transmural flow distribution in the non-collateral-dependent anterior region. In group II dogs, from 30 sec to 4 min after coronary occlusion no significant changes in mean myocardial flow or in the transmural flow distribution were observed in the collateral-dependent area. Mean circumflex coronary pressure increased slightly but significantly (p ≤ .05) from 20 ± 5 to 24 ± 8 mm Hg.

Conductance changes from 30 sec to 4 min during coronary occlusion are shown for all 24 dogs in figure 2. Collateral conductance for group II dogs changed minimally from 0.001 ± 0.001 to 0.002 ± 0.002 (ml/min/g)/mm Hg (p ≤ .02). Only one of the dogs in group II had collateral conductance changes of more than 0.002 (ml/min/g)/mm Hg. In group I dogs, however, mean collateral conductance was 0.017 ± 0.017 (ml/min/g)/mm Hg at 30 sec and significantly increased to 0.021 ± 0.021 (ml/min/g)/mm Hg at 4 min (p ≤ .005) (figure 2, A). In 11 of 16 group I dogs, collateral conductance increased by greater than 0.002 (ml/min/g)/mm Hg. The change in distal conductance was quite variable and did not reach statistical significance (figure 2, B).

The relationship between initial collateral conductance and the change in collateral conductance during coronary occlusion was examined (figure 3). In dogs with low levels of collateral development (group II), little change in conductance was observed during coronary occlusion. In dogs with evidence of collateral development (group I), variable increases of collateral conductance were observed during the occlusion, but a trend indicating a relationship between the magnitude of the initial conductance and the change was apparent. The overall correlation was r = .69.

The transmural flow distribution (endocardial/epicardial) at 30 sec and 4 min of circumflex occlusion are compared in figure 4. In group II dogs no significant trend in coronary pressure or in the endocardial/epicardial flow ratio was apparent during the occlusion. In group I dogs the endocardial/epicardial flow ratio increased as coronary pressure increased. In three group I dogs coronary pressure increased despite the fact that the endocardial/epicardial flow ratios were greater than unity at 30 sec.

The reproducibility of the change in collateral conductance during coronary occlusion was evaluated in eight dogs (four from each group). These dogs under-
went two circumflex coronary occlusions separated by 2 hr to allow baseline conditions to return. The change in conductance was not significantly different during the first and the second occlusions in dogs in either group. Hemodynamic parameters were also similar during each of the occlusions.

When differences between group I and group II were examined under control conditions, hemodynamics were similar as were blood flows to the posterior papillary and anterior regions and endocardial/epicardial blood flow ratios ($p \geq .15$) (table 1). Under control conditions the only difference between groups was in the aortic-coronary pressure drop ($p \leq .02$). Differences were found between groups at both 30 sec and 4 min during coronary occlusion in heart rate, posterior papillary blood flow, and the endocardial/epicardial blood flow ratio ($p \leq .02$). The change in coronary collateral conductance from 30 sec to 4 min was significantly greater for group I, $0.004 \pm 0.002$ (ml/min/g)/mm Hg, than group II, $0.001 \pm 0.000$ (ml/min/g)/mm Hg ($p \leq .04$). The separation of dogs into groups I and II was something of an artificial one since they represent a continuum. A certain amount of collateral vasculature was present in all the animals and appeared to respond in a similar manner during the two occlusions. It is clear, however, that the magnitude of the changes in collateral conductance were a function of the degree of collateralization and thus were greater in group II (figure 3).

**Discussion**

The primary purpose of this research was to evaluate coronary collateral function during brief occlusion of a...
major coronary artery. Previous investigators have described an experimental preparation of partial coronary stenosis that often results in rapid collateral development over a period of approximately 2 weeks. This preparation produces an area of myocardium that has a dual blood supply. The resting mean circumflex coronary flow in 11 dogs with flow probes in group I was 27 ± 15 ml/min. Data from our laboratory indicate that the mean circumflex flow in dogs without coronary stenosis studied in the awake state is in the range of 34 ml/min. Also, the aortic-to-coronary pressure gradient was small under control conditions compared with during occlusion (table 1). Thus, under resting conditions the segment of myocardium is perfused primarily by flow through the stenotic vessel rather than the collateral vessels. These studies provided an opportunity to observe how rapidly immature collateral channels function after a brief coronary occlusion. The experimental preparation is analogous to spasm or thrombus occurring in the setting of partial coronary stenosis, which may result in coronary occlusion with a brief interruption of antegrade blood flow.

Blood flow into a region of myocardium perfused by collateral channels may be regulated by a number of factors including the resistance in (1) the collateral vessels themselves, (2) the arteriolar or precapillary and the penetrating vessels in the distal myocardial bed, or (3) a combination of both. The data obtained in these dogs can be used to compute separately the conductance at the level of the collateral channels and that occurring in the distal myocardial bed. To make this distinction, the pressure drop across the collateral network and a measurement of collateral blood flow must be obtained. During coronary occlusion, it was assumed that the pressure drop from the central aorta to the distal circumflex coronary artery represented the pressure drop across the collateral network. Previous studies have indicated that in the absence of coronary stenosis the gradient along the epicardial coronary artery is small. The current study supports these data in that group II dogs had only a 3 mm Hg resting aortic-circumflex pressure gradient. This suggests that the major amount of change in pressure gradient occurred over the collateral network rather than from the aorta to the point of origin of the collateral vessels. The precise location and determinants of the pressure gradient across the distal myocardial bed is uncertain. For the purpose of this study it was assumed that the difference between distal circumflex coronary pressure and left ventricular end-diastolic pressure would at least provide a directional estimate of this pressure gradient. It is likely that this is at best a very gross estimate since evidence points to the existence of a "vascular waterfall" occurring in the distal myocardial bed. It is likely that the conductance of the distal myocardial bed as calculated here is a rather insensitive index of the dynamics occurring at the level of the penetrating vessels or the distal arterioles. No correlations of distal bed conductance with collateral conductance change during coronary occlusion or with the extent of collateral stimulation were apparent. However, the lack of correlation may be due to the limitations inherent in the computation of distal bed conductance as an index of vasomotion in the distal bed.

The dogs with evidence of collateral development invariably had an increase in collateral conductance from 30 sec to 4 min during occlusion of the circumflex coronary artery. These conductance changes were not associated with significant changes in heart rate, arterial pressure, or left ventricular end-diastolic pressure. At 4 min the endocardial/epicardial flow ratio, mean myocardial flow, and distal coronary pressure were significantly increased as compared with 30 sec. Furthermore, the improvement in collateral conductance during occlusion correlated with the initial level of conductance during coronary occlusion. These observations suggest that immature collateral channels do not function maximally at the onset of a coronary occlusion but may gradually improve function during the occlusion.

Thirty seconds was chosen as the time of the initial measurement because contraction of the ischemic muscle has ceased by this time and the coronary pressure is at a reliable steady state. The time of 4 min was chosen because it was believed that this would allow sufficient time for a detectable change in collateral function to have occurred. The observation that collateral conductance increases from 30 sec to 4 min during coronary occlusion is consistent with previous findings in the peripheral circulation. Rosenthal and Guyton found in the dog that with occlusion of the femoral artery, peripheral conductance of collateral blood flow increased 277% during the first 70 sec, suggesting that the collateral network may not reach maximal function immediately but may increase function rapidly after femoral artery occlusion. The overall increase in distal pressure in the peripheral circulation observed by Rosenthal and Guyton was approximately 30 mm Hg, compared with the 7 mm Hg observed in the coronary circulation in the present study. These differences may relate to differences in the anatomy, physiology, or the degree of collateralization of the leg as compared with the heart in dogs.

The mechanism of the increase in collateral conduc-
tance after coronary occlusion is uncertain. Several possible mechanisms could explain this phenomenon: ischemic, hemodynamic, myogenic, or neural mechanisms could be involved. Ischemia could effect an improvement in perfusion of the collateral-dependent myocardium in at least two ways. First, a potent humoral effect on the collateral vessels could be produced by release of a vasoactive metabolite from inadequately perfused myocardium. Improved collateral conductance correlated with improved transmural perfusion during the occlusion, suggesting that collateral conductance changes may be related in some way to the recovery from subendocardial underperfusion.

Second, hypokinesis of the collateral-dependent region during occlusion could result in decreased systolic wall forces. Theoretically, the collateral-dependent myocardium might benefit in this situation by allowing collateral blood flow during both diastole and systole.

Arguing against the hypothesis that subendocardial ischemia is responsible for the increase in collateral conductance after circumflex occlusion is the fact that in three of our dogs in which there was no evidence of subendocardial underperfusion after 30 sec of occlusion collateral conductance increased over the course of the occlusion. It would appear, then, that the observed increase in collateral conductance during coronary occlusion cannot be explained as a consequence of release of a vasoactive substance from underperfused myocardium.

There are several ways in which physical forces may effect a change in the collateral vessels. One possible mechanism is that changes in the distending pressure may have resulted in a dilatation or opening of collateral channels. Pressure was not measured directly inside the collateral vessels, but was measured in the distal circumflex coronary artery. This pressure fell during coronary occlusion, suggesting that pressure inside collateral vessels was lower during coronary occlusion than under control conditions. It would seem unlikely, therefore, that an increase in distending pressure occurred during the coronary occlusion and “popped” the collaterals open.

A physical force acting on the collateral vessels that potentially could be increased during coronary occlusion is the collateral flow velocity. The mean pressure gradient under control conditions was relatively low across the collateral network, suggesting that little collateral flow occurred at rest. During occlusion, the pressure gradient across the collateral network markedly increased, suggesting that the collateral flow velocity also increased. Increased flow velocity across the collateral channels would be expected to result in an increase in the shearing stress exerted on the luminal wall of the collateral vessel. In small vessels shearing stress, even under conditions of moderate changes in flow velocity, could conceivably become quite high. It is possible that increased flow velocity may alter the endothelial lining of the vessel wall to cause a release of a vasodilating substance such as prostacyclin.

A possible myogenic mechanism must be considered. According to the myogenic hypothesis the vascular tone of the collateral vessel would be regulated in response to changes in a force applied by the distending pressure. If pressure fell in the collateral vessel then it would dilate, resulting in a decrease in collateral vasculature resistance or enhanced collateral conductance. However, the poor correlation (r = .57) between the degree of pressure drop during the occlusion and the change in conductance perhaps indicates that myogenic factors were not of paramount importance.

Evidence from the present study against both release of a vasodilator substance and a myogenic mechanism is the fact that the immature collateral vessels do not have well-developed vascular smooth muscle. Without the presence of smooth muscle both responses would seem improbable. The vessels develop smooth muscle as part of the vessel growth process but it is not known whether these cells respond as mature vascular smooth muscle. The distal and proximal connections of collaterals to large arteries probably do contain smooth muscle. The amount these vessels contribute to collateral conductance is unknown. The possible involvement of neural influences was not investigated.

The data obtained in these studies may have important implications for the mechanism of the relief of angina pectoris in patients with significant coronary artery disease. If collateral vessels are present, the rapidity with which they open and become functional may be highly significant during coronary artery spasm or with the increased need for flow in a stenosed vessel during exercise. The data obtained in these studies clearly demonstrate that collateral conductance increases over a 4 min period during total occlusion of a partially stenosed coronary artery. Thus, it seems reasonable to conclude that these collateral vessels did not function at maximal capacity immediately. If minutes are required to achieve the maximal collateral flow, this finding may explain the relief of ischemic pain that occurs after several minutes in patients with resting angina or the “walk through” phenomena, which occurs in some patients with exercise-induced angina.

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