Determination of Coronary Collateral Flow by a Load Line Analysis

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SUMMARY. We have examined the feasibility of determining coronary collateral blood flow in an open-chest dog by a "load line" type of analysis as is often employed to analyze transistors and vacuum tubes. The load line equation states that collateral flow is given by the quantity:

$$ Q_{col} \left( 1 - \frac{P_P}{K \cdot AOP} \right) $$

where $P_P$ is peripheral coronary pressure, $AOP$ is aortic pressure, $Q_{ret}$ is retrograde flow, and $K$ is a constant. The validity of this equation was critically tested in a series of dog experiments in which the collateral vessels were found to approximate a linear resistance, the source pressure for the collaterals ($K$ in the equation) was found to be 0.8 of aortic pressure, and the retrograde flow with zero back pressure was found to account for all of the collateral flow. Finally, we found that estimates from the equation correlated well with direct microsphere measurements of collateral flow. All of these findings support the use of the proposed technique which determines collateral flow by three easily measured laboratory parameters. (Circ Res 50: 663-670, 1982)

WHEN a coronary artery is occluded, blood flow to the region of myocardium served by that vessel does not totally cease but rather continues at a greatly reduced rate. This residual flow is delivered by coronary collateral vessels. Most authorities agree that the collateral flow rate is a major determinant of the amount of myocardial cell survival following coronary artery occlusion (Rivas et al., 1976) and that improved coronary collateral flow is a meritorious therapeutic goal. Unfortunately, investigations into identifying interventions which can augment coronary collateral flow have been continuously thwarted because of the lack of a suitable method for measuring coronary collateral blood flow in an in situ heart.

One of the earliest methods for estimating collateral flow was to measure the quantity of blood which flowed retrograde from a coronary artery that had been opened to the atmosphere distal to an occlusion (Anrep and Hausler, 1928). A criticism of this retrograde flow technique has been that it overestimates collateral flow, since flow occurs retrograde against atmospheric pressure rather than peripheral coronary pressure, and, thus, the pressure gradient for flow would be enhanced (Epstein, 1954). On the other hand, Scheel (1979) has argued that the resistance of the cannulas employed by most investigators for retrograde flow collection is sufficiently high to impede flow, causing the results to be artifactually low. It becomes clear, then, that it would be only a fortuitous coincidence if retrograde flow did actually equal the true collateral flow in any given instance.

More recently, radio microspheres have become the method of choice for measuring collateral flow. Unfortunately, they have several shortcomings as well. Due to counting restraints, relatively few measurements can be made in any single heart. More important, Patterson and Kirk (1979) have shown that identification of collateral-dependent tissue is no small problem. Because collateral flow is quite low, even a small percentage of normally perfused myocardium included in a sample thought to be collateral dependent can introduce a large artifact. The methods required to eliminate this problem, the so-called "shadow technique" (Hirzel et al., 1976), are cumbersome and have not been adopted by most investigators.

In the present study, we have employed a "load line" technique to analyze the collateral flow. This scheme is similar to that used to analyze transistors and vacuum tubes. This approach was taken because, in the presence of coronary occlusion, the coronary microcirculation, which has very discontinuous resistance characteristics (Downey and Kirk, 1974), is in series with the collateral circulation which should have linear resistance characteristics (Scheel et al., 1977). If the conditions of the theoretical model below are met, then collateral flow can be determined simply by the pressure gradient across the collateral vessels, divided by the resistance of those vessels.

Figure 1 shows a simplified model of the load line concept. In this model, the left anterior descending coronary branch (LAD) is ligated. Its microcirculation, $R_{LAD}$, must then be supplied via the collateral vessels, $R_{col}$. The patent circumflex branch is perfused by aortic pressure, since it has not been ligated. Flow through $R_{LAD}$ is ultimately determined by the pressure at Node A. If we cannulate the distal segment of the LAD, we can provide an alternative path for...
collateral flow by allowing flow to occur retrograde out of the cannula. By varying the back pressure to retrograde flow, the amount of blood diverted through $R_{LAD}$ can be varied from none—by producing zero back pressure—to 100% of the collateral flow, by providing a back pressure equal to that which existed at Node A before it was cannulated. This latter pressure is often referred to as the peripheral coronary pressure (PCP). The relationship between the back pressure and the retrograde flow is shown by the broken line on the graph.

If the collaterals behave as a linear resistance, then the relationship between flow through $R_{col}$ and the pressure at Node A will be described by the solid line in the graph, the load line. When the pressure at Node A equals aortic pressure, no flow will occur through the collaterals. Likewise, when Node A has zero pressure, the full aortic pressure is realized across the collaterals, and flow will equal AoP/$R_{col}$. Since there is no gradient for antegrade flow, the retrograde flow will also equal the collateral flow. According to circuit theory, the load line will be a straight line between these two points. Finally, the true collateral flow through $R_{LAD}$ when there is no retrograde flow diversion is determined by the intersection of peripheral coronary pressure and the load line. In this case, retrograde flow is zero, so that collateral flow will equal the antegrade flow. One can calculate that

$$Q_{col} = Q_{ret} \left( 1 - \frac{PCP}{AOP} \right).$$

Notice that this serves for the true collateral flow as a function of three easily measured parameters, i.e., the retrograde flow at zero back pressure ($Q_{ret}$), the peripheral coronary pressure and the aortic pressure ($AOP$).

The conditions of the model which must be met for the above equation to be valid are, first, that the collaterals must have a linear pressure flow relationship; second, that the retrograde flow at zero back pressure must account for all or at least a predictable percentage of the collateral flow, and last, that the load line’s zero flow intercept must be equal to, or a predictable percentage of, aortic pressure.

Animal studies were therefore undertaken to critically test these three assumptions to see whether this technique could be used as a practical method for measuring coronary collateral blood flow. In addition, a series of experiments was conducted in which microsphere estimates of collateral flow were compared to calculations as a further test of the validity of the technique.

### Methods

#### The Animal Model

Mongrel dogs of either sex ranging from 12 to 20 kg were anesthetized with sodium pentobarbital, 30/mg kg, iv. The chests were opened in the 4th left interspace and the hearts exposed. The dogs were ventilated with room air from a Harvard respirator while the chests were opened. The left anterior descending coronary artery was dissected free of the heart and cannulated with a short cannula made from 15-gauge hypodermic needle stock. Heparin (10,000 units) was administered intravenously to prevent clotting in the perfusion lines. Figure 2 shows the perfusion scheme. Arterial blood from a femoral artery passed through a Carolina Medical Electronics blood flow transducer and into the coronary artery. Pressure in the line was measured by a Statham P23Db transducer positioned at left atrial level and connected to a side branch of the tubing. A second side branch went to a photoelectric drop counter. The free end of the drop counter was on a track which could be raised above or lowered below left atrial level to vary the hydrostatic head in the side branch. The drop counter was interfaced to a Commodore PET microcomputer which calculated the blood flow rate by measuring the intervals between a predetermined number of successive drops (Lee and Downey, 1981). Both a mean flow rate and the standard error of that rate were output by the computer for each run.

Clamps on the perfusion line allowed either normal perfusion of the artery (clamp A off and clamp B on), or retrograde flow collection (clamp A on and clamp B off). A catheter was advanced through the left carotid and into the left ventricle for left ventricular pressure measurement. A second catheter was inserted via the right femoral artery into the area of the aorta for arterial pressure measurement. The proximal end of the subclavian artery was cannulated and connected via 1⁄8-inch ID tubing to a 500-ml reservoir about 1 meter above the dog; this was used to stabilize

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**Figure 1.** A model of the coronary circulation in which the left anterior descending artery has been ligated. The collateral vessels are represented by $R_{col}$ and the anterior descending by $R_{LAD}$. The bottom graph shows retrograde flow (the interrupted line) and collateral flow (the solid line) as a function of the pressure at Node A. Note that, at zero back pressure, all of the collateral flow appears in the retrograde flow. Similarly, when back pressure equals peripheral coronary pressure, all of the collateral flow goes through $R_{LAD}$. The intersection of peripheral coronary pressure with the solid line should therefore be the true collateral flow. The equation for that point is:

$$Q_{col} = Q_{ret} \left( 1 - \frac{PCP}{AOP} \right).$$

Notice that this serves for the true collateral flow as a function of three easily measured parameters, i.e., the retrograde flow at zero back pressure ($Q_{ret}$), the peripheral coronary pressure and the aortic pressure ($AOP$).
coronary pressure was measured by putting both clamps on the tubing and noting the perfusion pressure. Next, clamp level. When the preparation was in a stable state, peripheral thoracic aorta, normotension, and hypotension caused by conditions: arterial hypertension caused by occluding the above, except with the addition of a catheter into the left lower the subclavian artery reservoir. For each measurement, we briefly reestablished retrograde flow was measured. The coronary pressure. As back pressure is reduced, the drop counter was then adjusted to the necessary height to provide the desired back pressure, and the drop rate was measured with the microcomputer. Each flow rate measurement required about 15 seconds. Successive measurements were made at various back pressures until 5 minutes of interrupted perfusion had elapsed, at which time the perfusion was re-established and the heart allowed to recover. When the reactive hyperemia had subsided, usually after about 5-10 minutes, the procedure was repeated.

Occlusion of the Collateral-Dependent Vessels

By occluding the microcirculation of the left anterior descending coronary artery, we created a condition where the retrograde flow would equal all of the collateral flow. This was accomplished by infusing 100 mg of 25-μm carbonized microspheres into the arteries' perfusate while it was perfused with arterial pressure. This was administered by slow injection over about a 60 second period. Total occlusion was verified by a zero reading on the flow meter. After each retrograde flow measurement, we briefly reestablished aortic pressure to verify that the vessel was still occluded.

Microsphere Measurements

We directly measured collateral flow in six dogs with radiolabeled microspheres. The dogs were instrumented as above, except with the addition of a catheter into the left atrium. In addition, a snare was placed around the thoracic aorta. Microspheres were injected under three different conditions: arterial hypertension caused by occluding the thoracic aorta, normotension, and hypotension caused by lowering the subclavian artery reservoir. For each measurement, we first adjusted the aortic pressure to the desired level. When the preparation was in a stable state, peripheral coronary pressure was measured by putting both clamps on the tubing and noting the perfusion pressure. Next, clamp B was removed and retrograde flow was measured. The height of the drop counter was adjusted to be 2-3 cm below atrial level. Clamp B was then replaced and one million 15-μm radiolabeled microspheres (3M Corp.) were injected as a bolus into the left atrium. Arterial blood was withdrawn at 15 ml/min via another pump from a catheter in the arch of the aorta. Blood was collected in three successive counting vials over a 90-second period and served as reference standards (Domenech et al., 1969; Russell et al., 1977). The arterial pressure then was changed and the procedure repeated. Two measurements were made in four dogs, and measurements were made under all three conditions in two of the dogs. After the measurements had been completed, 1 ml of fluorescein dye was injected into the perfusate to mark the ischemic region, and the heart was quickly removed.

The object of the microsphere measurements was to measure the total collateral flow in these hearts. There is, of course, no reliable method for measuring this quantity, hence the rationale for this study. We attempted to approximate this measurement, however, by the following procedure. The microsphere method only yields a flow rate per gram tissue. If we knew the mass of the perfusion field and the flow rate per gram within it, the product of these two quantities would equal the total flow rate. We calculated the flow rate per gram of the ischemic zone by cutting a uniformly stained transmural sample from the center of the anterior descending region and then determined the flow rate for each of the isotopes injected (Russell et al., 1977). We determined the mass of the region by cutting a second transmural sample from the posterior wall of the ventricle and determining flow rate per gram. The latter represented the flow rate for normally perfused myocardium. We then divided the flow to the anterior descending artery, as indicated by the flowmeter just before the perfusion line was clamped, by the normally perfused flow rate as measured in the posterior wall. If the perfused anterior descending region received a flow per gram that was similar to the rest of the heart, then this value should yield the mass of the myocardium served by the anterior descending artery. Next, we multiplied the flow per gram figure, which is determined for the stained sample by this mass, to arrive at a total collateral flow figure. These values were then compared to the comparable collateral flow as calculated from the proposed equation.

**Results**

Retrograde Flow as a Function of Back Pressure

Retrograde flow was measured as a function of back pressure with the microcirculation patent in nine dogs. A typical plot of this relationship is shown by the squares in Figure 3. The plot intersects the pressure axis at about 30 mm Hg. This is the peripheral coronary pressure. As back pressure is reduced, the flow rate increased until it intersected the flow axis at about 4 ml/min. One reproducible feature of these plots was that the slope always decreased at lower pressures. We found that by arbitrarily breaking this relationship into two data sets, those above 10 mm Hg and those below 10 mm Hg, two fairly linear line segments were obtained. Figure 4 shows the composite data as per this analysis. Peripheral coronary pressure, by the least square fits, was found to be 28.7% ± 1.9% of the aortic pressure. The extrapolated pressure intercepts from the points below 10 mm Hg.
FIGURE 3. Data from a representative experiment. Retrograde flow is plotted against back pressure at the tip of the cannula. Pressure at the tip was calculated as pressure behind the cannula plus the retrograde flow times the cannula's resistance. Squares represent flows before microcirculatory occlusion and crosses represent flows after occlusion.

However, was much higher at 78% ± 6.28% of aortic pressure, showing the differences in slope of the two data sets. These intercepts were found to be significantly different from each other at the $P < 0.001$ level (paired t-test).

We next occluded the microcirculation of these dogs' left anterior descending coronary artery and repeated the retrograde flow measurements. Care was taken to be sure that aortic pressure had not changed between the two measurements. The crosses in Figure 3 show a typical result after microcirculation occlusion. Note that the flow intercept was still about 4 ml/min, but the pressure axis intercept had increased to 65 mm Hg. When least squares fits were made to all of these data, the upper line in Figure 4 resulted. Note that the pressure intercept was 81.7% ± 4.25% of the aortic pressure and was not significantly different from the extrapolated intercept of the unoccluded data points taken with back pressures below 10 mm Hg. Retrograde flow for the nine dogs was 3.72 ± 0.51 ml/min before occlusion with microspheres and was 4.1 ± 0.68 ml/min after occlusion. A paired t-test yielded a t-value of 0.82 which indicated no significant difference. Of the nine experiments, three animals showed a decrease retrograde flow after occlusion, five showed a net increase and one did not change. Thus, it would appear that the collateral vessels have a pressure at their source of 0.81 times aortic pressure. Furthermore, the relationship between retrograde flow and back pressure is the same whether the antegrade vasculature is plugged or patent as long as back pressure is 10 mm Hg or less.

When the clamps on the perfusion line were arranged so that the coronary arteries once again experienced aortic pressure after several retrograde flow measurements had been performed, the vessel was still found to be occluded. In two dogs, we attempted to occlude the microcirculation with 50-μm microspheres. Although these were effective in dropping flow to zero initially, appreciable forward flow was observed after a period of retrograde flow. Thus, the 50-μm microspheres were dislodged under retrograde flow conditions while the 25-μm spheres were not.

Figure 5 shows the results of the experiments in which coronary collateral flow was measured directly with microspheres. The horizontal axis is the collateral flow as calculated by the load line equation, and the vertical axis shows the total collateral flow as determined by the microsphere measurements. Flows, as calculated by the proposed technique, correlated to

FIGURE 4. Composite data from nine dogs in which the pressure and flow intercepts were calculated both before (upper line) and after (lower line) microsphere occlusion of the microcirculation. Coronary back pressure appears on the horizontal axis, and retrograde flow appears on the vertical axis.

FIGURE 5. Correlation of collateral flow as calculated by the load line equation (horizontal) to that calculated by microspheres (vertical). The r value of the fit was 0.88.
0.76 times the microsphere calculations plus 0.48 ml/min per g. The r value for the fit was 0.88, and we considered that to be a fair correlation. A slope of 1 and an intercept of 0 would have indicated that they were exactly equivalent.

Discussion

In the introduction, we listed three conditions that would have to be met before the load line equation could be accepted as yielding true collateral blood flow. The first of these was that the collateral vessels would have to behave as linear resistances. If they possessed linear resistance characteristics, then the load line should be straight. In these experiments, the load line for the collateral circulation was the plot of retrograde flow as a function of back pressure after microcirculatory occlusion (the upper lines in Figures 3 and 4). Although an almost straight line was usually observed, the curves were consistently concave to the pressure axis as seen in Figure 3. The most probable explanation for this deviation from linearity is that elasticity in the walls of the collateral vessels caused them to expand when the pressure inside of them was increased. As they expanded, their resistance would fall. Figure 6 shows the predicted effects on the load line when collateral resistance becomes an inverse function of the pressure at Node A. The numbers on the curves indicate the minimum value of resistance achieved. The line in which resistance fell to two-thirds of its starting value when Node A equaled the source pressure best approximates the actual data. It should also be noted that the greatest change in resistance in this model occurs at high back pressures and at back pressures below 25 mm Hg, less than an 8% change in resistance would be seen. Thus, we conclude that the linearity of the collateral resistance is indeed adequate for this technique.

The second condition which had to be met was that the retrograde flow had to account for all of the collateral flow. This would certainly be the case if all of the collateral vessels emptied directly into the left anterior descending artery with only artery-to-artery type connections. If, on the other hand, many of these vessels ran directly to capillary networks as artery-to-capillary type connections, then much of the collateral flow would not be present in the retrograde flow. Levy et al. (1961) first proposed artery-to-capillary connections when it was seen that some regional flow persisted when retrograde bleeding occurred. Bloor et al. (1965), however, showed that the apparent residual flow under those conditions was an artifact related to unaccounted for intravascular rubidium associated with the regional flow measurement. More recently, Downey et al. (1973) have revived the artery-to-capillary theory, showing that regional flow to the subendocardium persists during retrograde flow diversion when flow is measured with radio microspheres, a technique which overcomes the objections of Bloor et al. The experiment by Downey et al. (1973) seems to have had an artifact as well, however. Kirk (1980) has shown that the residual flow which appeared in the subendocardial samples probably was due to inclusion of a small amount of normally perfused tissue in the samples which were thought to be collateral dependent. When Kirk (1980) repeated the Downey et al. (1973) experiment, taking the necessary steps to avoid such contamination (Hirzel et al., 1976), no residual flow was seen. It would thus appear that virtually all of the collateral vessels are artery to artery in nature and that, in theory, the retrograde flow could indeed account for all collateral flow.

Scheel (1979) has argued that the resistance of the cannulas which most investigators use is sufficiently high to divert some of the collateral flow in the antegrade direction by creating a back pressure-to-retrograde flow. In the present study, the resistance of the cannula was carefully measured with dog blood and the drop across it was calculated from the flow rate. This pressure drop was added to the pressure recorded by the transducer to calculate the pressure at the cannula’s tip. This latter pressure was used for the pressure-flow plots. Pressure at the tip of the cannula could be taken to zero simply by causing the back pressure to be slightly negative. Actually, the pressure drop across the cannula never exceeded 5 mm Hg in any of these experiments because the flow rates were so low.

The fact that retrograde flow in the absence of microcirculatory occlusion was not different from the load line in the range between 0 and 10 mm Hg indicates that antegrade diversion of flow is not a major technological problem. This behavior almost certainly is the result of vascular waterfall formation in the antegrade bed. Numerous researchers have shown that there is a critical pressure below which the coronary arteries are not perfused (Bellamy, 1978; Ellis and Klocke, 1980; Sherman and Grayson, 1980). This value has been reported to be as high as 40-50 mm Hg when tone is present, but seems to be much lower when it is absent. Undoubtedly, at low back pressures, antegrade diversion of flow was prevented.
by this vascular waterfall mechanism in our preparation. Only when back pressure exceeded 10 mm Hg did any appreciable antegrade diversion occur. Ten mm Hg is a little lower than the value most researchers have reported for the critical closing pressure with maximal dilation; however, it should be pointed out that this value was rather arbitrarily chosen by eye to best fit our data and is not a precise measurement. What is more important, recent evidence from this (Downey et al., 1981) and other laboratories (Eng et al., 1980) indicates that a serious capacitance artifact is present in the previously reported values of critical closing pressure, causing these values to be 10 mm Hg or higher than they actually are. Thus, the value of 10 mm Hg may be fairly accurate.

The net effect of this waterfall behavior is that the slope of the retrograde flow-back pressure curve is quite shallow up to 10 mm Hg so that cannula resistance could be fairly high before an antegrade diversion artifact would adversely affect the retrograde flow measurement for the proposed technique. Scheel's (1979) prediction of antegrade flow diversion was based on the assumption that the coronary vessels behaved as linear resistors. That assumption is not supported by our findings. In their method, they calculate an antegrade flow component based on the pressure drop across the cannula which was then added on to the retrograde flow to derive what they considered to be the true collateral flow (Scheel et al., 1977). Since their calculated antegrade flow would considerably overestimate the actual antegrade flow, it must be concluded that these calculations contain an unavoidable error.

When the microcirculation was plugged with microspheres, the retrograde flow at zero pressure did not change. This further proved that negligible antegrade flow diversion had occurred. Wichman et al. (1978) found a large increase in retrograde flow when the microcirculation was plugged, using essentially the same technique. We have no explanation for the discrepant data except that possibly they did not maintain zero pressure at the tip of their cannula. As can be seen in Figure 4, an elevation in back pressure can result in an appreciable difference in retrograde flow under two conditions. It should be noted, however, that the increase in back pressure has to be fairly large—about 10 mm Hg—for differences to occur.

The other possible explanation is that aortic pressure was not carefully controlled. We found that the greatest determinant of the retrograde flow was the aortic pressure. In the present study, we had to resort to a pressure-regulating system to prevent any aortic pressure changes between the control and the occluded measurements before we could get reproducible results.

The third criterion which needed to be met to validate the technique was that the source pressure for the coronary collaterals had to equal or at least be a predictable percentage of aortic pressure. When the coronary microcirculation was plugged, the peripheral coronary pressure, PCP, was consistently found to be about 80% of the aortic pressure. Since antegrade flow would be impossible at this time, this means that the PCP with occlusion represents the pressure at the node where the collaterals leave the parent circulation. Figure 7 shows a refinement of the model presented in Figure 1. Note that a vascular waterfall, as per the discussion above, has been added to the R_{LAD} by the addition of the battery and the diode. In addition, a resistance, R_c, is added upstream of where the collaterals leave the circumflex circulation. Since the pressure at this node was found to be 80% of aortic pressure, R_c must be one-fifth of the total LAD resistance. The 80% value is the same as that reported by Wickman et al. (1978).

This means that the equation presented in the introduction must be modified to represent the source pressure for the collaterals as 0.8 AOP instead of AOP. The equation then becomes:

\[ R_{coll} = Q_{coll} \left( 1 - \frac{P_c P_{AOP}}{0.8 AOP} \right) \]

Although the collaterals may act as artery-to-artery connections, some of them exist at quite small-size vessels. Hirzel and Kirk (1976) showed that 50 μm microspheres passed through the coronary collateral circulation, so that many of these connections must be 50 μm or larger. In the present experiment, however, we found that occlusion of the antegrade bed could not be maintained with 50-μm spheres. We
interpret that finding to mean that an appreciable number of collaterals entered the anterior descending in vessels having diameters between 25 and 50 μm. As shown in Figure 8, a period of retrograde flow would result in the 50-μm spheres being dislodged and washed out. However the 25-μm spheres would continue to be packed into the microcirculation during retrograde flow collection.

If a resistance existed between the point at which the collaterals exit the circumflex artery and the coronary ostium, then a similar resistance undoubtedly existed between the entrance of the collaterals into the anterior descending artery and the coronary cannula. Since retrograde flow is only about one-fourth of the antegrade flow in the LAD, the drop across this resistance would be one-fourth of 20 mm Hg, or about 5 mm Hg. This is not enough pressure at Node A to exceed the critical closing pressure for antegrade flow diversion and, therefore, would not cause a problem with the proposed technique. In the presence of collateral development due to long-standing ischemia, such as that produced by an ameroid constrictor (Gregg, 1974; Schaper, 1971), this resistance could cause appreciable diversion. In a recent study by Downey et al. (1980), dogs were prepared with ameroid constrictors to induce collateral development. In those chronically ischemic dogs, retrograde flow becomes about equal to the normal antegrade flow. Appreciable flow was found in the region served by the occluded vessel even when retrograde flow was diverted. Furthermore, care was taken to avoid contamination of the ischemic samples with normally perfused tissue. A likely explanation is that existing collaterals simply increased their lumen size and the pressure drop across the Rₒ increased as the retrograde flow increased. In those experiments, retrograde flow was about equal to normal antegrade flow. Thus the pressure gradient should have been about equal to the normal gradient across Rₒ, nearly 20 mm Hg. This would be sufficiently high to cause a significant diversion.

When we tried to directly correlate collateral flow by the proposed technique to an alternative technique using microspheres, a reasonable correlation was observed. It is not known how accurate the microsphere measurements were, since we did not rigorously check for contamination of the samples with normally perfused myocardium (Patterson and Kirk, 1979). Another source of error is that flow calculations were based on a transmural sample of the ischemic zone. The distribution of flow across the wall of an ischemic zone is quite non-uniform, however, with the subendocardium receiving less than one-half of the flow to the subepicardium (Russell et al., 1977). Only if flow to the collateral-dependent zone were uniformly distributed between the epicardium and the endocardium would this calculation be exact. In light of these shortcomings, most of the variability is likely to be in the microsphere measurements rather than the retrograde flow—PCP calculations.

In our equation, collateral flow is found to be inversely related to PCP. This at first may appear strange, because PCP has traditionally been considered to be a good indicator of collateral flow. The answer to this apparent discrepancy lies in the fact that PCP can be caused to rise by either an increase in the antegrade bed’s resistance or a decrease in the collateral resistance. If the cause is due to a decreased collateral resistance, then the retrograde flow will be increased as well. Thus, PCP and retrograde flow are not independent variables in the equation but, rather, are covariant whenever collateral resistance is varied. Nevertheless, conditions can occur in which the antegrade bed’s resistance is increased—for example, when it was occluded with microspheres in the present study. In that case, PCP rose and collateral flow did indeed fall. This points out the importance of the proposed equation, since PCP alone can be misleading under some conditions.

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