The Effect of Cardiac Contraction on Collateral Resistance in the Canine Heart

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SUMMARY We determined whether the coronary collateral vessels develop an increased resistance to blood flow during systole as does the cognate vascular bed. Collateral resistance was estimated by measuring retrograde flow rate from a distal branch of the left anterior descending coronary artery while the main left coronary artery was perfused at a constant pressure. Retrograde flow rate was measured before and during vagal arrest. We found that in 10 dogs the prolonged diastole experienced when the heart was stopped caused no significant change in the retrograde flow rate, which indicated that systole has little effect on the collateral resistance. However, when left ventricular end-diastolic pressure was altered by changing afterload or contractility, a direct relationship between end-diastolic pressure and collateral resistance was noted.

CONTRACTION of the heart compresses the coronary arteries and impedes blood flow through them. Systole does not completely occlude the coronary vasculature, but rather creates a gradient for flow across the heart wall ranging from little changes in flow at the subepicardium to near zero flow at the subendocardium. Thus a considerable fraction of coronary inflow occurs during systole. Several workers have examined the collateral vasculature to see whether it is compressed during systole as is the cognate bed. Cibulski et al. analyzed phasic flow records in acute canine preparations and concluded that only 5% of the collateral flow occurred during systole. More recently Brown et al. independently varied either the systolic or the diastolic component of the aortic pressure and measured retrograde flow from an occluded branch. Their data indicated that the collateral vessels, unlike the cognate bed, are completely pinched off during systole. This is a surprising finding, since blood flowing retrograde from an open artery is thought to derive primarily from collateral vessels near the epicardium, where tissue pressure during systole is low.

The present experiment further tested the hypothesis that systole completely occludes collateral channels. This was done by measuring retrograde flow as the coronary arteries were perfused at constant pressure and the heart was arrested by vagal stimulation. If, indeed, the collateral vessels were totally occluded during the systolic period, then the prolonged diastole associated with arrest should cause retrograde flow to increase in proportion to the time the heart previously was in systole.

Methods

Ten mongrel dogs of either sex, weighing 11–17 kg were anesthetized with sodium pentobarbital (30 mg/kg, iv). The chest was opened in the 5th interspace and the dog was ventilated with 100% O₂. The left common coronary artery was exposed by blunt dissection at its origin. A coronary cannula with perfusion tubing attached was inserted through the subclavian artery and advanced into the left common coronary artery, where it was tied securely in place. Heparin (10,000 U, iv) prevented clotting. The perfusion apparatus is shown in Figure 1. The cannula was a double-lumen type which withdrew blood from the aorta via the outer lumen. After passing through the exterior circuit, blood entered the coronary artery through the inner lumen. The tubing (Tyrone) with inner diameter (i.d.) = 1/16 in., passed through the fingers of a Harvard model 1215 pump. It then led to a 20-ml air-filled buffer bottle which damped the pulsations from the pump. An extracorporeal electromagnetic flow probe (Carolina Medical Electronics) was used to measure flow in the circuit near the coronary cannula. To provide a constant perfusion pressure the perfusion pressure signal was compared to a set point voltage by an integrating circuit. The output of the integrating circuit controlled the pump speed.
through a Harvard model 550 pump speed modulator. Thus perfusion pressure was controlled in a servo mode to equal the set point.

The left anterior descending coronary artery (LAD) was isolated, usually distal to the first major branch, and cannulated with a cannula made from a 16-gauge hypodermic needle. This was connected via Tygon tubing (i.d. = \( \frac{1}{8} \) in.) to both the main perfusion line, as shown in Figure 1, and either a drop counter (eight experiments) or an electromagnetic flowmeter (two experiments). With the clamp on B closed and the one at A removed the LAD segment was normally perfused. When the clamp at A was closed and that on B removed, blood supplied to that vessel through collateral channels flowed retrograde through the tubing and was measured with the flowmeter or drop counter. The retrograde flow which was collected in the reservoir was periodically reinfused into a femoral vein. Retrograde flow always was allowed to occur for 2 minutes before any measurements were made and flow to the LAD segment was reestablished within 10 minutes after the onset of retrograde flow.

Silver stimulating electrodes were placed on the vagus nerves and a rectangular wave (90 V, 30 cycles/sec) was used to stop the heart for 5-10 seconds. When the heart was arrested, enough blood remained in the central aorta to provide inflow to the perfusion system during the arrest period.\(^7\)

Arterial pressure was measured from a catheter passed into the thoracic aorta via a femoral artery; ventricular pressure was measured via a Teflon catheter passed into the left ventricle from the left carotid artery.

**Results**

Figure 2 shows a typical record of retrograde flow during a period of vagal arrest. The sudden asystole caused a marked increase in antegrade flow while retrograde flow in this case fell. The undamped perfusion pressure record indicates that perfusion pressure remained constant through the experiment. The retrograde flow rates from the 10 dogs are shown in Table 1, where they are normal-

ized by expressing the rates during arrest as a percentage of that prior to arrest. Each number represents the average of two or more repetitions of this maneuver. The range was 77–117%, with a mean of 95%. The antegrade coronary flow, however, always increased. The flow during arrest, expressed as a percent of that during beating, ranged from 115% to 166%, with a mean of 140%. In no case was the increase in retrograde flow with arrest as great as the increase in main left coronary flow. Table 1 indicates that these hearts spent an average of 51% of the cardiac cycle in systole (ventricular pressure in excess of 25 mm Hg). In a system in which the collateral channels are completely occluded during systole a doubling or retrograde flow would be expected with arrest. In fact retrograde flow actually fell in eight of the 10 experiments when the heart was stopped.

Since the perfusion apparatus did not maintain pressure in the right coronary during a vagal arrest, the contribution from the right coronary artery to the LAD segment under study was estimated by the following maneuver. The pump was turned off and the change in retrograde flow rate was noted. The pump turned off the only source of retrograde flow would have been from aortic pressure through the right coronary artery. In all but one dog the contribution from the right coronary artery calculated by this method was 8% or less of the total flow. In the remaining dog there was a 25% contribution from the right coronary artery (Table 1).

In an effort to determine the contribution of heart size to the collateral resistance, three maneuvers were used to vary end-diastolic pressure. The first consisted of injecting 15 mg of sodium pentobarbital into the coronary perfusion line to depress the heart. This was done in three of the dogs (experiments 8-10, Table 1). The mean response to the drug was an increase in left ventricular end-diastolic pressure.

![Figure 2](https://example.com/figure2.png)  
*Figure 2. Retrograde flow during cardiac arrest. The perfusion pressure record is undamped. LV = left ventricular; LCA = left coronary artery.*
TABLE 1  Retrograde Flow Data from 10 Dogs

<table>
<thead>
<tr>
<th>Expt no.</th>
<th>Dog wt (kg)</th>
<th>Flow with arrest (% beating)</th>
<th>Retrograde flow at 125 mm Hg (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Retr.</td>
<td>Ant.</td>
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<tr>
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<td>SD</td>
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LV = left ventricle including the septum; % systole = the percent of the cardiac cycle during which left ventricular pressure was in excess of 25 mm Hg; % R. coronary = percent of retrograde flow derived from the right coronary artery; NA = not available.

pressure of 88%, a fall in peak left ventricular pressure of 50%, and an increase in coronary perfusion rate of 230%. The latter response probably was due to the vasodilatory action of sodium pentobarbital. In all three dogs this maneuver depressed retrograde flow rate (mean decrease was 21%).

In the second procedure the coronary perfusion was interrupted until the hearts were ischemically depressed as evidenced by a falling aortic pressure and a rising left ventricular diastolic pressure. When the pump was re-started the gradual return of function allowed retrograde flow to be measured at a variety of end-diastolic pressures. This procedure, performed in six of the dogs (experiments 5-10, Table 1), also without exception depressed the collateral flow rate. Figure 3 shows a representative record of this experiment. To eliminate the possibility that the large changes in flow in the perfused segment associated with reactive hyperemia might be affecting the results, the following protocol was used to produce Figure 3. The coronary arteries were maximally dilated by interrupting the coronary blood flow for 20 seconds. After flow was resumed left ventricular diastolic pressure quickly returned to the control level. Before coronary flow began to subside, however, perfusion again was stopped as shown in Figure 3. When left ventricular diastolic pressure had risen flow was reinstated. Although the perfusion rate returned to the preclosure value the retrograde flow was reduced.

![Figure 3](http://circres.ahajournals.org/lookup/fig/29945285)  
**Figure 3** The effects of ischemically induced failure on retrograde flow. Flow to the main left coronary artery (LCA) was interrupted by clamping the perfusion line between the pressure transducer and the coronary cannula. This causes the off-scale artifacts in the perfusion pressure record. Notice that retrograde flow fell to zero when the left coronary flow was stopped, indicating little contribution from the right coronary.

![Figure 4](http://circres.ahajournals.org/lookup/fig/29945286)  
**Figure 4** Retrograde flow as a function of left ventricle end-diastolic pressure (LVEDP) during increased afterload. Flow has been normalized by expressing each flow as a percent of flow before afterload was augmented (the three far left points on the graph). The data are from three dogs.
Finally, three dogs (experiments 7, 9, and 10, Table 1) were subjected to 5 seconds of aortic constriction, which increased peak systolic pressure. Since the ventricle was already moderately depressed due to the large akinetic LAD segment, moderate changes in afterload caused marked changes in end-diastolic pressure. Raising peak systolic pressure from 95 mm Hg to 150 mm Hg typically increased left ventricular end-diastolic pressure from a resting value of 5 mm Hg to 25 mm Hg in these hearts. This did not elicit any appreciable increase in the perfusion rate due to the brief duration of the constriction. Figure 4 shows the relationship between end-diastolic pressure and normalized retrograde flow in these experiments. It can be seen that increasing left ventricular diastolic pressure by this procedure also increases collateral resistance.

Discussion

Retrograde flow rate was essentially unchanged when the hearts were stopped by vagal stimulation. It appears that systole has little or no effect on the resistance of the vessels supplying the retrograde flow. Brown et al. found that varying the systolic component of the aortic pressure while holding the diastolic component constant caused no change in retrograde flow. They concluded that the collateral channels were pinched off completely during systole, a conclusion incompatible with the present data. The probable explanation for the disagreement is provided by the present finding that the collateral resistance is a function of left ventricular diastolic pressure. All procedures that increased diastolic pressure in the ventricle increased collateral resistance regardless of the directional change in mean ventricular pressure.

This finding is not surprising, because these changes in diastolic pressure probably reflect similar changes in diastolic volume. Since the collateral vessels run in a tangential direction in the ventricular wall, distention of the ventricle should exert a traction force on these vessels increasing their length, decreasing their caliber and thus augmenting their resistance. When systolic pressure was varied in the study by Brown et al., similar changes in diastolic pressure and thus heart size were inescapable. It appears that the increased perfusion pressure realized when systolic pressure was augmented was compensated for by a size-related increase in collateral resistance. This explanation is especially attractive since we have found diastolic pressure in these hearts to be quite sensitive to afterload because of the large akinetic region.

The retrograde flow rate in the present experiment cannot be equated with collateral flow to the ischemic zone. Ample evidence indicates that alternate channels exist to supply flow to the region, especially to the subendocardium, which do not anastomose directly with the large coronary arteries. However, this measurement should provide an accurate estimate of the resistance of the collateral vessels which supplied the retrograde flow.

Those vessels are thought to be primarily subepicardial in location, and it is not surprising that systole has little effect on flow through them since the vascular compression in this region is low. Whether the resistance of those channels which directly supply the subendocardium is affected by contraction has yet to be determined. Because their location is probably nearer to the subendocardium, such a possibility is much more likely.

Cibulski et al. found that when the left anterior branch was occluded the increase in flow to the circumflex branch of the left coronary artery occurred primarily in diastole. They concluded from this "donor" technique for estimating collateral blood flow that 5% of that flow occurs in systole. Elliot et al. placed flow probes on small branches of the circumflex coronary artery which has occluded centrally. In several of their dogs collateral flow was clearly revealed by blood flowing retrograde through the segments. As in the study of Cibulski et al., this flow was greatly reduced during systole but did not cease. Although the resistance of the collateral channels may be unaffected by contraction, this does not mean that systole should not inhibit the collateral flow. A vascular waterfall system, as previously described for the coronary vessels, should still be operative on the downstream segment in the ischemic zones. Furthermore, since driving pressure for the waterfall system is perfusion pressure minus tissue pressure and since the perfusion pressure provided by the collateral channels is low, systole should markedly inhibit collateral flow, but not because of compression of the collateral vessels. Thus, the conclusion of Cibulski et al. still could be correct.

References

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