Effects of Myocardial Strains on Coronary Blood Flow

By James M. Downey, H. Fred Downey, and Edward S. Kirk

ABSTRACT

Systole causes a redistribution of coronary blood flow away from the subendocardium. In the present study the relative contribution of shortening of the myocardial fibers (wall strains) and of pressure development in the ventricular lumen to redistribution were determined. The distribution of coronary blood flow during systole in hearts ejecting into a severed aorta (large wall strains and near-zero afterload) was compared with that in isovolumetrically contracting hearts (reduced wall strains and significant afterload). A quantitative index of the distribution of coronary blood flow during systole was provided by the myocardial uptake of a bolus of $^{86}$Rb or $^{42}$K injected when constant-pressure perfusion of the left coronary artery was restricted with a solenoid-controlled pump to the period of systole. The coronary blood flow during systole in the subendocardium of the ejecting heart was 62% of that in the subepicardium. A similar gradient in the systolic flow with the endocardium receiving 37% of the blood flow to the epicardium was observed in the hearts contracting isovolumetrically. Removing the afterload by severing the aorta abolished the transmural differences in coronary blood flow. In the present experiment cardiac strains per se did not redistribute coronary blood flow through shear or traction forces on the coronary vasculature, but rather, coronary blood flow was affected only by compressive stresses in the myocardium. Contraction in the absence of afterload influenced overall coronary resistance, however; 18% of the resting coronary resistance was associated with shortening alone. An additional 11% of the resting coronary resistance appeared when pressure development accompanied shortening. Coronary blood flow patterns indicated two separate compressive stresses in the left ventricle. The first stress was associated with pressure development and increased with myocardial depth. The second stress was smaller, it was associated with shortening and uniformly distributed.

KEY WORDS

intramyocardial stress vascular waterfall intramyocardial pressure blood flow in systole $^{86}$Rb subendocardial perfusion extravascular coronary resistance blood flow distribution $^{42}$K

The contracting heart deforms its coronary vessels and thereby restricts coronary blood flow (1). This restriction is least near the subepicardium and increases with myocardial depth (2). However, the mechanism whereby contraction inhibits coronary flow has not been defined. The coronary vessels should respond to compressive stresses in the myocardium by forming vascular waterfalls (3). Since compressive stresses within the myocardium associated with pressure development in the ventricular cavity increase with myocardial depth (4-7), the presence of waterfalls alone could explain the effect of systole on coronary blood flow. Other mechanisms, however, must be considered. Because of the vascular anatomy of the heart, any process that narrows the coronary arteries in the midwall results in reduced flow to the subendocardium. The large dimensional changes (wall strains) that occur in the ventricle during contraction may deform the vessels supplying the subendocardium by a mechanism quite different from vascular waterfalls. To investigate this possibility coronary blood flow in hearts experiencing large wall strains but no luminal pressure was compared with coronary blood flow in hearts experiencing significant pressure development and greatly reduced wall strains.

Methods

Three series of experiments were performed with mongrel dogs of either sex (9.6-21 kg) anesthetized with sodium pentobarbital (30 mg/kg, iv); additional anesthesia was administered as required. The hearts were exposed by a left thoracotomy in the fourth inter-
Diagram of the pumping system that was used to provide a pulsatile perfusion pressure. A solenoid-operated valve electrically synchronized to the heart beat directed compressed air to the air side of the diaphragm. The pressure was transmitted through the diaphragm to the blood forcing it into the coronary artery. As the valve vented the air side, pressure on the blood side likewise fell, and the chamber filled with blood from the Sigmamotor pump.

Costal space, and electrocautery was used to promote hemostasis. Ventilation with room air was maintained with a positive-pressure respirator. Heparin (500 units/kg, iv) was administered to prevent clotting in the perfusion tubing.

**GROUP 1**

In this series of experiments left ventricular strains were minimized by causing the heart to contract isovolumetrically, and the effects on the transmural distribution of coronary blood flow during systole were measured. A Gregg cannula was tied into the left coronary artery of a donor dog, which was perfused with arterial blood from a support dog. While coronary blood flow was maintained with a peristaltic pump, the heart was removed by cutting the great vessels and mounted on a stand. A balloon filled with approximately 25 ml of saline was inserted past the mitral valve into the lumen of the left ventricle. The beating heart was secured to the stand with a purse-string suture through the atria and a loop of heavy cord around the atrioventricular ring. The saline-filled balloon was incompressible and, although the ventricular pressure increased during systole, the ventricular volume remained constant throughout the cardiac cycle. Coronary venous blood was collected in a large glass funnel beneath the heart and returned to the support dog via a cannulated femoral vein. No provision was made for right coronary flow, because it supplies only a small portion of the right ventricular myocardium.

The transmural distribution of coronary blood flow was measured by injecting either $^{42}$K or $^{86}$Rb into the coronary perfusate. Both of these isotopes are extracted from the arterial blood by the myocardium at essentially the same rate (8). The uptake of the isotopes by the myocardium was then directly measured at various sites in the left ventricle. The isotope was administered under two conditions. First $^{86}$Rb was injected while the left coronary artery was continuously perfused by a Sigmamotor peristaltic pump. Thus, $^{86}$Rb indicated the intramyocardial distribution of coronary blood flow over the entire cardiac cycle. Following the $^{86}$Rb injection no coronary venous blood was returned to the support dog.

The second measurement was made when forward coronary blood flow was confined to the period of systole. To accomplish this measurement, the continuous perfusion was replaced by one in which pressure alternated between zero during diastole and a normal aortic pressure (133 mm Hg) during systole. $^{42}$K was injected into the perfusate at the onset of this pulsatile perfusion so that its intramyocardial distribution would indicate the distribution of the coronary blood flowing only during systole. Contaminated blood was not returned to the support dog; therefore, the arterial blood that received the $^{42}$K contained no $^{86}$Rb.

This pulsatile perfusion was provided by a special pumping system diagramed in Figure 1. Arterial blood was pumped by a peristaltic pump at a constant flow from either a femoral artery or a reservoir to the blood side of the diaphragm pump. A solenoid valve that was synchronized with the heart beat directed compressed air at 150 mm Hg to the dry side of the diaphragm. These pulses of compressed air were transmitted through the diaphragm to the blood side forcing blood down the coronary cannula. When the diaphragm pump was vented to the atmosphere during diastole, the
peristaltic pump replenished the chamber with blood. The solenoid valve was synchronized through appropriate pulse and delay circuits that were in turn triggered by signals arising from an electrocardiographic electrode on the ventricular surface.

No more than 1.5 minutes elapsed between the injection of $^{86}$Rb and the injection of $^{42}$K. Thirty seconds after the injection of $^{42}$K, the pump was turned off, and the heart was removed from the stand.

Each excised heart was rinsed under tap water, and the atria and free wall of the right ventricle were removed. The remaining left ventricle was weighed and placed in a domestic freezer. When the tissue was completely frozen, 15-cm$^2$ sections that included the full thickness of the ventricular wall were cut from the posterior and anterior apex and the posterior and the anterior base. These four sections were in turn sliced into four layers from the epicardium to the endocardium. Thus, four myocardial depths were sampled from four locations on the ventricle. Each of the 16 samples was weighed to the nearest milligram and deposited in a test tube containing 3 ml of nitric acid. When the samples were completely digested to ensure a uniform geometry, they were counted on a dual-channel gamma detector (Nuclear Chicago), and the activities of the two isotopes were separated by gamma spectroscopy. The corrected count rate for each isotope was divided by the sample weight to yield an activity in counts/g tissue for each sample. Since no consistent differences were observed between the regions sampled, all of the data were pooled and analyzed only with respect to myocardial depth. The data were normalized by dividing the activity of each sample by the activity of the entire transmural section from which it came. The average activity of the four samples representing each depth was calculated for each heart. Then the means ± SE of these average activities were determined for each depth.

**GROUP 2**

In a second series of experiments, cardiac strains were maximized in the absence of luminal pressure, and the effects on the transmural distribution of the systolic blood flow were measured. The left coronary artery of the in situ heart was cannulated with a Gregg cannula. The pulsatile pump described for group 1 was used, but...
TABLE 1

Hemodynamic Data from All Experiments

<table>
<thead>
<tr>
<th>Dog</th>
<th>Left ventricular weight (g)</th>
<th>Heart rate (beats/min)</th>
<th>Peak ventricular pressure (mm Hg)</th>
<th>Aorta cut</th>
<th>Coronary perfusion pressure* (mm Hg)</th>
<th>Mean coronary perfusion pressure † (mm Hg)</th>
</tr>
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<tbody>
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<td>Developing pressure</td>
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<td>Continuous (Mean)</td>
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<td></td>
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<td></td>
<td>Aorta</td>
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<td>Pulsatile (Peak)</td>
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<td>205</td>
<td>90</td>
<td>125</td>
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<tr>
<td>Mean ± SD</td>
<td>67 ± 18</td>
<td>175 ± 20</td>
<td>103 ± 24</td>
<td>109 ± 22</td>
<td>124 ± 17</td>
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Group 1

1. 40                        150          95                  < 25        140                        
2. 118                       166          115                 < 10       135                        
3. 63                        145          75                  < 5         135                        
4. 42                        174          65                  < 5         150                        
5. 66                        185          73                  < 15        105                        
6. 59                        120          120                 < 10        130                        
7. 44                        150          65                  < 10        140                        
Mean ± SD | 61 ± 27                | 155 ± 21               | 87 ± 23                         | 133 ± 14 |                                       |

Group 2

1. 80                        165          82                  < 10        140                        
2. 90                        142          87                  < 25        77                         
3. 85                        192          100                 < 10        82                         
4. 85                        165          90                  < 15        75                         
5. 74                        174          85                  < 10        60                         
6. 82                        186          100                 < 15        93                         
Mean ± SD | 83 ± 5                 | 171 ± 19               | 91 ± 8                          | 82 ± 9   | 73 ± 13                              | 59 ± 14                                |

Left ventricular weight refers to weight of the excised heart minus the atria, the great vessels, and the right ventricular free wall.

*Groups 1 and 2.
†Group 3.

In this experiment arterial blood was drawn from a femoral artery of the experimental dog instead of a support dog.

The reservoir in the line to the femoral artery (Fig. 1) was filled with 100 ml of arterial blood. For a control measurement the systolic distribution of the coronary blood flow with significant wall strains and afterload was obtained by using the pulsatile pump to perfuse the coronary circulation with blood from the femoral artery; $^{42}$K in 0.1 ml of saline was injected into the perfusate near the coronary cannula. Thirty seconds later the pump was turned off, and the heart was returned to a continuous perfusion. After a 60-second interval the pump was restarted, but this time arterial blood was drawn from the reservoir. As soon as pulsatile perfusion was resumed, the aorta was abruptly severed just distal to the left subclavian artery. Simultaneously a bolus of $^{86}$Rb in the same form as the $^{42}$K was injected into the perfusate. Thirty seconds later perfusion was stopped, and the heart was removed for analysis as described for group 1.

GROUP 3

In a third series of experiments the effects of cardiac strains in the absence of ventricular pressure on overall coronary resistance were examined. The left coronary arteries of in situ hearts were cannulated and perfused with arterial blood from a femoral artery. Flow in the perfusion line was held constant with a Sigmamotor peristaltic pump, and changes in coronary resistance were revealed by changes in perfusion pressure. To interpret changes in coronary resistance only as changes in the degree of compression experienced by the coronary vessels, all vascular tone was removed by continuous infusion of adenosine at 0.85 mg/min into the coronary perfusate. A reservoir in the line between the Sigmamotor pump and the femoral artery was filled with 100 ml of arterial blood. While the coronary vessels were perfused at a constant rate with blood from the reservoir the aorta was severed as it was in the group 2 experiments. After ventricular pressure had fallen to zero, the heart was arrested by bilaterally stimulating the vagus nerves. The nerves had been crushed and cauterized proximal to the stimulation site. The changes in perfusion pressure resulting from removal of afterload only and removal of afterload with arrest were noted.

Results

GROUP 1

In these experiments perfusion to the
isovolumetric hearts was limited to systole by using the pumping system described in Methods. Figure 2 is a record of the pulsatile perfusion pressure generated by the pump. The administration of $^{42}$K during pulsatile perfusion caused the isotope to be distributed in the myocardial tissue as shown by the solid line in Figure 3. Because the uptake of the isotope by the tissue is primarily limited by the plasma flow rate (9), the vertical axis is proportional to tissue blood flow. Since the perfusion was pulsatile, the blood flow distribution reflected that occurring during systole. A marked gradient that favored the outer layers was observed.

The broken line in Figure 3 illustrates the intramyocardial distribution of the $^{86}$Rb that was injected during continuous perfusion; it shows the distribution of blood flowing over the entire cardiac cycle. A gradient that favored the subendocardium and was opposite to that occurring in systole was observed in this experiment. The difference between these two flow distributions indicated a selective impediment to blood flowing to the subendocardium during systole. Hemodynamic data for these dogs are given in Table 1.

GROUP 2

In these experiments the distribution of coronary blood flow during systole was measured under two conditions in each heart. First, the hearts were contracting against a significant afterload. The flow distribution under this condition was indicated by the uptake of $^{42}$K (Fig. 4). An appreciable impediment to subendocardial blood flow during systole was apparent from the transmural gradient that favored the epicardium. Second, the afterload was removed by cutting the aorta. The transmural gradient of systolic blood flow, as revealed by the uptake of $^{86}$Rb, was lost (Fig. 4). Hemodynamic data for these dogs are given in Table 1.

GROUP 3

The coronary arteries were perfused at a constant flow rate so that changes in perfusion pressure corresponded to changes in coronary resistance. Furthermore, because the coronary vessels were in a state of maximal dilation due to the infusion of adenosine, all changes in coronary resistance were due to changes in the degree of compression which they experienced. When the ventricular pressure was effectively removed by cutting the thoracic aorta, coronary resistance fell to 88.6 ± 2.3% (SE) of the control value. Stopping the heart beat by vagus nerve stimulation after ventricular pressure had been abolished resulted in a further decline in coronary resistance to 71 ± 2.9% of the control value (Fig. 5B). Thus, removing the afterload alone in the presence of myocardial shortening clearly did not remove all extravascular compression of the coronary vessels. In Figure 6 the coronary resistance is separated into its components. Arresting the heart revealed that 29% of the resistance came from compression of the coronary arteries, and 18% of the coronary resistance was associated with shortening alone. The presence of shortening with pressure development revealed that the remaining 11% was afterload dependent.

Figure 5 also shows the effect of arrest on coronary resistance with the aorta intact. Figure 5A reveals that the fall in coronary resistance with arrest was the same whether the aorta was intact or severed. Hemodynamic data for these dogs are given in Table 1.

Discussion

In group 1 the transmural uptake of $^{86}$Rb had a gradient that favored the endocardium. Since this isotope was administered during continuous perfusion it reflected the distribution of coronary blood flow over the entire cardiac cycle. The flow during systole was distributed away from the endocardium. Thus a large reverse gradient was present during diastole. Gradients during the diastolic perfusion probably result from gradients in coronary pressure.
Separation of coronary resistance into its components. Sev-  ering the aorta revealed that 11% of the coronary resistance resulted from extravascular compression associated with ventricular pressure development (afterload). When shortening was also prevented by arresting the heart, it was found that an additional 18% of the coronary resistance resulted from compression associated with shortening alone and thus was independent of afterload. The data were obtained from six dogs.

tone, since intramyocardial compression is minimal at this time (10). Reduced epicardial tone was probably the result of handling and cooling of the epicardial surface during preparation. Thus, compression during systole in the isovolumetric hearts so altered coronary resistance that it reversed a flow gradient that was ongoing in the diastolic period. Although the distribution of the total coronary flow was not measured in group 2, it is unlikely that it was nonuniformly distributed as was that in group 1. These hearts were studied in situ and experienced a minimum of manipulation. Hearts similarly prepared in this laboratory previously have been found to have a uniformly distributed flow when they are perfused with constant pressure (11).

The myocardial distribution of coronary blood flow has been previously examined (12) as a function of ventricular pressure in both beating and nonbeating hearts. Cutarelli and Levy (12) found that coronary flow was distributed uniformly in contracting myocardium independent of afterload. Since, however, distribution of flow was a function of ventricular pressure in ischemically depressed tissue, they concluded that the differences in vascular compression across the ventricular wall only existed in tissue where shortening was prevented by ischemia. The present data argue against such an interpretation. Luminal pressure development preferentially inhibited subendocardial perfusion regardless of the degree of myocardial shortening. It has been previously suggested (13) that the effects of altered afterload in the experiments of Cutarelli and Levy (12) were masked by local autoregulation except when tone was abolished by ischemia. The present results support the latter interpretation.

The coronary arteries course over the surface of the heart and send tributaries at right angles into the ventricular wall to supply the underlying tissue. Thus, any process that deforms the vessels passing through the midwall will have its greatest effect on flow reaching the terminal vasculature in the subendocardium. Several types of deformation associated with dimensional changes in the ventricular wall can be hypothesized. The left ventricle is composed of multiple muscle fibers; the orientation of these muscle fibers changes in a rotational manner with myocardial depth (14). This rotational change causes shear strains between adjacent layers (15) that could kink or otherwise restrict flow in arteries passing through the tissue. Also thickening of the ventricular wall accompanies contraction. Resulting traction forces might extend the length and diminish the caliber of vessels oriented perpendicular to the ventricular surface and thus augment their resistance. The results of the present experiments, however, indicate that these mechanisms have a negligible effect on coronary distribution. Clearly the development of pressure in the ventricle is responsible for redistributing systolic perfusion. Ventricular strains per se contribute little if any to this process.

Compressive stresses in the ventricle probably reduce tissue perfusion locally through a vascular waterfall mechanism. In this process the difference between perfusion pressure and pressure surrounding the vessels is the primary determinant of flow (3). If this theory is correct the compressive intramyocardial stresses can be determined by the blood flow patterns they create. For example, under the constant-flow conditions of group 3, changes in vascular compression will elicit an equal change in perfusion pressure because flow is proportional to the difference between perfusion pressure and tissue pressure (3). Thus, if flow is to remain constant, pressure difference must also re-
main constant. Such a calculation is only valid if the stress is uniformly distributed in the myocardium. The distribution of systolic flow observed in hearts contracting against zero afterload indicates that these conditions were fulfilled. Shortening in the absence of afterload caused mean perfusion pressure to increase 14 mm Hg over that of the arrested state (Fig. 6). Assuming that the compression was limited to the systolic period (60% of the cardiac cycle), an intramyocardial stress of 14/0.6 or 23 mm Hg was calculated for that period. Because the systolic portion of the coronary blood flow was uniformly distributed in these hearts, stress was also assumed to be similarly disturbed. The stress resulting from shortening of myocardial fibers probably arose from a crowding effect on vessels between adjacent fibers as they thickened, thus making the stress normal to the axis of individual fibers. But since fiber orientation is variable in the ventricle, no single orientation can be assigned to this stress. These hearts were contracting against a near-zero afterload so strains were probably exaggerated. Thus, the stress associated with shortening undoubtedly would be lower still in a normally ejecting heart. In Figure 6, the magnitude of the afterload-dependent component of the extravascular resistance was, therefore, underestimated, because the afterload-independent component should have increased with removal of ventricular pressure.

Hearts arrested with the aorta intact presumably continued to fill in excess of their normal diastolic volume. Yet they had the same coronary resistance as the arrested hearts with severed aortas which should have had greatly reduced volumes. Although myocardial shortening augmented coronary resistance, increasing fiber length apparently did not cause a comparable change.

Pressure in the ventricular lumen created a different set of intramyocardial stresses which in the normal heart presumably coexist with those resulting from shortening. The flow data indicates that only the latter stress was nonuniformly distributed.

Redistribution of coronary blood flow during systole resulted from pressure development in the ventricular lumen and was independent of cardiac wall strains. Shortening, however, increased coronary resistance uniformly across the ventricle wall in the absence of ventricular pressure. No comparable changes in coronary resistance were associated with augmented fiber length. These data indicate that systole redistributes coronary flow only by forming vascular sluices in response to compressive stresses in the myocardium as opposed to deformation of the vasculature resulting directly from dimensional changes.

References

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