In addition to the obvious advantages of data compression for storage and retrieval of map data, the method also has significant advantages for analysis and comparison of maps. The 216 coefficients that uniquely characterize each map are a magnitude of information that is manageable by pattern recognition techniques and may permit automated classification of maps as a screening process. Map data expressed as 216 coefficients can be handled for statistical analyses aimed at quantitating the diagnostic utility of maps. Such analyses would be impossible for the 100,000 numbers that characterize a typical QRST map prior to data compression. Since QRS and ST-T data are represented separately—that is, 144 of the 216 coefficients represent QRS and 72 represent ST-T—it will be possible to apply pattern recognition techniques or other statistical analyses independently to QRS and ST-T data. This may be desirable since cardiac diseases may affect QRS and ST-T differently. It is not possible at this time to comment on the diagnostic utility of the 216 coefficients since no standards exist for evaluating the diagnostic ability of any of the current map interpretation methods. However, studies are in progress to evaluate the diagnostic performance of these 216 coefficients.

References


Redistribution of Canine Left Ventricular Myocardial Blood Flow in Unloaded Systole

RICHARD B. WILLIAMS, HERTA M. TREMER, AND SIDNEY S. SOBIN

SUMMARY The left coronary arteries of dogs were cannulated and perfused with blood from support dogs. The experimental hearts were unloaded by severing the aortas to maximize strains and minimize fiber stress. In each heart we compared the transmural distribution of blood flow in two states: (1) provision of perfusion pressure (40 mm Hg) only during systole and then (2) provision of perfusion pressure throughout the cardiac cycle. The distribution of flow in each of these perfusion states was labeled with a diffusible radioisotope (^1K or ^8Rb, one labeling the first state; the other labeling the second). Quantitative, paired autoradiography was used to visualize the two flow distributions. The differences between the two distributions after standardization was plotted as differences between activity vs. depth in the myocardium (r > 0.91). This was fitted with a line by least squares, the slope of which was significantly different from zero at the 0.0005 level. The magnitude of the gradient of the systolic flow was represented by the ratio of deep to shallow flow. The mean of these ratios was 0.54 ± 0.12 (95% confidence interval). A graphical analysis shows that the data are consistent with a gradient of extravascular compression across the left ventricular wall. Circ Res 49: 203-211, 1981
gradient of compression could result from the development of fiber stress and ventricular pressure (Streeter et al., 1970). Kirk and Honig (1964) suggested that systolic ventricular wall thickening, which is part of fiber shortening strain, also could contribute to myocardial extravascular compression. However, in 1974, Downey et al. concluded that, although myocardial fiber shortening strain contributed to extravascular compression, this effect was distributed evenly across the left ventricular wall and consequently did not contribute to the gradient of compression. They based this conclusion on their finding that systolic perfusion in the empty beating heart was distributed evenly across the wall.

We thought, however, that there were some problems with this interpretation. First, their method of flow measurement underestimates flow gradients as Downey and Kirk (1974) noted in a previous report. A technique that underestimates gradients can be used to demonstrate that a gradient does exist but cannot logically be used to demonstrate that one does not exist. Next, even if the actual systolic blood flow were equal across the wall, it could not be assumed that this indicated that systolic compression was evenly distributed across the wall because: (1) autoregulation was not abolished in their preparation, (2) they did not establish a control state that represented the flow distribution in the absence of systole; that is, they did not establish the distribution of resistance across the wall. In view of the above and since the work of Downey et al. (1974) is cited widely as proof that fiber shortening does not redistribute myocardial blood flow, we re-investigated this question. Our results indicate that systolic fiber shortening does influence perfusion patterns across the left ventricular wall.

**Methods**

**Experimental Design**

To determine the effect of systolic fiber shortening on myocardial blood flow distribution, we compared the distribution of systolic flow with the distribution of total cardiac cycle flow. Systolic flow was isolated by providing coronary perfusion pressure only during systole. Total cardiac cycle flow was the result of constant coronary perfusion pressure. Both flows were measured in the empty beating heart to maximize fiber shortening and obviate luminal pressure development (Downey et al., 1974). Perfusion blood was provided by a donor dog in order to provide a stable preparation. Also, we maximally dilated the coronary vessels with adenosine so as to minimize autoregulation.

As shown by Kety (1960), the deposition of a freely diffusible substance is a good indication of local blood flow. The two flow distributions were determined by autoradiography of two different diffusible radioisotopes. One isotope was deposited from the coronary perfusate during systolic perfusion; the other was deposited during total cardiac cycle perfusion. We used autoradiography because it permits higher spatial resolution of isotope deposition than techniques which cut the heart into discrete pieces and then determine the isotope content in each piece.

The radioisotopes used were \(^{86}\)Rb and \(^{42}\)K. These isotopes permitted paired autoradiography, i.e., two radiographs of each tissue sample because of their very different half-lives; \(^{86}\)Rb has a half-life of 18.5 days and \(^{42}\)K has a half-life of 12.5 hours. A far greater activity of \(^{42}\)K, the shorter lived isotope, was used than \(^{86}\)Rb. One autoradiograph was exposed immediately after the experiment (within 18 hours). The exposure lasted for a relatively short time (<5 hours). This radiograph showed the distribution of the high activity isotope \(^{42}\)K. After waiting for several days for the \(^{42}\)K to decay, another longer exposure (10–14 days) of the same section was performed. This showed the distribution of \(^{86}\)Rb. Thus, both flow distributions for systole and total cycle flow were measured in the same tissue sample. The isotope order for the flow states was randomly selected.

These isotopes are appropriate for a reason other than their relative half-lives; due to their large extravascular distribution in the myocardium, they do not wash out nearly as fast as they wash in. This means that the second flow state does not wash out the isotope deposited during the first. The data of Downey and Kirk (1970) demonstrate that the time constant for equilibration is many minutes and our second infusion lasted 30 seconds, well within the equilibration period.

**Preparation of Experimental Animal**

Three mongrel male dogs, 20–30 kg, were used. Each was initially anesthetized with pentobarbital, 30 mg/kg, and additional anesthetic was given as required. The animals were ventilated with 100% O\(_2\) and end-expiratory CO\(_2\) concentration was monitored and maintained at 5.3%.

A thoracotomy was performed by splitting the sternum and then making an incision in the left 4th or 5th intercostal space. The ribs cranial to this incision were cracked close to the vertebral column, thus permitting the entire left thoracic wall to be folded back out of the field. The left coronary artery was dissected free at its origin and a strip of umbilical tape placed around it.

**Preparation of Donor Animal**

Simultaneously with the coronary dissection in the experimental animal, a donor dog was anesthetized with pentobarbital, 30 mg/kg, and the following cannulae installed: a tube for monitoring arterial pressure (PE 320) into the abdominal aorta via a femoral artery, a cephalic vein cannula (PE 320) to provide access for additional anesthetic, volume
expander, and heparin when needed, and three one-fourth inch metal cannulae. The latter were installed in a femoral artery, a femoral vein, and a carotid artery. The femoral artery cannula supplied blood to a blood reservoir (reservoir A, see Fig. 1) and the femoral vein cannula returned this blood to the animal. The carotid artery cannula supplied the coronary perfusion apparatus of the experimental heart.

Reservoir A was included in order to keep the donor's intracorporeal blood volume as constant as possible during the coronary artery perfusion and prevent the release of vasoactive substances. This reservoir was arranged so that it could empty into the donor's femoral vein at approximately the same rate that the donor's carotid artery supplied blood to the coronary perfusion apparatus. After giving the donor 500 units of heparin per kg body weight, reservoir A was filled by letting blood flow from the femoral artery through the reservoir and back into the femoral vein with the amount held in the reservoir slowly increasing. As the volume of blood in reservoir A increased to 1 liter, dextran 40 (10% in 0.9% saline) was simultaneously dripped into the cephalic vein to match the volume lost by the animal. Thus, neither the filling of the reservoir nor the subsequent perfusion dramatically changed the intracorporeal blood volume of the donor.

**Perfusion System**

The perfusion system between the donor and the experimental animal consisted of (Fig. 1) a peristaltic pump, reservoir B, a pulsatile pump, and the coronary artery cannula. Reservoir B had three ports: the input from the peristaltic pump, the output to the pulsatile pump, and an air inlet. The latter could either be open to the atmosphere or connected to one of two compressed air sources by changing the position of a tubing clamp. The pulsatile pump generated the rectangular wave of perfusion pressure for "systolic-only" perfusion. Very thick-walled vinyl tubing (1/4" lumen; 1/8" wall approximately 14" long) was used to connect the pulsatile pump to the stainless steel coronary artery cannula. Near the junction of the vinyl tubing and stainless steel cannula, two adjacent 18-gauge needles penetrated the wall of the vinyl tubing. One was used to inject the isotopes and their saline rinse; the other was used to infuse adenosine continuously at approximately 2 mg/min.

Three modes of coronary perfusion were used. Two were defined by steady (non-pulsatile) perfusion pressures at either 90 or 40 mm Hg; the third was defined by pulsatile perfusion pressure (40 mm Hg during systole and zero during diastole). In the steady modes, reservoir B was pressurized as shown in Figure 1 at either 90 or 40 mm Hg and the pulsatile pump was not activated. In the pulsatile mode, reservoir B was open to ambient air and the pulsatile pump activated.

The pulsatile pump was similar to the one described by Downey et al., 1974. It consisted of a blood chamber and an air chamber separated by a thin latex septum. A metal grid prevented the latex septum from swelling into the air chamber when the pressure in the blood chamber was higher than that in the air chamber. Retrograde flow into reservoir B was prevented by a latex flap over the entrance to the blood chamber; the flap thus functioned as a one-way valve. The blood chamber was...
placed at the level of the coronary ostium and the chamber pressure was recorded. The entrance to the air chamber was governed by a three-way solenoid valve activated by the R wave of the ECG; the chamber was connected to a 40 mm Hg compressed air source when the solenoid was activated and to ambient air when the solenoid was inactivated. Synchrony between the solenoid activation and systole was achieved by varying the duration of activation as well as the interval between the R wave and activation of the solenoid. (see Fig. 2)

Coronary Artery Cannulation and Experimental Protocol

Just before the cannula was installed in the coronary artery, 150-200 ml of blood were transferred from reservoir A to reservoir B by increasing the femoral vein inflow to the donor and opening the donor’s carotid artery flow to reservoir B. The donor’s arterial pressure and heart rate did not change substantially throughout the experiment. The pressure of reservoir B was set at 90 mm Hg for steady perfusion and the blood chamber and coronary cannula were primed with blood. The left coronary artery then was cannulated by introducing the cannula into the left subclavian artery and guiding it down the ascending aorta to the left coronary ostium. Once the cannula tip entered the ostium, it was secured by clamping the umbilical tape (which had been placed around the artery earlier) with a small Mixter clamp. Perfusion was initiated immediately.

At this point, the pericardium was opened to reveal the areas supplied by both the circumflex and anterior descending arteries. If the cannula placement was such that one of these branches was occluded, myocardial cyanosis quickly developed. The cannula was then repositioned so that this did not occur or, if this failed, the preparation was discarded. The solenoid trigger was set so that the pressure pulse coincided with early systole.

The experiment began by severing both cervical...

![Figure 2](http://circres.ahajournals.org/)

**Figure 2** This recording shows the phase relationship between systole and the perfusion pressure pulse: the lower tracing is perfusion pressure; the upper tracing is the ECG. Point A is the “S” wave. Point B is the termination of the “T” wave. The interval between the “S” wave and end of “T” wave includes most of the mechanical systole.
vagi (in order to obviate reflexes resulting from an empty heart) and then severing the thoracic aorta and waiting 5 seconds for the heart to unload itself. Then reservoir B was opened to the atmosphere. The blood level of reservoir B was raised a little more than 1 cm above the blood chamber of the pulsatile pump. Because of the low resistance of the tubing between reservoir B and the blood chamber, this hydrostatic head kept the chamber filled. With the pulse chamber in operation and the pulse height of 40 mm Hg, one isotope of a pair (= 1 mCi 42K or 10 µCi 86Rb) was injected as a single bolus. (The isotopes were in 0.55 ml of saline and were flushed in with 0.3 ml of saline.) After waiting 30 seconds for the first isotope to wash into the myocardium, we turned off the pulse chamber and allowed the heart to recover for 1 minute at 90 mm Hg perfusion pressure. Reservoir B was then set at the same pressure as the previous pulse height (i.e., steady perfusion mode 44 mm Hg), and the second isotope of the pair was injected. After 30 seconds, perfusion was stopped.

Tissue Removal and Preparation for Autoradiography

Immediately after the experiment, the free wall of the left ventricle was excised. A transmural strip approximately 2 cm wide and extending completely across one dimension of the face of the wall was removed. This was frozen by submersion in CCl4 at −10°C for 1 hour. CCl4 was chosen as a medium because, being a non-polar liquid at this temperature, it did not penetrate the myocardium and disturb the sequestration of the radioactive ions. Giger-Muller tube survey of the used CCl4 consistently failed to detect any counts over background.

Sections 500 µm thick were cut on a sliding microtome maintained at −10°C in a freezer and arrayed between two sheets of plastic, each a maximum of 1 mil thick, precut to the dimensions of the film used for autoradiography. The two sheets were sealed together at the edges to protect the tissue from dehydration. Each heart was represented by an array of at least 15 sections. A randomly selected section from each heart was used to represent that heart. Five transmural lines perpendicular to the epicardial surface were randomly selected on the representative section. The gradients of exposure along these lines were analyzed on the two radiographic images of the section corresponding to the two flow states.

Autoradiographic Exposure

The array of tissue sections was placed on a sheet of Kodak X-OMAT G film and the two held closely apposed for the duration of exposure. The tissue was kept frozen until both radiographs were complete. All films were developed using the automated Kodak X-OMAT system.

We found that a good index of necessary exposure time could be obtained by assuming that the activity per unit area of section was proportional to the total activity injected adjusted for decay between the time of injection and the beginning of the exposure. Thus the total of all counts over a given time per unit area of section (the total radiographic "exposure") was assumed to be roughly proportional to the total counts given off by the total injected isotope during that time:

$$\text{Total counts} = \int_0^t \text{exp} - \left( \frac{0.693}{t_{1/2}} \right) \text{dt}$$

where $A_o$ = total injected activity; $A_t = A_o \exp - \left( \frac{0.693}{t_{1/2}} \right)$

where $t_{1/2}$ = half-life of isotope; $t = $ time of exposure.

We refer to this index of the total exposing counts as the total count index (TCI). Its units are mCi days. Both preliminary and in vivo results indicated that TCI values of 0.04 to 0.08 mCi days gave good autoradiographic exposure for both isotopes.

In the method of paired autoradiography used, each autoradiograph visualizes one isotope predominantly. The degree to which the other isotope influenced the radiography can be estimated using the TCI. Taking into consideration the decay of both isotopes, the lowest ratio of 42K to 86Rb activities was 36.9 at the beginning of an exposure to visualize 42K. The exposure time was 4.5 hours (0.1875 day). The TCI for 42K was 0.087 mCi days; for 86Rb, 0.0018. The 86Rb TCI was 5.1% of that for 42K.

The least amount of time that was permitted for 42K decay before the 86Rb exposure ended was 11 days after the calibration of the 42K. At the start of the exposure to visualize 86Rb, the ratio of 86Rb to 42K activities was 1.5 $\times 10^4$. The exposure time was 7 days, after which the TCI values were 3.3 $\times 10^{-7}$ and 0.041 for 42K and 86Rb, respectively. Their ratio was 8.1 $\times 10^{-6}$.

Sample Selection

Each heart had many (>15) tissue sections (samples) associated with it. The images of some of these were unusable because they overlapped with moisture and static electricity artifacts. These sections were excluded from further consideration. The remaining tissue sections were numbered sequentially from an arbitrary and convenient starting point as one. A sample was selected for study by identifying it with a random number generated in the appropriate range, and the sample so chosen was representative of that heart.

In order to determine the distribution of isotope across the wall, we sequentially analyzed the two autoradiographs (42K and 86Rb), corresponding to a
selected sample, along the five lines extending transmurally from epicardium to endocardium. The positions of these lines were determined by measuring the length of the epicardial border of the section and then multiplying the length by five random coefficients between 0 and 1. These five products represent lengths from one end of the epicardial border (arbitrarily chosen as the "zero" end) and the positions of the lines. The wall thickness along each line (which was variable) was divided into tenths and the absorbance (defined as $-\log T$, $T = \%$ transmittance) at each tenth was measured and recorded.

This procedure was done first with the $^{42}$K autoradiographs and then with the $^{86}$Rb radiographs by superimposing the films and marking the sample points. That is, the same points on the sections were measured for both autoradiographs.

A relative exposure vs. absorbance standard was constructed by varying the exposure time of a fixed but not calibrated radiation source. Exposure is defined as $I \times t$, where $t$ = exposure duration and $I$ = the number of particles striking the film per unit time. To the extent that isotope deposition is defined as $I \times t$, where $t$ = exposure duration and $I$ = the number of particles striking the film per unit time. To the extent that isotope deposition is flow limited, $I = C_i \cdot Q$, $Q_i$ = flow to observed region. $C_i = constant$. Therefore, relative exposure $= C_i \cdot Q / t$.

The relative exposure for each transmural line was standardized by the average for that line $Q$.

Standardized relative exposure

$$= C_i \cdot Q_i / t / C_i \cdot Q / t \cdot Q_i / Q$$

To determine whether "redistribution" of the labeled blood flow occurred between the two perfusion states, we subtracted the respective standardized values through the wall for systolic perfusion from those for full cycle perfusion. The regression of these differences on myocardial depth was analyzed. Since autocorrelation of the least squares errors was not greater than 0.6, 28 degrees of freedom were used (Durbin and Watson, 1950, 1951). As an index of the magnitude of the systolic gradient, a ratio of the standardized relative exposure of the 30% most shallow myocardium to the 30% deepest was determined for systolic perfusion. This was evaluated with two degrees of freedom.

**Results**

Figure 3 shows the regression of differences in pairs of systolic- and total cycle-standardized relative exposure values against depth in the ventricular wall. If the distribution of isotope resulting from systolic perfusion were the same as that from full cycle perfusion, the points would follow the "line of no redistribution" and have zero slope. However, the least squares line for the data has a slope which is significantly different from zero ($P < 0.0005$).

To illustrate the magnitude of the systolic gradient, the ratios of endocardial to epicardial flows (relative exposure) for systolic perfusion are shown in Table 1. Those for full cycle perfusion are given in Table 2.

**Discussion**

The regression analysis indicated that systolic fiber shortening does indeed cause a statistically significant redistribution of coronary blood flow away from deep myocardium. The ratio of deep to shallow flow indicates further that the systolic gradient resulting from fiber shortening is large enough to be physiologically significant.

Two factors tend to strengthen these statements: (1) It is possible deposition was somewhat diffusion limited. This would tend to underestimate both flow gradients. Therefore, the observation of a sizable gradient of systolic label deposition (roughly twice as much in the subepicardium as in the sub-endocardium) permits the inference of an actual systolic flow gradient which is at least this great. It was because both isotopes lose their flow-limited characteristics at high flow rates that we used the low 40 mm Hg perfusion pressures in the maximally diluted coronary vessels. (2) The difference between the diastolic flow gradient and the systolic gradient (i.e., the "redistribution") was also underestimated. This was because of two factors. First, because the coronary arteries are somewhat compliant, limiting the perfusion pressure to systole does not prevent the occurrence of some diastolic flow (Downey and Kirk, 1974), so that some of the systolic flow tracer was deposited during diastole. Second, and more important, the control distribution was deposited throughout the cardiac cycle and not just during diastole. That is, a significant part of the control flow tracer was deposited during systole. Since both of these factors tend to underestimate the difference in gradients, the present data unequivocally indicate that a flow redistribution due to systole in the unloaded heart does exist transmurally and is at least as great as the deposition gradient observed.

Our results differ from those of Downey et al. (1974) in that we found a strong systolic blood flow gradient, whereas their experiment implied that blood flow was evenly distributed in unloaded systole. As noted above, their experimental design will not necessarily demonstrate the absence of a gradient of either blood flow or extravascular compression. On the other hand, it is possible that the discrepancy between our results and theirs is due only to the difference in perfusion pressure used. Downey et al. attributed the strain-dependent flow impedance to extravascular compression. If a gradient of such compression exists in the unloaded heart and if there is a gradient of conductance per mass of tissue across the ventricular wall, then the blood flow gradient depends on the perfusion pressure used (Fig. 4). It has been claimed that a gradient of conductance does exist in the relaxed heart, even in the absence of autoregulation, and that it

Discussion
favors the endocardium (Downey et al., 1975). This may or may not apply in a maximally fiber shortened heart. Downey and Kirk (1975) found during maximal vasodilation that myocardial vascular resistance was the same in loaded systole as in diastole. However, Downey et al. (1979) have since published results that show no gradient of conductance in the fibrillating, and presumably somewhat deformed, heart. This contrasts with the finding of Downey et al. (1975) in the fibrillating heart with vented left ventricle, which showed a strong gradient of conductance in the maximally vasodilated myocardium favoring the endocardium.

We should say here that the use of adenosine was necessary to properly interpret the results; it enabled us to distinguish purely "physical forces" affecting the blood flow from active autoregulation. This distinction is most important in the coronary circulation when varying degrees of myocardial ischemia are present and "physical forces" begin to determine myocardial blood flow distribution. (Griggs and Nakamura, 1968).

In view of the Downey et al. (1974) attribution of the strain-dependent flow impediment to extravascular compression, an interesting hypothesis suggests itself to account for the present findings. Extravascular compression could result from stresses necessary to thicken the wall during systole. It was suggested by Kirk and Honig (1964) that systolic wall thickening changed the cross-sectional shape of the myocardial fibers and that the stress necessary to do this would be a strain-dependent extravascular pressure component. Although Streeter (1970) notes that the fibers seem to roll over one another rather than changing their cross-sectional shape with systolic strain, one must inquire whether there are other structures present in the ventricular wall which might contain stress due to systolic wall thickening. The most prevalent anatomical entities within the left ventricular wall, other than muscle fibers, are blood vessels. Coronary arteries supplying myocardium other than that immediately epicardial run in a radial direction through the wall (Estes et al., 1966). This suggests that wall thickening during systole stretches these vessels. Since it is generally accepted that vessels in the size range of these radial conducting arteries (>0.5 mm) do not contribute significantly to total resistance, the change in total resistance caused by their deformation may not be significant. However, the longitudinal tension generated by elongation of these numerous vessels would be exerted as intramyocardial pressure at sites of vessel tethering. Since there is more thickening in deeper myocardium (Feigl and Fry, 1964), this tension might be expected to increase deep IMP more than shallow, and result in the relative underperfusion of the deep myocardium observed in this study.

**Table 1**

<table>
<thead>
<tr>
<th>Heart</th>
<th>A</th>
<th>B</th>
<th>A:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-21</td>
<td>1.19</td>
<td>2.63</td>
<td>0.45</td>
</tr>
<tr>
<td>6-28</td>
<td>1.05</td>
<td>1.85</td>
<td>0.57</td>
</tr>
<tr>
<td>8-9</td>
<td>1.88</td>
<td>3.11</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Average of all: 0.54 ± 0.197 (95% C.I.).

**Table 2**

<table>
<thead>
<tr>
<th>Heart</th>
<th>A</th>
<th>B</th>
<th>A:B</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-21</td>
<td>1.25</td>
<td>1.43</td>
<td>0.87</td>
</tr>
<tr>
<td>6-28</td>
<td>1.15</td>
<td>1.35</td>
<td>0.85</td>
</tr>
<tr>
<td>8-9</td>
<td>2.11</td>
<td>2.61</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Average of all: 0.846 ± 0.08 (95% C.I.).
Although quantitations of strain blood flow redistribution in the loaded ventricle must wait for techniques which can distinguish between the redistribution caused by ventricular pressure development and that caused by fiber shortening strain, the contribution of these stressed radial vessels is important to consider. This is because, if it is true, changing the length-tension characteristics of these vessels would influence the distribution of myocardial blood flow. The family of drugs consisting of the nitrites and the organic nitrates have been claimed to preferentially relax prearteriolar smooth muscle in coronary arteries (Harder et al., 1979). Because of the large amount of longitudinal smooth muscle in the radial coronary arteries (Elias, 1966), these drugs might be expected to influence the length-tension characteristics of these vessels. Interestingly, these agents seem to augment deep myocardial blood flow simultaneously with relaxing prearteriolar smooth muscle (Winbury et al., 1969). This seems to be the second and longer phase of a biphasic response; the shorter first phase, dilation of arteriolar vessels, may well cause redistribution away from deep myocardium (Forman et al., 1973). Although these drugs are very effective clinically for the relief of myocardial ischemia, there is reservation about their use in life-threatening situations because their mechanism of action is not understood. If modulation of the strain-dependent blood flow redistribution contributes to their action this knowledge could be of considerable practical importance.

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PASSIVE STIFFNESS OF HYPERTROPHIED MYOCARDIUM/Williams and Potter

Passive Stiffness of Pressure-Induced Hypertrophied Cat Myocardium

JOHN F. WILLIAMS, JR., AND RALPH D. POTTER

SUMMARY The effect of myocardial hypertrophy on passive stiffness was determined from the stress (o)-strain relationship of right ventricular papillary muscles from 18 pulmonary artery-banded and 21 non-banded cats. By use of Lagrangian strain, \( (1 - \frac{L}{L_0}) \), where \( L \) is initial muscle length, and instantaneous stress elastic constants \( \beta \) and \( \alpha \) were calculated from the equation \( \alpha = \alpha(e^\beta - 1) \). Elastic stiffness \( \left( \frac{d\alpha}{de} \right) \) was determined from the formula \( \frac{d\alpha}{de} = \beta \alpha + \alpha \beta \). Banding produced an average increase in RV mass of 70%. \( \beta \) averaged 14.2 ± 0.9 (SEM) and 16.0 ± 0.8 in the non-hypertrophied and hypertrophied muscles, respectively (0.10 > \( P > 0.05 \)), whereas \( \alpha \) averaged 0.17 ± 0.01 and 0.19 ± 0.01 g/mm², respectively (NS). However, elastic stiffness was significantly greater in hypertrophied muscles over the entire stress range. Contractile function varied widely among hypertrophied muscles but was not related to changes in stiffness. Thus, moderate degrees of pressure-induced hypertrophy are associated with a modest increase in the passive stiffness properties of the muscle, independent of changes in contractile function. Circ Res 49: 211-215, 1981

IT IS generally accepted that resistance to ventricular filling is increased in hearts hypertrophied by pressure loading. However, it has not been possible to determine conclusively which of the several determinants of ventricular diastolic stiffness are altered and in particular whether intrinsic muscle stiffness is changed (for review, see Grossman and McLaurin, 1976; Mirdsky, 1976; Glantz and Parmley, 1978). Although in vitro measurements of passive muscle stiffness circumvent many of the problems associated with measurements in intact hearts and a large amount of data is available from such studies, conflicting conclusions have been reported. Thus, some studies have reported unaltered stiffness of hypertrophied muscle (Grimm et al., 1963; Williams et al., 1966; Spann et al., 1967; Pannier, 1971; Bassett and Gelband, 1973; Cooper et al., 1973; Williams and Potter, 1974; Jouannet and Hatt, 1975), whereas others have found muscle stiffness to be increased (Mirsks and Parmley, 1973; Alpert et al., 1974; Bing et al., 1978).

Assessment of passive muscle stiffness in vitro has been based almost exclusively on the comparison of resting length-tension relationships in normal and hypertrophied muscles. However, the validity of assessing muscle stiffness solely from resting length-tension relations has been challenged by Mirsky (1976), who has proposed the elastic stiffness-stress relationship as a more accurate measure of passive stiffness. To emphasize this point, Mirsky (1976) determined the elastic stiffness-stress relationship from resting length-tension data published in a previous study (Spann et al., 1967) in which the resting length-tension relation of hypertrophied muscles was similar to that of non-hypertrophied muscles. According to Mirsky's (1976) calculations, the slope of the elastic stiffness-stress relationship and elastic stiffness at any stress level was greater in the hypertrophied muscles.

In addition to the use of different methods for assessing passive stiffness, it seemed possible that variations in contractile state of the muscles might also contribute to the varying conclusions regarding...
Redistribution of canine left ventricular myocardial blood flow in unloaded systole.

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