Left Ventricular Pressure-Volume Relationships and Myocardial Oxygen Consumption in the Isolated Heart

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THE HYPOTHESIS that the physical work performed during ventricular systole is largely determined by ventricular diastolic volume has had currency for the last 45 years. The oxygen cost of the heart's contraction has likewise been related to diastolic volume, and also to stroke work, mean arterial blood pressure times the heart rate, the integral of systolic pressure in time, and ventricular wall tension.

Many have attempted to identify the factors that determine the oxygen needs of the heart. Their conclusions have not been without controversy. As early as 1915, it was noted that "an increase of [cardiac] output was more economically performed than a comparable increase of 'aortic pressure'," in 1927 Starling and Visscher, and Hemingway and Fee, indicated that myocardial oxygen consumption was dependent on diastolic volume even when distention of the ventricle had progressed to the point of diminished stroke work. Later studies relating myocardial oxygen consumption to the area under the systolic pressure tracing were interpreted to show that at a constant heart rate systolic pressure was the preponderant, if not the sole, determinant of myocardial oxygen consumption, and strongly implied that the metabolic needs of the heart were not determined by diastolic volume or diastolic fiber length. Recent work in which left ventricular circumference was measured is consistent with this concept.

In these studies stroke volumes were known, but absolute volumes were not measured. The experiments described in this paper were designed to control absolute ventricular volume accurately.

The intact left ventricle of the dog has a fairly discrete blood supply and lends itself to metabolic determinations. By means of a previously described preparation, a combined pressure-volume and metabolic study was performed on an isovolumetrically contracting left ventricle. The preparation was also arranged to allow volume changes during systole and to permit the measurement of absolute volume. The isovolumetric pressure-volume studies, studies involving changes, and the results of concomitant metabolic determinations are reported in this paper. The intent was to relate myocardial oxygen consumption to ventricular pressure and volume, and to test specifically whether or not myocardial oxygen consumption is determined by diastolic volume.

Methods

Isovolumetric Studies

The isolated heart preparation has been described previously in full and will be described briefly herein. A schematic diagram of the preparation used for isovolumetric studies is seen in figure 1.

Hearts from healthy mongrel dogs were rapidly excised under chloralose-urethane anesthesia. A lucite button was ligated in the vicinity of the aortic cusps with a suture passed under the left coronary artery. By this procedure the left ventricular cavity was completely isolated from the coronary circulation. The right coronary artery was ligated, as were the bundle of His and the inferior and superior venae cavae. A catheter was placed in the coronary sinus and led to the outside through a perforation in the right atrium. Cannulas were ligated in the pulmonary artery, aorta, and mitral orifice.

The isolated heart was then perfused with arterial blood from a healthy anesthetized donor. Blood was pumped from the donor dog to a reservoir of adjustable height from which it passed through a filter, a Shipley-Wilson rotameter, and...
warming coils, and entered the coronary circulation of the isolated heart through the aortic cannula. Blood was withdrawn from the pulmonary cannula under slight negative pressure and returned to the donor through a second reservoir and filter.

One opening in the mitral cannula was connected to a pressure transducer* that continually monitored intraventricular pressure on a Sanborn polyviso recorder. The other opening was connected to a syringe with which absolute ventricular volume could be determined, and varied at will; the ventricular cavity was evacuated and known volumes of saline injected. Volumes were rechecked by aspiration after each experimental run. Pressure-volume points were determined from the injected volumes and the recorded systolic and diastolic pressures. After each change in volume, time was allowed before recording and sampling for stabilization to occur.

Small leads were attached to the epicardium for stimulation of contraction and recording of the electrocardiogram. The stimulus was provided by an electronic pulse generator† for defibrillation, 1 to 3 amperes of 110 volts 60—A.C. was used. Throughout this study heparin was used as an anticoagulant.

Studies Involving Stroke Volume

In order to study volume changes during systole, the preparation was modified so as to allow the ventricle to compress air. A schematic diagram of the modified preparation is shown in figure 2.

For use in this report, the terms "isovolumetric" and "isobaric" were selected advisedly in contrast to "isotonic" and "isometric." Although isotonicity and isometricity were approached, the experimental conditions do not permit the strict use of these terms.

The heart was prepared in exactly the same manner as described for the isovolumetric studies, except that the ventricular cavity contained air instead of saline. The mitral cannula was connected to a Krogh spirometer by tygon tubing (2 cm. I.D.) through an arrangement of hand valves. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber. The Krogh spirometer, in turn, was enclosed in a 100-L chamber which was maintained at the desired diastolic pressure. When both hand valves shown in figure 2 were open, the relatively small stroke volume of the heart caused a negligible rise of pressure in the 100-L chamber.
Results

Isovolumetric Studies

Effect of Heart Rate on Ventricular Pressure-Volume Relationships

Using the preparation in which the heart contracted isovolumetrically, it was possible to plot peak systolic pressure and end-diastolic pressure against a range of ventricular volumes. The effect of heart rate on ventricular pressure-volume relationships was studied in six hearts. Figure 3 is an example of one experiment in which peak systolic and end-diastolic pressure-volume points were obtained at heart rates of 30, 122, 182, and 254. Points obtained in diastole at the lower rates could be superimposed. At the higher rates the ventricle appeared to be less compliant in diastole. The reason for this is suggested by the rapid tracings in the lower half of figure 3, which show diastolic pressures while the ventricle contracted at three different heart rates and while ventricular volume was maintained constant. From these tracings, it can be seen that relaxation was virtually complete at rates of 122 and 182, but was incomplete at 254. In one experiment performed under hypothermic conditions (29 C.), the ventricle was unable to relax completely even at low heart rates, illustrating the temperature dependency of the rate of relaxation. At any given volume, the ventricle was capable of a higher peak systolic pressure at a higher heart rate, demonstrating the treppe phenomenon.

Effect of Epinephrine and Digitalis Glycosides on Ventricular Pressure-Volume Relationships

With the heart contracting isovolumetrically, pressure-volume points were obtained during control periods and after the infusion of drugs into the perfusing blood. As illustrated in figure 4, the location of points obtained in diastole showed no significant change from control points after digitalization (0.2 to 0.36 mg. lanatoside C [0.8 to 2.4 cat units]) in six hearts. In one additional experiment, digitalization with a relatively larger dose (4 cat units of acetylstrophanthin) shifted the diastolic pressure-volume curve 4 mm. Hg upward, indicating a slight decrease in the compliance of the ventricle in diastole.

Digitalis was given in increments to toxicity. Reported pressure-volume determinations
were taken following the dose prior to that which produced dysrhythmia. During these determinations, there was invariably an augmented contraction and usually a change in the position of the S-T segment of the electrocardiogram when compared with controls.

In five hearts, pressure-volume points were obtained before, during, and after infusion of epinephrine (10 μg./min.) or norepinephrine (38 μg./min.) into the perfusing blood. Again the location of points obtained in diastole during infusion of these drugs showed no significant change from control points. As illustrated in figure 4, the peak systolic pressure-volume points alone reflected the effect of the drug on ventricular pressure-volume relationships. On the lower part of figure 4 is a pressure tracing taken before and during the infusion of epinephrine at approximately equal ventricular volumes. It is included to show that at the heart rate chosen for these studies, relaxation was virtually complete in diastole. Throughout each experiment heart rate was maintained constant.

Studies Involving Stroke Volume
Pressure-Volume Studies at a Constant Diastolic Volume

For studies involving volume changes, the second preparation described under "Methods" was used. Figure 5 is an example of the polyviso tracings obtained in one experiment. On the four panels from top to bottom are left coronary flow, electrocardiogram, left ventricular volume, and intraventricular pressure. In this experiment, the heart at a constant diastolic volume was allowed to compress air into successively smaller air chambers, developing more pressure as the size of the air chamber was decreased (sections A to E). Under these circumstances, the Krogh spirometer recorded only the diastolic volume. Between successive decreases in the size of the air chamber the heart was allowed to contract isobarically (sections A' to E'). Here the Krogh spirometer recorded absolute volume during both systole and diastole. On the far right of the third panel is a rapid trace of the volume changes during the isobaric contractions (section E').

From tracings like those in figure 5, it became evident that the heart was capable of developing a wide range of peak systolic pressures without an accompanying change in diastolic pressure or volume. An incidental finding shown by figure 5 was that left coronary flow increased while the heart was developing pressure and decreased while the heart contracted isobarically, despite the fact that the perfusion pressure remained constant.

With this altered preparation it was possible to plot pressure-volume diagrams similar to those presented for the isovolumetric studies, except that volume changes accompanied each contraction. Knowledge of both diastolic pressure and volume allowed the plotting of diastolic pressure-volume points. Knowledge of peak systolic pressure combined with the determination of volume as described previously enabled the plotting of peak systolic pressure-volume points. As illustrated in one experiment by the control peak systolic pressure-volume points connected by a heavy line on the left-hand side of figure 6, the ventricle at a constant diastolic volume was
Polyviso tracing of coronary flow, electrocardiogram, diastolic ventricular volume, and ventricular pressure of the heart compressing air into successively smaller chambers (A to E). Sections (A' to E') show isobaric contractions with volume changes, rapid tracing at far right (E'). Note that the heart could develop a wide range of peak systolic pressures without any accompanying change in diastolic pressure and volume.

In 23 out of 29 experiments in which the ventricle compressed air into a series of different volumes, the relationship between peak systolic pressure and systolic volume was linear, describing a straight peak systolic pressure-volume line, as illustrated by the heavy line joining the control points on the left-hand side of figure 6. In six experiments, there was a slight but definite concavity of this line to the right. In general, the peak systolic pressure-volume line was straighter at the higher systolic pressures.

Pressure-Volume Studies at Multiple Diastolic Volumes

In 10 experiments, peak systolic pressure-volume lines were determined as described before from contractions that originated from two or more well-separated points on the diastolic pressure-volume curve. One of these experiments is illustrated on the right-hand side of figure 6 where the thin compression lines have been omitted except for the two parallel ones. In 8 out of 10 experiments, the location of the higher portions of the peak systolic pressure-volume lines could be superimposed regardless of the diastolic volume. Again the determination and the superimposability of these lines were questionable at the lower pressures.

Epinephrine and Digitalis Glycosides

In two experiments, the infusion of nor-epinephrine (0.38 μg./min.) into the perfusing blood shifted the peak systolic pressure-volume points upward and to the left, as illustrated on the left-hand side of figure 6. In two additional experiments, similar effects were obtained with digitalis glycosides (0.2 μg. cetalanid). Invariably, poor myocardial performance induced by the infusion of toxic levels of potassium or procaine amide or frequent attempts at electrical defibrillation was manifested by a decrease in the slope of the peak systolic pressure-volume line. Recovery, in turn, was accompanied by an increase in this slope as it approached control levels.

Development of Pressure Following Isobaric Contractions

In 10 experiments, the lower hand valve in figure 2 was replaced by an electronically operated solenoid valve timed to close at any preselected time interval after the stimulus. The upper hand valve remained open and the tube leading to the compression chambers was closed. With this modification, the heart was allowed to develop pressure into a small volume after first undergoing an isobaric contraction. On the left of figure 7 is a pressure-
Figure 6

(Left panel—heavy line) control. Pressure-volume plot of peak systolic pressure-volume points when the heart is compressing air into chambers of varying sizes. The (thin lines) represent the pressure-volume change during systole. Above control are peak systolic pressure-volume points obtained during infusion of epinephrine. Note that all contractions originate from the same diastolic pressure-volume point. (Right panel—solid and dashed lines) pressure-volume plot of peak systolic pressure-volume points when the heart is compressing air into different sized chambers from different diastolic volumes. All but two thin compression lines have been omitted. Note that the peak systolic pressure-volume lines can be superimposed despite moderate changes in the diastolic pressure-volume point.

Figure 7

(Left panel) pressure-volume plot of peak systolic pressure-volume points attained by contractions originating from the same point (X) on the diastolic pressure-volume curve, proceeding to eject different volumes isobarically, and subsequently at points (A, B, C, etc.) compressing air into a small chamber. Note that the capacity of the heart to develop pressure diminishes as the isobaric portion of the contraction increases. (Right panel) pressure-volume plot of peak systolic pressure-volume points attained by contractions originating from different points on the diastolic pressure-volume curve (X, Y, Z), proceeding to eject varying volumes isobarically, and subsequently compressing air into a small chamber.

lines was not found in all experiments. Again, the position of the peak systolic pressure-volume lines was not shown to be consistently and significantly altered by a moderate range of diastolic pressures and volumes.

Isobaric Ejection of Volume at Different Systolic Pressures

In seven experiments, the upper hand valve in figure 2 was closed and the Japanese valve reversed, preventing any passage of air from the 100-L. chamber to the heart. The compression chambers were removed, and through the tube originally leading to the compression chambers, the ventricle was maintained at a preselected diastolic pressure from an external air-pressure source. The 100-L. chamber was maintained at a chosen systolic pressure. During systole, the heart compressed the air within the ventricle and the connecting tubing until it achieved a pressure equal to that of the 100-L chamber; at this point the Japanese valve opened, preventing any fur-
Figure 8

(Lower left panel) pressure-volume plot of peak systolic pressure-volume points attained by contractions originating from the same point (X) on the diastolic pressure-volume curve, proceeding to develop pressure into a small chamber, and subsequently (J to O) ejecting a volume isobarically at the indicated systolic pressure. Note that the capacity of the heart to eject a volume diminishes with increases in the pressure at which that volume is ejected. (Lower right panel) pressure-volume plot of peak systolic pressure-volume points attained by contractions originating from different points on the diastolic pressure-volume curve (P to Q), proceeding to compress air into a small chamber, and subsequently ejecting the volume isobarically at different pressures. (Top) rapid trace of pressure and volume changes in the above experiment. Note the flat-topped pressure wave while volume is being ejected.

Metabolic Studies

Isovolumetric Loading

In 14 experiments, myocardial oxygen consumption was determined while the heart contracted isovolumetrically. In each experiment the ventricular cavity was first evacuated with a syringe. A known volume of saline was then injected, and after allowing two minutes to achieve a steady state, blood samples were obtained from the coronary sinus and aortic stump while the intraventricular pressure and coronary flow were continuously monitored. The procedure was repeated in the order of increasing volumes. Pressure-volume relationships were plotted as shown in figure 9, together with their associated myocardial oxygen consumptions in cc. per minute. In all 14 experiments, a rise in contained volume was accompanied by a rise in both systolic pressure and myocardial oxygen consumption. While contracting isovolumetrically, the hearts consumed substantial amounts of oxygen despite the fact that there was no stroke volume and hence no mechanical stroke work.

In nine hearts, myocardial oxygen consumption was compared at identical volumes and different rates. The treppe phenomenon was demonstrated in that increases in rate were accompanied by increases in systolic pressure. The oxygen consumed per minute by the isovolumetrically beating heart invariably increased with an increase in heart rate. In those experiments in which the treppe effect was substantial, the oxygen consumed per beat likewise increased with an increase in heart rate.
In figure 10, myocardial oxygen consumption is plotted against peak developed pressure times rate, volume times rate, and the area under the systolic portion of the pressure tracing times rate. To the extent that ventricular wall tension could be estimated by the application of the Laplace relationship between pressure and tension of a sphere, (\(T = \frac{P \times 4\sqrt{\text{vol.}}}{3}\)), myocardial oxygen consumption could also be plotted against peak developed tension times rate. As illustrated by figure 10, the oxygen consumption of the isovolumetrically contracting heart could be equally well correlated with each of these parameters in the absence of stroke work.

Isobaric Loading

In nine experiments, the isolated heart was allowed to eject a stroke volume of air without developing pressure, as described above in "Methods: Studies Involving Stroke Volume." The heart was prepared as shown in figure 2. All isobaric studies were conducted as a constant heart rate.

With data obtained in the above manner, pressure-volume relationships of the isobarically contracting ventricle were plotted, together with their myocardial oxygen consumptions, as illustrated in one experiment by the horizontal lines in figure 11. In all experiments, an increase in intraventricular pressure was accompanied by an increase in systolic and diastolic volume and an attending increase in myocardial oxygen consumption, despite the fact that there was no developed pressure. In nine additional experiments in which the ventricle contracted isobarically at a pressure of 20 mm. Hg and at a mean heart rate of 100, the hearts consumed an average of 3.36 cc. O2/100 Gm. left ventricle per minute. The Laplace principle, described in the results of the isovolumetric study, could again be applied to permit the estimation of ventricular wall tension. During isobaric contractions, where there were volume changes in the absence of pressure changes, peak systolic tension was less than diastolic tension.

Isobaric and Air-Compression Loading

In 12 experiments, myocardial oxygen consumption was determined while the heart contracted isobarically, as previously described. Following this control study, the upper hand valve was closed (fig. 2) so that during systole the heart compressed air into a small chamber while diastolic pressure remained unchanged. Diastolic volume was continuously monitored and stroke volume could be determined by the application of Boyle’s law. After a two-minute period, repeat blood samples were obtained and myocardial oxygen consumption was again determined. Throughout these studies heart rate was maintained constant.

In all experiments, the heart consumed more oxygen when it compressed air into the small chamber than it did during the preceding isobaric control period, despite the fact that the diastolic pressure and volume did not change. Figure 11 is a pressure-volume diagram of an experiment performed at one...
diastolic volume and later repeated at another. The horizontal lines are the isobaric controls. The diagonal lines leaning to the left show the systolic pressure-volume course of the ventricular cavity compressing air into the small chamber. These are drawn straight but actually are short segments of a large hyperbola. Oxygen consumptions are shown at the peak systolic portion of each line. Since widely different oxygen consumptions were obtained from contractions originating from the same diastolic pressure-volume point, it follows that myocardial oxygen consumption is not determined by diastolic volume.

In seven experiments, oxygen consumptions were obtained while the heart compressed air into different-sized chambers from two diastolic volumes. Again heart rate was maintained constant. Figure 12 is an example of one of these experiments. In these seven studies, myocardial oxygen consumption could be equally well correlated with peak systolic pressure, peak systolic tension, systolic volume, and the area under the systolic portion of the pressure tracing. As seen in figure 13, these correlations do not appear to be consistently affected by diastolic pressure or volume within the accuracy of the method.

**Discussion**

**Isovolumetric Studies**

The systolic pressure augmentary effect of increased heart rate (treppe) is accompanied by apparent decreased diastolic compliance only at very rapid rates. During hypothermia where relaxation is prolonged, this effect is greatly enhanced. Such findings are consistent with studies in which measurements of ventricular circumference in an open-chest preparation were made.14

The increased force of contraction produced
by epinephrine or digitalis glycosides is not accompanied by an increase in ventricular compliance during diastole. This would tend to favor the hypothesis that the positive inotropic effect of both these drugs is essentially due to an increased systolic force rather than a change in diastolic compliance. In view of the fact that epinephrine shortens relaxation time, it is quite likely that at rapid rates where relaxation is incomplete the infusion of epinephrine could appear to increase diastolic compliance.

Studies Involving Stroke Volume

From the experiments illustrated by the left-hand side of figure 6, it is apparent that at a given diastolic volume the heart is capable of a spectrum of developed pressures and stroke volumes, depending on the manner in which the ventricle is loaded. The spectrum of developed pressures and stroke volumes—and hence stroke work—is obtained from a constant diastolic volume and in no way invokes Starling’s law. To be sure, the heart has the ability to develop greater pressures and stroke volumes when the diastolic volume is large, providing load conditions remain unchanged. This is illustrated by the parallel lines on the right-hand side of figure 6 which represent the pressure-volume course of the ventricle while it is compressing air into identical chambers from different diastolic volumes. These observations illustrate that at a constant diastolic volume the heart is capable of a wide pattern of pressure-volume work, depending on load conditions, and that Starling’s law applies only in the special case where load conditions remain more or less unchanged.

The experiments illustrated by figures 6, 7, and 8 imply that the pressure-volume diagram of the isolated heart is described by a line formed by a full range of peak systolic-pressure-volume points, and the diastolic-pressure-volume line. Thus, from any diastolic-volume, the ventricle develops maximum pressure under isovolumetric conditions, and maximum stroke volume at or near isobaric conditions. This pressure-volume diagram is analogous and, incidentally, similar to the length-tension diagrams of striated muscle (from length 100 down), and describes the potential energy in terms of pressure-volume work that the ventricle is capable of delivering. A peak systolic pressure-volume line appears regardless of whether pressure and volume changes occur simultaneously (fig. 6), whether volume is expelled first and pressure developed afterward as illustrated by figure 7, or pressure is developed first followed by ejection of volume (fig. 8). From experiments illustrated by figure 7, it appears that at a constant diastolic volume the capacity of the ventricle to develop pressure diminishes with stroke volume. Likewise, from experiments illustrated by figure 8, at a constant diastolic volume.

Figure 12

Pressure-volume diagram of the heart during isobaric contractions (horizontal line) and during air-compression studies in which the heart compressed air into chambers of varying volume (lines diagonally to the left). VO₂ in cc/min. at the peak systolic portion of each line. Heart rate constant.
volume the capacity of the heart to eject a volume lessens with increases in the pressure at which that volume is ejected. At first approximation these relationships are roughly linear. Within the accuracy of the method, they do not appear to be greatly altered by moderate changes in diastolic volume.

The manner whereby epinephrine and digitalis affect the pressure-volume diagram of the isolated heart may help to describe more accurately the pharmacological action of these drugs. Essentially, epinephrine increases the slope of the peak systolic pressure-volume line so that the effect of the drug is greater as isometricity is approached. As illustrated by the left-hand side of figure 6, the infusion of epinephrine under isobaric loading was accompanied by little volume change. As the heart was allowed to develop more pressure, the identical dose of epinephrine caused at least a twofold volume change as well as a sizable increase in developed pressure when compared with controls. Similar findings were observed with digitalis glycosides.

It is not suggested that these findings be directly applied to an explanation of the variable clinical efficacy of epinephrine and digitalis. Nevertheless, at least for the isolated heart, they serve to illustrate its physiological and pharmacological dependency on load conditions.

**Metabolic Studies**

In the isovolumetric studies, in which there was no stroke volume and therefore no stroke work, the heart consumed substantial quantities of oxygen. This does not imply that individual muscle fibers were not performing work. Such an implication would necessitate isometric contraction of all the muscle fibers, a circumstance which doubtless did not exist. It does imply, as suggested by others, that stroke work in itself does not determine the oxygen needs of the heart.

While the heart contracted isobarically, myocardial oxygen consumption was considerably lower than in the isovolumetric studies, but was nevertheless above basal levels for isolated hearts. In view of this and the fact that the ventricle developed no measurable pressure during contraction, it is evident that the development of pressure cannot be the sole factor that establishes the amount of oxygen required by the heart.

Likewise, the systolic change in ventricular wall tension cannot be the only determinant of myocardial oxygen consumption, unless one postulates a metabolic cost to the decrease of tension during systole. In order to apply the Laplace principle as described, one has to make assumptions such as a spherical ventricular shape, an infinitely thin ventricular wall, as well as equal distribution and orientation of all the muscle fibers. To the extent that these assumptions are accepted, one can conclude that during an isobaric contraction, in which oxygen consumption is above basal levels, tension diminishes during systole.

As shown by the air-compression studies, a spectrum of oxygen consumption levels could be obtained while the heart contracted.
MYOCARDIAL OXYGEN CONSUMPTION

from the same diastolic pressure-volume point. From these experiments it follows that myocardial oxygen consumption is not determined by diastolic volume, as previously claimed. This does not mean that myocardial oxygen consumption is completely unaffected by diastolic volume. It does imply, however, that the energy required for the contraction of a particular muscle fiber is not dictated by its preceding diastolic fiber length, and that the state of the heart in systole rather than diastole determines its oxygen needs.

In the air-compression studies, in which the load components of pressure changes and volume changes were varied, myocardial oxygen consumption could be related to both peak systolic pressure and systolic volume. In addition, there appears to be a consistent relationship between peak systolic pressure and systolic volume, regardless of the sequence of pressure and volume changes in the loading, and irrespective of moderate changes in diastolic pressure. By means of pressure-volume plots this relationship has been expressed as a peak systolic pressure-volume line that is stable barring deterioration or enhancement of myocardial performance. In view of the relationship between peak systolic pressure and systolic volume, it is evident that if oxygen consumption is related to one it would have to be related to the other.

Peak systolic pressure and systolic volume, in turn, are largely determined by the manner of loading. When the heart compressed air into progressively smaller chambers, peak systolic pressure increased, stroke volume decreased, and the ventricle consumed more oxygen as it approached an isovolumetric contraction. It is reasonable to assume that as the heart approached an isovolumetric contraction, the muscle fibers likewise approached an isometric contraction and that this was accompanied by an attending increase in their oxygen use. Within the limits measured, these findings are consistent with those of others who measured the oxygen uptake of isolated muscle strips and illustrate the dependency of myocardial oxygen consumption on load conditions.

Summary

An isolated dog-heart preparation, in which absolute volumes were known, was employed to determine left ventricular pressure-volume relationships and myocardial oxygen consumption. Loading was varied from the extreme of zero pressure change to zero volume change during systole. Maximum peak systolic pressures were developed by isovolumetric, and maximum stroke volumes by isobaric contractions. When the load was varied to allow both pressure and volume to change in systole, the peak systolic pressures and the simultaneously determined ventricular volumes could be plotted as a "peak systolic pressure-volume line." Moderate changes in diastolic volume had little effect on the position of the line, and the mechanical work of the heart appeared to depend on the nature of the load rather than the diastolic volume. Epinephrine and digitalis glycosides did not affect diastolic pressure-volume relationships. Heart rate affected the diastolic pressure-volume curve only at rapid rates, where changes in the rate of relaxation produced apparent differences in compliance. Myocardial oxygen consumption is shown to be correlated with peak systolic pressure or volume, and is not mainly determined by either diastolic volume or stroke work.

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References


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