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Inhibition of Coronary Blood Flow by a Vascular Waterfall Mechanism

By James M. Downey and Edward S. Kirk

ABSTRACT

The mechanism whereby systole inhibits coronary blood flow was examined. A branch of the left coronary artery was maximally dilated with an adenosine infusion, and the pressure-flow relationship was obtained for beating and arrested states. The pressure-flow curve for the arrested state was linear from below 20 to beyond 200 mm Hg. The curve for the beating state was shifted toward higher pressures and in the range of pressures above peak ventricular pressure was linear and parallel to that for the arrested state. Below this range the curve for the beating state converged toward that for the arrested state and was convex to the pressure axis. These results were compared with a model of the coronary vasculature that consisted of numerous parallel channels, each responding to local intramyocardial pressure by forming vascular waterfalls. When intramyocardial pressure in the model was assigned values from zero at the epicardium to peak ventricular pressure at the endocardium, pressure-flow curves similar to the experimental ones resulted. Thus, we conclude that systole inhibits coronary perfusion by the formation of vascular waterfalls and that the intramyocardial pressures responsible for this inhibition do not significantly exceed peak ventricular pressure.

KEY WORDS

intramyocardial pressure pressure-flow relationship maximal dilation dogs extravascular resistance blood flow model

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The waterfall model. **Top:** A collapsible tube surrounded by a pressure, $P_T$. When $P_T$ is between the inflow pressure, $P_A$, and the outflow pressure, $P_V$, a region of partial collapse occurs at the outflow end. **Middle:** Graph of flow as a function of $P_A$ in this system. The line at the left results when $P_T = 0$ and the line at the right results when $P_T = 1$. **Bottom:** Electrical analogue of this system. The voltage, $V_A$, is analogous to $P_A$, and $V_T$ is analogous to $P_T$. Current in the circuit is analogous to fluid flow in the model.

To see if this model is quantitatively predictive, however, two more refinements were included. These are presented in Figure 3. First, since intramyocardial tissue pressure varies not only with depth but also with time, local battery voltage must be calculated as some fraction of ventricular pressure at any given moment. Leg 1 to the right represents an epicardial channel in which the tissue pressure coefficient, $1/N$, is near zero. The coefficient increases linearly until it reaches 1 at the Nth line is shifted to the right of the broken line by an amount equal to the average of the battery voltages. If the resistances are not of equal value, however, the shift becomes a resistance-weighted average.

the slope. The bottom section of Figure 1 shows an electrical analogue of this system. The battery and the diode prevent current flow until $V_A$ (analogous to $P_A$) exceeds the battery voltage, $V_T$ (analogous to $P_T$).

The model just described, however, is too simple to apply to the heart, since cardiac tissue pressure varies with depth in the tissue (8–11). Consider, therefore, the more complex model in Figure 2. In the top section, coronary vessels at various depths in the heart wall are represented by parallel legs in the circuit. The top leg, A, represents one near the endocardium, and the bottom leg represents one near the epicardium. Battery voltage increases with myocardial depth to simulate the gradient of intramyocardial pressure across the heart wall. In the center section, individual leg currents are plotted against $V_A$. The intercept is different for each leg, since the battery voltages are different. The solid line in the bottom section shows the sum of these currents. When $V_A$ is above the highest battery voltage, the function is linear. Below 90 v however the line curves toward the left as the current in individual legs drops to zero. If all of the battery voltages are reduced to zero, the broken line at the left results. Notice that this line is parallel to the solid line in the range in which $V_A$ exceeds the highest battery voltage. In this case, the linear portion of the solid

**FIGURE 1**

**FIGURE 2**
T-tube was placed in the thoracic aorta, and tubing was passed from the side arm of the T-tube to an elevated reservoir. During data collection, the distal aortic segment was clamped as shown to increase the volume of blood in the reservoir. Thus, mean aortic pressure could be held constant, even when the heart was briefly stopped. A branch from the reservoir passed through the fingers of a Sigmmamotor model T8 peristaltic pump to a cannulated branch of the left anterior descending coronary artery. Pullations created by the pump were damped by an air-filled buffer in the perfusion line. Adenosine in saline was infused into the perfusate at 1.6 mg/min to keep the vessels maximally dilated. Flow was monitored by a Statham K2000 flowmeter recording from an In Vivo Metrics cannulating type of probe in the perfusion circuit. Perfusion pressure was measured from a branch between the pump and the cannula. A stiff vinyl catheter was advanced through a carotid artery into the left ventricle to obtain a ventricular pressure record. Finally, stimulating electrodes were placed distal to crushed segments on both vagi. By repetitive supramaximal stimulation, an asystole of 5-7 seconds could be obtained in most dogs.

The experimental protocol was as follows. While the segment was perfused at a constant rate with the Sigmmamotor pump, the vagi were stimulated and the heart stopped for 5-7 seconds. The perfusion pressure and the setting on the pump before and during arrest were noted. This procedure was repeated over a wide range of flows. In several dogs fluorescein dye was injected into the perfusate at the end of the experiment, and the heart, on removal, was sectioned and examined to verify that the entire thickness of the ventricular wall had been perfused.

After each experiment, the pump was calibrated by pumping blood through the perfusion line and timing the filling of a volumetric flask. This procedure was carried out for all settings used in the experiment. The Sigmmamotor pump had a 15-turn vernier dial, and flows were reproducible to within 2%. At the same time, the pressure drop across the cannula was noted for each flow rate. This pressure drop was subtracted from the measured perfusion pressure to give perfusion pressure distal to the cannula. These calibrations then made it possible to plot perfusion pressure (distal to the cannula) against coronary blood flow for both the beating and the arrested state in each experiment.

**Results**

**Theoretical Model**

Solutions to the equations generated by the model appear in Figure 5; coronary blood flow appears on the vertical axis and perfusion pressure on the horizontal axis. When peak ventricular and aortic pressures were specified at 90 mm Hg and K at 1 and the collateral resistance was ten times the vascular resistance, the line to the right resulted. Notice that this curve exhibits the same features as those predicted by the basic model in Figure 2. It is linear in the range above the highest tissue pressure, which in this case is equal to ventricular pressure since K = 1. Below this point it curves to the left. The line at the left results when all tissue
pressures are zero over the entire cardiac cycle. Notice that it is linear and has the same slope as the linear portion of the right curve. The separation between the linear segments in Figure 5 is 23 mm Hg.

The effect of the collateral circulation is to prevent the pressure-flow curves from going through the origin. At zero flow, the distal vasculature is entirely supplied by the collateral vessels, and a positive perfusion pressure is recorded. A change in tissue pressure still affects this back-pressure. At zero perfusion pressure, all of the collateral flow passes retrograde into the perfusion apparatus and none passes forward through the distal vessels. Therefore, a change in tissue pressure does not affect this perfusion pressure. Thus, the lines converge at zero perfusion pressure.

ANIMAL EXPERIMENTS

Records from a typical experiment appear in Figure 6. Coronary flow rate was held constant by the peristaltic pump. When the heart was briefly arrested by vagal stimulation, indicated by the gaps in the ventricular pressure record, coronary perfusion pressure fell. Since the coronary vasculature was already dilated to the maximum by

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adrenosine, the reduced coronary resistance was interpreted to be the result of reduced tissue pressure compressing the coronary vessels. The drop in pressure increased as a function of the prearrest perfusion pressure. The return to the prearrest perfusion pressure in these records was delayed due to a transient period of bradycardia that reduced the time spent in systole and thus the degree of vascular compression. The flowmeter record indicates that, with arrest, flow transiently increased (due to a change in the volume of the buffer) but returned to the prearrest value before the heart beat resumed.

When perfusion pressure (measured at the time when flow had returned to the prearrest level and corrected for the drop across the cannula) is plotted against flow, the graph in Figure 7 results; the right line connects the prearrest points and the left line the arrested points. When the heart is arrested, tissue pressures are thought to be minimized (1). Over the entire range of perfusion pressures, the left line appears to be linear as predicted by the model when tissue pressures are set equal to zero (Fig. 5). This finding was consistent in all six dogs studied. The line to the right in Figure 7 resulted when the heart was beating, and its shift to the right was, therefore, the result of tissue pressure within the heart compressing the coronary vessels. In the range of pressures above about 100 mm Hg, it also was linear. Below 100 mm Hg, it curved to the left. The linear portion was parallel to the line obtained during arrest. This curve exhibits the same essential features as does that generated by the model in Figure 5, that is, a linear segment at high pressures and a curved segment at lower pressures. These features are best observed when the fall in perfusion pressure with arrest is plotted as a function of the prearrest perfusion pressure as is done in Figure 8.

In Figure 8 the data from all six experiments are presented. The separation between the two curves varied considerably, 25 to 40 mm Hg, from experiment to experiment. Because, at this point our interest was only in the shape of the curves, specifically where the transition point from linear to nonlinear occurred, the pressure drop data were normalized to account for the differences in separation. Normalization was accomplished by dividing

*INHIBITION OF CORONARY BLOOD FLOW*

**FIGURE 6**

Effect of asystole at several flow rates. In these records coronary flow was held constant with the pump, and the heart was momentarily arrested as indicated by the gaps in the ventricular pressure record. The pump speed is different for each section of the figure as indicated by the flow record. Notice that perfusion pressure dropped less when the flow rate was low than it did when the flow rate was high.
Peak ventricular pressure ranged between 75 and 105 mm Hg, and at perfusion pressures beyond this range the function appeared to be horizontal indicating that the two pressure-flow curves were parallel in this range. Below 100 mm Hg, the function broke toward the origin, indicating a diminishing pressure drop and revealing that the two pressure-flow curves were converging at lower pressures. The model clearly showed that this break occurred at the highest tissue pressure in the system. The break was consistently found to be at a perfusion pressure near the peak ventricular pressure. Thus, the tissue pressure coefficient, K, must have a value near 1. The solid line in Figure 8 indicates the relationship predicted by the model for a K value of 1.

In all of the dogs the following features were consistently observed. (1) The pressure-flow relationship obtained during arrest was linear over its entire length. (2) The pressure-flow relationship obtained while the heart was beating appeared to be linear and parallel to the arrested line in the range of pressures above peak ventricular pressure and nonlinear in the range below. Although there is a certain degree of uncertainty associated with the determination of absolute flow rates in these experiments, the parallelism of the two linear segments can be determined with considerable precision. The points were collected under constant flow conditions, so that, if the pressure drop on arrest is equal for successive points, then the lines must be parallel in that region. The separation between the linear portions of the curves averaged 31 mm Hg (range 25 to 40 mm Hg).

**Discussion**

A linear pressure-flow relationship was observed for the maximally dilated coronary artery under conditions of minimal tissue pressure (asystole). A linear pressure-flow relationship has been reported for other maximally dilated beds as well. Green and co-workers (14) have reported that flow is a logarithmic function of pressure in the hind limb with the logarithmic slope proportional to the vascular tone. As maximal dilation is approached, however, the logarithmic slope approaches unity, resulting in a linear pressure-flow relationship (14). Levy and Share (15) have also reported a linear pressure-flow relationship for the maximally dilated hind limb; moreover, they have found that linearity is not affected by varying the hematocrit from 2.5 to 73.8%. It seems to be a basic property of vascular beds, including the coronary system, that...
they behave as rigid indistensible tubes when they are maximally dilated.

The effect of contraction in the heart is to shift the pressure-flow curve to the right. Basically two mechanisms could result in this modification. One possible mechanism involves the creation of vascular waterfalls where the segments downstream from the major resistance are partially collapsed by local tissue pressure; the other possible mechanism involves other alterations in the dimensions of the resistance vessels by pinching, kinking, etc. These two processes are not mutually exclusive, and obviously both could occur in the same bed. The relative contribution of each process can be assessed, however, from the pressure-flow curves that we have presented. If resistance changes not associated with vascular waterfalls are involved, the slope of the linear segment would be altered. But, because the linear segment obtained from the beating state was parallel to that obtained during arrest, it appears that only vascular waterfalls as described by the model are actually occurring.

A key feature of the waterfall mechanism is that a partial collapse occurs at the distal end of the segment as it exits the region of high surrounding pressure. Because of the unusual anatomy of the heart, it is necessary to hypothesize the site of the partial collapse. The arteries course over the epicardial surface sending branches perpendicularly into the underlying myocardium (16). The pressure surrounding these vessels increases with myocardial depth. These vessels reach their deepest point at the capillaries, whereupon they return toward the epicardium as veins. The ascending veins, being distal to most of the vessel’s resistance and being a passage toward lower tissue pressures in the overlying tissues, probably are the site of partial collapse. If this assumption is correct, then the entire ascending segment should be in a state of partial collapse with the pressure in the vein at each level being in equilibrium with the local surrounding pressure. A large volume of venous blood would be expelled as these veins collapse. This phenomenon could explain why the coronary sinus blood flow is highest during systole (17).

The present experiments were conducted on a section of myocardium in which the vasculature was dilated to the maximum, but the effect of tissue pressure on vessels with tone, as are present in the normal heart, should be similar, since, with a waterfall mechanism, flow remains proportional to perfusion pressure minus tissue pressure regardless of tone (7). Vasomotion could alter the critical closing pressure of the coronary vessels, which should be additive to tissue pressure effects in such a waterfall system. This change, however, would only tend to shift the pressure-flow curves in Figure 7 to the right as a pair and should not affect the spacing between them. This hypothesis is supported by the observation that the ratio between coronary inflow rate during systole and diastole does not significantly change when the coronary vessels are caused to dilate (18). Furthermore, when coronary tone is present, the fall in perfusion pressure which accompanies arrest is similar to that when the vessels are maximally dilated (unpublished observation).

Before the present data can be extrapolated to the normal heart, it must be determined if the perfused segment was functioning normally. In the present experiment contractile activity was not measured, but in a previous experiment using similar methodology an isometric force gauge was attached in the field of the perfused branch. In these experiments contractile force was maintained when maximal dilation was effected with adenosine infusion (19). Also, since the vessels were dilated, flow did not fall below normal except at perfusion pressures of 50 mm Hg or less so that it is not likely that the segments were ischemically depressed.

Although the experimentally derived pressure-flow curves exhibit many of the same features as do the theoretical curves, they differ in one important respect: the separation between the lines representing the beating and the arrested states was greater for all of the experimental curves. The degree to which systole should shift the pressure-flow curve to the right is determined by several factors. The distribution of the coronary vessels within the tissue pressure field is critical. The model assumes a section of tissue with vessels uniformly distributed at all depths. In several hearts in which dye was injected into the perfusate when the experiment was terminated, a keystone-shaped perfusion field was observed in which the broad edge of the keystone was against the endocardium. Thus, a greater percent of the perfused vessels probably resided nearer the endocardium, where compression is greatest, than was assumed by the model. For the sake of simplicity, a linear distribution of tissue pressure was assumed to exist across the heart wall since such a distribution is compatible with the available data (2, 9-11). Tissue pressure may decrease from endocardium to epicardium more gradually than the linear gradient assumed for the model, resulting in a greater tissue pressure at any depth. This effect could also enhance the

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separation between the beating and the arrested curves. The shape of the theoretical curve in Figure 8 is determined by the distribution of the vessels within the tissue pressure field. A misestimate of this distribution with the vessel population distributed toward lower pressures would elevate the leftmost portion of the curve. Because most of the experimental points fall below the theoretical line in this region, it would appear that the most likely source of the discrepancy lies in a misestimate of this distribution.

A similar situation also existed in choosing a time course for the tissue pressure. Data from direct measurements indicate that it is similar to that for the ventricular pressure (10, 11). Also it has been suggested that the radially oriented stress in equilibrium with the ventricular pressure predominates in the heart wall (4). This stress would have a time course identical with ventricular pressure as was employed in the model. Nevertheless, it is possible that some compression, perhaps related to shortening, persists longer than the ventricular pressure. Such compression could augment the effect of systole on flow.

The model predicts that the pressure-flow curve from the beating heart will break at the perfusion pressure which equals the highest tissue pressure in the system. Our data consistently showed a break point at a perfusion pressure that was nearly equal to peak ventricular pressure. Thus, if tissue pressures in excess of peak ventricular pressure existed in the section of myocardium which we were perfusing, they either did not involve much tissue or they were present for a very short portion of the cardiac cycle. Interestingly, most studies in which a measuring device has been inserted directly into the beating myocardium report pressures well in excess of peak ventricular pressure (8–10). Brandi and McGregor (11), however, have demonstrated that a foreign body in the myocardium experiences a pressure which is proportional to its size. Therefore, the direct measurements may be artifactually high, thus explaining the apparent discrepancy with the present data. Alternatively, the coronary vessels may be so arranged within the structure of the myocardium that they are not fully exposed to the compressive stresses which are present.

The experimental and theoretical results indicate that systole impedes coronary blood flow primarily through the formation of vascular waterfalls and that the intramyocardial pressures which create these waterfalls do not significantly exceed peak ventricular pressure.

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