Effect of Left Ventricular Hypertension, Ischemia and Vasoactive Drugs on the Myocardial Distribution of Coronary Flow

By Thomas W. Moir, M.D., and Don W. DeBra, M.D.

ABSTRACT

Distribution of coronary flow to the inner and outer layers of the left ventricle of the anesthetized, open chest dog was estimated by the myocardial uptake of \(^{86}\)Rb chloride infused into the cannulated common left coronary artery. With normal relationship of coronary perfusion pressure and left intraventricular pressure, there was no significant underperfusion of the endocardium. When left intraventricular pressure was raised and coronary perfusion pressure was held at levels sufficient to provide normal coronary flow, endocardial distribution remained equal to or slightly greater than that to the epicardium. However, when coronary perfusion pressure was lowered, particularly to levels causing obvious signs of myocardial hypoxia, maintenance of a normal left intraventricular pressure resulted in marked underperfusion of the endocardium. The coronary vasoactive drugs, dipyridamole, norepinephrine, vasopressin, and the \(\beta\)-adrenergic receptor blocking agent, propranolol, increased the flow distribution to the endocardium of both the normotensive and hypertensive left ventricle. It is concluded that the systolic tissue pressure which increases from epicardium to endocardium does not cause significant underperfusion of the endocardium in either the normotensive or hypertensive left ventricle as long as normal coronary perfusion pressure and flow are maintained.

ADDITIONAL KEY WORDS

systolic tissue pressure gradient
epicardial flow diastolic coronary resistance coronary perfusion pressure endocardial flow \(^{86}\)rubidium dipyridamole norepinephrine vasopressin propranolol anesthetized dog

From the Department of Medicine, School of Medicine, Western Reserve University, Cleveland, Ohio. This work was supported by Public Health Service Research Grant 5 P01 HE 08304 from the National Heart Institute. Dr. Moir is a Markle Scholar in Academic Medicine. Accepted for publication April 27, 1967.
The purpose of the present study was the estimation of endocardial distribution of common left coronary flow under a variety of conditions of coronary perfusion pressure, left intraventricular pressure, myocardial ischemia and after administration of coronary vasodilator drugs, using as an index the myocardial uptake of \(^{86}\)Rb chloride infused directly into the common left coronary artery. With this method of infusion, excessively high concentrations of \(^{86}\)Rb in the left ventricular cavity were avoided and distribution studies were done after subsidence of the reactive hyperemia of cannulation.

**Methods**

Fifty-six mongrel dogs weighing between 18 and 22 kg were anesthetized with morphine (1 mg/kg sc) and pentobarbital (20 mg/kg iv) and positive pressure breathing was established through an occlusive intratracheal tube. After the left chest was opened and the pericardium incised, heparin (10 mg/kg) was given and the left jugular vein and left common carotid artery were cannulated. The common left coronary artery was cannulated through its aortic ostium via the left subclavian artery and perfused through a recording rotameter from an air-presurized blood reservoir. The reservoir was kept filled with blood delivered from the left carotid artery by a pump. Left coronary perfusion pressure could be held constant at any desired level independent of aortic pressure by appropriate setting of the air pressure in this chamber. The right coronary artery was perfused from the aorta.

The thoracic aorta was then ligated and the proximal portion cannulated and allowed to bleed into a similar air-presurized blood reservoir so that aortic pressure could also be held at any desired level independent of left coronary perfusion pressure.

Mean left coronary perfusion pressure, mean aortic pressure, and phasic left intraventricular pressure were continuously monitored by pressure transducers and recorded, together with the rotameter flow curve, on an electronic recorder. An electrocardiogram was recorded by a direct writing electrocardiograph.

With these arrangements the distribution of the common left coronary flow was studied under four pressure-flow conditions in different groups of dogs:

1. **Normal**: normal perfusion pressure in the common left coronary artery, normal coronary flow, normal left intraventricular pressure, normal ECG.
2. **Hypertension**: normal coronary perfusion pressure, high coronary flow, high left intraventricular systolic pressure, normal left intraventricular diastolic pressure, normal ECG.
3. **Ischemia**: low coronary perfusion pressure, low coronary flow, normal left intraventricular systolic pressure, elevated left intraventricular diastolic pressure, ischemic ECG changes.
4. **Low CP**: low coronary perfusion pressure, low coronary flow, normal left intraventricular pressure, normal ECG.

In four additional groups of dogs, the effect of dipyridamole\(^1\) (10 to 20 mg instantaneously iv), vasopressin (Pitressin) (0.1 pressor units/kg per min infused continuously into the coronary artery), norepinephrine (1 \(\mu\)g/kg per min infused continuously iv), and propranolol\(^2\) (0.5 mg/kg instantaneously iv) on the distribution of coronary flow in both the normotensive and hypertensive left ventricle was also studied.

In these latter groups of animals, and in groups 2, 3, and 4 above, control common left coronary flow rates were obtained before administration of the drugs or alteration of the pressure-flow conditions. Bilateral cervical vagotomy was done in half of the dogs in which left ventricular pressure was raised by increasing aortic pressure.

When the conditions of the study were established, 20 \(\mu\)c of \(^{86}\)Rb chloride mixed in arterial blood was infused at a constant rate into the common left coronary artery cannula tubing proximal to the rotameter for a period of exactly 2 min. At the end of the infusion period, the heart was electrically fibrillated, immediately excised, washed, and blotted dry. Ten full thickness biopsy specimens were obtained from the free wall of the left ventricle and the interventricular septum, divided into inner and outer halves, and weighed in previously tared plastic tubes on an analytical balance. These specimens were then assayed for radioactivity in a scintillation counter at counting rates sufficient to ensure a counting error of less than 2%. The uptake of \(^{86}\)Rb was expressed as counts per minute per gram of myocardium and used as an index of the distribution of the metered common left coronary flow to the endocardium and epicardium. A comparison of the distribution of blood flow to these two areas was made by the ratio of uptake, the

---

\(^1\)Persantin, kindly supplied by Geigy Pharmaceuticals.

\(^2\)Inderal, kindly supplied by Alex Sahagian-Edward, M.D., Ayerst Laboratories.
CORONARY FLOW AND VENTRICULAR PRESSURE

<table>
<thead>
<tr>
<th>NO. OF DOGS</th>
<th>Normal</th>
<th>Hypertension</th>
<th>Ischemia</th>
<th>Low Cor. Pr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Observ.</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Aortic Pr. (mmHg)</td>
<td>113</td>
<td>160</td>
<td>105</td>
<td>104</td>
</tr>
<tr>
<td>Cor. Pr. (mmHg)</td>
<td>113</td>
<td>105</td>
<td>41</td>
<td>56</td>
</tr>
<tr>
<td>L.V. Pr. (mmHg)</td>
<td>128/3</td>
<td>208/8</td>
<td>125/15</td>
<td>125/6</td>
</tr>
<tr>
<td>Cor. Flow (ml/100g/min)</td>
<td>86</td>
<td>101</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

**Figure 1**

Left ventricular endocardium: epicardium (I:O) uptake under different conditions of coronary perfusion and left ventricular pressures. Aortic and coronary (Cor.) pressure (Pr.) = average mean pressure; L.V. Pr. = left ventricular systolic and diastolic pressures; Cor. flow = common left coronary artery flow. Bar in graph = mean I:O uptake; vertical lines = ± 1 SD.

$I:O$ ratio, where $I = \text{counts per minute per gram in the endocardial specimen}$ and $O = \text{counts per minute per gram in the epicardial specimen}$.

Immediately after the heart was electrically fibrillated, a blood sample was obtained from the left ventricular cavity and the $^{85}$Rb concentration measured. Aliquots of blood were also obtained from the coronary arterial cannula tubing for determination of the coronary arterial concentration of the isotope.

Left ventricular weight was determined by excision of the left ventricular mass prior to the biopsy specimens and the common left coronary artery flow rates obtained by the rotameter were expressed as milliliters per 100 g per minute.

**Results**

The ratios of radioactive uptake in the endocardial (I) and the epicardial (O) halves of the left ventricles of the animals in the four study groups in which pressure-flow conditions were changed are illustrated in Figure 1.

In those animals in which a normal relationship of coronary perfusion pressure and left ventricular pressure was maintained, the I-O ratio of 0.94 is suggestive of some underper-

fusion of the endocardium but the deviation from unity is not significant ($P>0.05$). The average common left coronary flow measured by the rotameter was 86 ml/100 g per min in this group. The electrocardiogram and left ventricular pressure pulse showed no evidence of deterioration during the period of study.

In those animals in which coronary perfusion pressure was held at a normal level while left ventricular hypertension was produced by raising aortic pressure, the I-O ratio of 1.07 is compatible with maintenance of normal distribution of forward coronary flow to the endocardium. In fact, the I-O ratio is suggestive of an increased flow to the endocardium under these conditions; although the deviation from unity is not significant ($P>0.05$), the average I-O ratio in this group differed significantly ($P<0.05$) from the normal study group. The increased cardiac work incident to the rise in aortic pressure resulted in an average metered common left flow of 101 ml/100 g per min, an average increase of 25% over control flows. There was no evidence of deterioration of left ventricular function reflected in either the electrocardiogram or the left ventricular pressure pulse. The average left ventricular pressure in this group was 208/8 (range 180/8 to 228/6). In non-vagotomized animals, slowing of the heart rate was observed when the aortic pressure was raised to produce left ventricular hypertension. However, no difference in I-O uptake ratios was noted between these animals and those in whom vagotomy prevented the reflex bradycardia.

In the group in which ischemia was produced by lowering the coronary perfusion pressure while left ventricular systolic pressure was held constant by maintenance of a normal aortic pressure, the I-O ratio of 0.28 reflects a markedly decreased flow in the endocardium. The deviation from unity was highly significant ($P<0.005$). The average common left coronary flow in these animals was 48 ml/100 g per min, a 42% decrease over their control flow. This reduction of flow was associated with marked electrocardiographic
ST-T wave changes of subendocardial ischemia, decrease in the rate of rise of the left ventricular pressure pulse, and a rise in left ventricular end-diastolic pressure. The average left ventricular pressure in this group was 125/15 (range 120/13 to 130/18).

In the final group of animals illustrated in Figure 1, the low CP group, coronary perfusion pressure was reduced less drastically than in the ischemic group; the average common left coronary flow was 60 ml/100 g per min, a rate which was only 10% less than their control. Although the ratios of these animals segregated statistically into two groups of 3 each, the average I-O ratio of each (0.84 and 0.39) was significantly less than unity \( P < 0.01 \) and \( P < 0.005 \). The ECG remained unchanged and there was no evidence of left ventricular deterioration reflected in the ventricular pressure pulse. Nonetheless, the uptake ratio reflects significant underperfusion of the endocardium.

Figures 2 and 3 illustrate the \(^{86}\)Rb uptake ratios obtained after the administration of various vasoactive drugs. With each drug the I-O ratios were obtained after pretreatment under normal pressure-flow conditions and then, in different dogs, with left ventricular hypertension and maintenance of normal coronary perfusion pressure.

The effects of dipyridamole and norepinephrine on the myocardial distribution of flow are shown in Figure 2. In the normotensive animals, the I-O ratio of 1.15 after dipyridamole was not significantly different from unity \( P > 0.05 \) but was significantly greater than that of the normal group \( P < 0.025 \) illustrated in Figure 1. The common left coronary flow of 115 ml/100 g per min represented an 81% increase over control flows. In the hypertensive animals, dipyridamole caused a significant increase in perfusion of the endocardium as indicated by the I-O ratio of 1.19, a figure both significantly different from unity \( P < 0.05 \) and from the normal group of Figure 1 \( P < 0.01 \). The coronary flow rate of 157 ml/100 g per min represents a 120% increase over control rates. In both of these dipyridamole groups, the ECG and left ventricular pressure pulses showed no evidence of myocardial deterioration.

As further illustrated in Figure 2, when norepinephrine was administered and the coronary perfusion pressure was adjusted so that it equaled the aortic pressure induced by the drug, a mean uptake ratio of 1.04 was obtained, a value not significantly different from unity \( P > 0.05 \) or from the previously described normal group. The coronary flow rate of 146 ml/100 g per min represents a 64% increase over the control flow in this group. In the animals in which
CORONARY FLOW AND VENTRICULAR PRESSURE

Coronary perfusion was held at normal levels while the aortic pressure and, consequently, the left ventricular pressure were elevated as a result of the norepinephrine infusion, the I-O ratio of 1.12 was significantly different from unity \((P < 0.05)\) and indicates a greater distribution of coronary flow to the inner half of the hypertensive left ventricle under these conditions. The coronary flow of 134 ml/100 g per min represents a 50% increase over the control rate in this group. The ECG and left ventricular pressure pulse showed no evidence of myocardial deterioration in either of the norepinephrine groups.

In Figure 3 similar plots of \(^{86}\)Rb uptake ratios are shown for the vasopressin and propranolol groups. In the normotensive ventricle of the vasopressin group, the coronary flow of 104 ml/100 g per min represents a 15% decrease in flow rate over the average, predrug control values. The I-O ratio of 1.07 is borderline significantly greater than unity \((0.10 > P > 0.05)\). A similarly borderline deviation from unity of the mean uptake ratio of 1.09 was found in the vasopressin group with left ventricular hypertension. In both groups the I-O ratios were significantly greater than the normal group. In the hypertensive animals, the average coronary flow of 99 ml/100 g per min was only 4% greater than the flow rates measured during the vasopressin infusion prior to induction of hypertension. Variable T-wave abnormalities were noted in the ECG during the vasopressin infusion in both of the vasopressin groups, although the left ventricular pressure pulses showed no evidence of deterioration.

As shown in Figure 3, after \(\beta\)-adrenergic receptor blockade by propranolol, the I-O ratio in the normotensive group was 1.23, a significant deviation from unity \((P < 0.01)\). The coronary flow of 79 ml/100 g per min represents a 36% decrease from the predrug control rate. In those animals in which left ventricular hypertension was induced after \(\beta\)-receptor blockade, the I-O ratio was also significantly greater than unity \((P < 0.01)\). In spite of the \(\beta\)-receptor blockade, the coronary flow rate rose to an average of 123 ml/100 g per min, a 21% increase over the predrug control rate. In both propranolol groups, \(\beta\)-receptor blockade produced a reduction in heart rate, decrease in the rate of rise of the left ventricular pressure pulse, and in the hypertensive group, deterioration of left ventricular function as manifested by rise of the end-diastolic pressure.

The average concentration of \(^{86}\)Rb in the left ventricular blood sample obtained in each animal immediately after fibrillation was expressed as a percent of the average concentration of the isotope in simultaneously obtained coronary arterial blood. This ratio varied among the study groups as shown in Table 1. In the normal, left ventricular hypertension, ischemia, low CP, and norepinephrine study groups, the average concentrations of \(^{86}\)Rb in the intracavitary blood was similar and ranged from 0 to 7% of the average coronary arterial concentration. However, in those animals treated with dipyridamole, vasopressin, and propranolol, the average concentration was higher and the range much wider, 4 to 22%. Consequently, this latter group was further analyzed as to the relationship of the intracavitary \(^{86}\)Rb concentration and the I-O ratio of myocardial isotope concentration. In those animals with I-O ratios of less than 1.0, the average concentration of \(^{86}\)Rb in the left ventricular blood sample averaged 13.0 ± 6.8% of the average coronary arterial concentration, while in animals of those groups with I-O ratios greater than 1.0, this figure was 9 ± 4.5%. These figures were not significantly different from each other.

Discussion

The primary purpose of this study was the assessment of the degree to which the intramyocardial systolic tissue pressure gradient impeded the distribution of coronary flow to the inner half of the left ventricle under normal pressure-flow conditions and also under circumstances which would be expected to increase the resistance to systolic flow, namely, low coronary perfusion pressure with normal left ventricular pressure and normal coronary perfusion pressure with left ventricular hypertension. Based on previous
studies (3), it was necessary to investigate the myocardial distribution of coronary flow under these conditions by methods which obviated reactive hyperemia at the time of the $^{86}$Rb infusion and which reduced the opportunity for the isotope to diffuse from the left ventricular cavity to the endocardium. Both conditions were met by the method of coronary artery infusion of $^{86}$Rb which permitted isotope infusion after subsidence of the reactive hyperemia of cannulation and which, by virtue of the high extraction rate of $^{86}$Rb by the myocardium, prevented high concentrations of isotope in the left ventricular cavity. Although the concentrations of $^{86}$Rb in left ventricular blood were variable and highest under those conditions in which the flow rate would be expected to limit myocardial extractions (9), there was no correlation between the intracavitary concentration of the isotope and the endocardial uptake as judged by the I-O ratio of intramyocardial radioactive contents. Thus, changes in the I-O uptake ratios of this study were believed to represent changes in the distribution of coronary blood flow incident to the pressure-flow conditions established prior to the infusion of the isotope.

Although Conn has questioned the accuracy of estimates of coronary blood flow rates by the $^{86}$Rb chloride method, particularly under conditions of myocardial hypoxia (8), we have recently reported a comparison of common left coronary flow rates measured by the rotameter and by the $^{86}$Rb clearance method (9). Although the $^{86}$Rb clearance method underestimated metered coronary flow at all levels of coronary perfusion pressure and flow rates, it gave correct directional changes of flow in all animals including those in which myocardial ischemia was manifested by electrocardiographic and ventricular pressure pulse abnormalities (9). In the present study we have used the myocardial uptake of $^{86}$Rb as a directional index of distribution of common left flow rather than as a measurement of flow rate. The latter was measured by the rotameter.

Although the mean I-O uptake ratios in the animals with a normal relationship of coronary perfusion pressure and left ventricular pressure suggested some underperfusion of the inner layers of the myocardium, the difference was not statistically significant. This differs from our previous study of the endocardial distribution of flow of the left circumflex
Coronary Flow and Ventricular Pressure

artery in which a small, but statistically significant, decrease in $^{86}$Rb uptake by the endocardium was found (3). The reasons for the difference in the significance of the I-O ratios in these two normal pressure groups is not known, but there were differences in technique. In the first study, the left circumflex artery alone was cannulated and the coronary sinus was bled during the period of isotope infusion; in the present study, the total common left coronary artery was cannulated and the coronary sinus was intact. What effect these differences had on the myocardial distribution of flow is unknown, but it should be pointed out that the differences between the I-O ratios of the two experiments are not markedly different, 0.89 for the previous study, 0.94 for the present, and that if inequality of distribution of flow to the endocardium and epicardium under normal pressure-flow conditions is present, it is not very great.

Recently, Kirk and Honig have reported data showing striking nonuniformity of distribution of intramyocardial coronary flow in the normotensive left ventricle which they believe is due to the effect of the intramyocardial tissue pressure gradient (10). Using both the $^{131}$NaI depot clearance method and the platinum cathode measurement of oxygen tension, they have reported that coronary flow in the endocardium was 25% less than in the epicardium and that there was a consequent gradient in oxygen tension in the myocardium, with the tension in the endocardium one-half that in the epicardium. From their data they have postulated the possibility of anaerobic metabolism in the endocardial layers of the left ventricle, particularly under "conditions of stress." As noted, the present study and those of others show no significant endocardial underperfusion in the normotensive left ventricle as measured by the $^{86}$Rb method.

At present there is no explanation of the difference between the two methods but the limitations of the tissue clearance method have been described (11, 12). In particular, Salisbury showed that there was no correlation between coronary flow and the rate of isotope removal from the myocardium of the beating dog heart (12). Possible conditions that limit tissue isotope clearance as an index of coronary flow include local edema and hemorrhage from the injection, local vasmotion, and the leakage of isotope up the needle track. Against the $^{86}$Rb method it might be argued that since myocardial extraction of the isotope is inversely related to the coronary flow rate (9), endocardial uptake will be high relative to epicardial uptake in situations where endocardial flow is lower than epicardial flow. However, this possibility as a source of error in the $^{86}$Rb method seems unlikely in view of the uptake data in the animals with myocardial ischemia in which electrocardiographic signs of subendocardial ischemia, presumably due to a decrease in coronary flow in the endocardium more marked than in the epicardium, were associated with a markedly decreased uptake of isotope by the inner layers of the myocardium. Based on these data and other studies (9), we believe the $^{86}$Rb method as used in the present study gives an accurate estimate of directional change in forward coronary flow.

If there were significant endocardial underperfusion in the normotensive ventricle, left ventricular hypertension would be expected to further impede endocardial flow. However, in the group of animals in which left ventricular hypertension was produced and a normal coronary perfusion was maintained, there was no evidence of underperfusion of the endocardium as judged by a normal, or slightly greater than normal, uptake of $^{86}$Rb. On the other hand, in those animals in which coronary perfusion pressure was lowered with a resultant decrease in coronary flow, a normally maintained left ventricular pressure caused a marked decrease in endocardial uptake of $^{86}$Rb and reflects a decrease in distribution of coronary flow to the endocardium under these conditions. These myocardial uptake studies correlate well with the physiologic and electrocardiographic studies of Salisbury et al., in which heart failure was pro-
duced either by lowering coronary perfusion pressure with maintenance of a normal aortic pressure, or by volume overload of the left ventricle with a normally maintained coronary perfusion pressure (13). In the first instance, heart failure as judged by an elevated end-diastolic left ventricular pressure was associated with ECG evidence of marked subendocardial ischemia together with other physiologic signs of myocardial hypoxia. In the second situation, where heart failure was produced by volume overload of the left ventricle, there was no evidence of subendocardial ischemia when coronary perfusion pressure was maintained within a normal range (100 mm Hg) even though mean aortic pressure rose as high as 200 mm Hg. We believe, therefore, that there is sufficient evidence from several methods of assessing endocardial coronary flow that the levels of coronary perfusion pressure and flow are the primary determinants of the adequacy of such flow rather than the intramyocardial tissue pressure gradient.

While our data confirm the results of Cutarelli and Levy regarding the adequacy of endocardial perfusion in both the normotensive and hypertensive left ventricle, it suggests a different explanation than theirs of the mechanism by which endocardial flow is maintained in the face of the intramyocardial tissue pressure gradient. They hypothesized that increases in intracavitary left ventricular pressure and the resultant intramyocardial tissue pressure would restrict endocardial perfusion only in areas of left ventricular myocardium which were nonbeating. In our ischemic group of animals in which marked underperfusion of the endocardium was demonstrated, there was clear evidence of abnormal myocardial function as judged by the left ventricular pressure pulses. However, the finding of a similar endocardial underperfusion in the low coronary perfusion pressure group of dogs in which there was no evidence of functional deterioration suggests that the low coronary perfusion pressure and coronary flow are the more important features. From these data we hypothesize a gradient in diastolic coronary flow which parallels the systolic tissue pressure gradient between epicardium and endocardium. Although systolic coronary flow is less in the endocardium than the epicardium, diastolic coronary flow is greater in the former than the latter as the result of a transmural gradient in diastolic coronary vascular resistance. This resistance gradient, in turn, is viewed as a response to the decrease in endocardial coronary flow during ventricular systole causing endocardial vessels to dilate more than those in the epicardium during diastole. When vasodilatation is induced maximally in the total myocardial vascular bed in response to ischemia, the differential in transmural diastolic coronary resistance is lost and the endocardium is underperfused because of the now uncompensated gradient in systolic coronary flow. Thus, in both the normotensive and the hypertensive ventricles the critical feature for maintenance of endocardial perfusion is the adequacy of coronary perfusion pressure and coronary blood flow.

The types of coronary vessels involved in our hypothesis are, of course, unknown but would seem most reasonably to be those capable of vasomotion. Although arteriolar vessels may predominate in such a transmural vasomotor gradient, there is evidence that the coronary capillary bed may be a feature in the maintenance of endocardial perfusion. Myers and Honig have demonstrated a vascularity gradient increasing from epicardium to endocardium in the normotensive canine left ventricle, and have calculated that this is primarily a difference in capillarity (14). Additionally, the study of Provenza and Scherlis in which precapillary sphincters were demonstrated in the myocardium suggests that the intramyocardial distribution of coronary flow may be, in part, the result of differences in myocardial capillarity which, in turn, might be controlled by vasomotion (15). More recently Fulton (16) and Estes et al. (17) have shown in post-mortem injection studies in the human heart that the endocardium is perfused via arterial vessels which are distinct from the vessels which perfuse the epi-
CORONARY FLOW AND VENTRICULAR PRESSURE

Indeed, Fulton has postulated that this subendocardial blood vessel plexus may serve as a "reservoir" for retrograde perfusion of more superficial layers of the myocardium during ventricular systole (16).

It was hoped that the use of coronary vasoactive drugs might give some insight into the possibility of vasomotor control of endocardial distribution of coronary flow, although it was realized that the drugs would most likely affect endocardial and epicardial vessels in a quantitatively similar fashion. It is not surprising, therefore, that the uptake studies show no significant difference in endocardial distribution between the normotensive and hypertensive left ventricle after drug treatment. Nonetheless, some interesting features emerged from these drug studies. In all cases except those animals treated with norepinephrine in which the coronary perfusion pressure was adjusted equal to aortic pressure, the I-O ratios in both the normotensive and hypertensive left ventricle were significantly greater than the normal group of animals illustrated in Figure 2. These data suggest that there is a preferential shift of blood flow toward the endocardium in response to coronary vasodilatation induced by either left ventricular hypertension or pharmacologic agents, or both, or when coronary vasoconstriction is produced by vasopressin. Additionally, the pattern of flow distribution after pretreatment with propranolol reflects increased endocardial flow with β-adrenergic receptor blockade. However, the mechanism for increased endocardial flow under these circumstances is undoubtedly complex since, on the one hand, β-receptor blockade would be expected to reduce the intramyocardial tissue pressure resistance to systolic coronary flow, while on the other, diastolic coronary vascular resistance would be increased as result of blocked β-receptor sites (18).

We have emphasized that endocardial flow is maintained at a level equal to that in the epicardium in the presence of left ventricular hypertension. Additionally, however, our uptake data indicate that endocardial flow may be somewhat greater than that in the epicardium under these pressure conditions. Reasons for this are not clear, but the possibility of an increased myocardial O₂ consumption in response to increased metabolic work in the inner layers of the hypertensive left ventricle must be considered. An increased tissue pressure in the myocardium as a consequence of the intracavitary hypertension would not of itself necessarily increase O₂ consumption; rather, if such a gradient in O₂ consumption exists between epicardium and endocardium under these conditions, it would seem more likely to be related to the mechanics of myocardial contraction. Under the circumstances of a beating heart with normal intraventricular pressures, myocardial fibers in the inner layers of the myocardium have been shown to shorten more than those in epicardial layers (6, 19). As shown by our I-O uptake ratios this shortening does not result in an increased coronary flow under these normal circumstances nor, for this thesis, an increase in O₂ consumption in the endocardium over that in the outer layers. With left ventricular hypertension, however, it is possible that a greater contractility is required in the inner layers of the myocardium either to maintain or increase the degree of fiber shortening in relation to that in more superficial layers; such an increase in contractility would be expected to increase O₂ consumption and coronary flow in the endocardium.

Acknowledgment

The authors wish to thank Mr. John Dattilo and Miss Eugenia Bobo for their devoted and expert help during this study. The authors are happy to acknowledge the interest and helpful suggestions of Dr. Richard W. Eckstein.

References


Effect of Left Ventricular Hypertension, Ischemia and Vasoactive Drugs on the Myocardial Distribution of Coronary Flow

THOMAS W. MOIR and DON W. DEBRA

doi: 10.1161/01.RES.21.1.65

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1967 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/21/1/65

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/