Registration of Left Ventricular Volume Curves in the Dog with the Systemic Circulation Intact

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A method is described whereby it is possible to obtain volume curves from the left ventricle of an open-chested dog with an essentially intact systemic circulation. Several applications of such univentricular records to the study of the heart's performance are suggested and examples of analyses from recorded curves are presented. Changes in the physicochemical properties of the myocardium are seen to accompany alterations in the chemical environment of the heart.

Volume curves have been obtained from the single ventricle of the reptilian heart and from both ventricles of the isolated mammalian heart. However, no satisfactory method has been available for obtaining such records from one ventricle of the mammalian heart in situ. Accurate determination of the volume changes of a single mammalian ventricle permits pursuit of several lines of study. Combined ventricular volume curves have proven unsatisfactory for these studies because the changes in the volume of one ventricle need not be proportional to those of the other and the end-diastolic volumes of the two may change in opposite directions. Some of the factors subject to investigation through the use of the volume curve of a single ventricle operating in situ are: (1) The role of end-diastolic volume in the regulation of cardiac work and the uptake of substrates and release of metabolites by the myocardium. (2) Variations in ventricular diastolic tone, i.e., the pressure-volume characteristics of the fully-relaxed ventricle. This can be evaluated by measuring simultaneously the end-diastolic volume and end-diastolic pressure. (3) Variations in the systolic residue of the heart and the latter in the response of the ventricle to altered conditions of work. (4) Variations in ventricular systolic tone, i.e. the pressure-volume characteristics of the ventricle at the end of systole. (5) The precise amount of useful work performed by the ventricle; while the product of mean systolic blood pressure and stroke output can be used as an index of useful work, the true quantity of the pressure-energy imparted to the ejected blood is the sum of the products of each unit of the stroke output and the pressure at which it is ejected (∑PdV); this latter quantity can be calculated from the pressure and volume curves of the ventricle. (6) The kinetic work of the heart, i.e. the work required to impart velocity to the ejected blood. The rate at which the blood leaves the ventricle from moment to moment can be measured directly from the volume curve. (7) Work diagrams for individual beats of the single ventricle. Such a work-diagram is the integrated pressure-volume relationship of the ventricle during the cardiac cycle. ∑PdV can be calculated from the systolic portion of this curve; and the impedance to filling during various phases of diastole can be obtained from the diastolic portion.

Methods

By using a previously described preparation, it was possible to obtain volume and pressure curves simultaneously from the left ventricle of an anesthetized, open-chested dog with an essentially intact systemic circulation. In addition, it was possible to make concurrent determinations of coronary flow and left ventricular minute output, of arteriovenous
oxygen differences across the heart and of pressures throughout the cardiovascular system.

With this preparation, left ventricular pressure was measured by means of an intraventricular catheter introduced through the tip of the left atrial appendage and connected to a Sanborn electromanometer. Ventricular volume was determined by placing a cardiometer in the usual manner over the ventricles after removing the pericardium. The rubber diaphragm rested upon the atrioventricular junction, making a tight seal. The side-arm of the cardiometer was connected to the top of a 500 cc. Kelly bottle in which an air-water junction was made. The resultant pressure changes were transmitted through water-filled lead tubing to a Statham strain-gauge and recorded simultaneously with the intraventricular pressure on a Sanborn Twinviso Cardiette. The volume recording system was calibrated at the end of the experiment by adding water from a calibrated syringe. The technical errors encountered in the recording of volume curves have been discussed in the original report on ventricular oncometry.

The right heart in this preparation was working under conditions of unusually low output and pressure because the systemic venous return was shunted from the venae cavae to the right pulmonary artery. The effects of changes in right ventricular volume were thus markedly reduced because the right ventricle was pumping only the coronary flow. This constituted method I. The volume curves presented in figure 1 were obtained with this method.

By further modification it was possible to practically eliminate variations in the diastolic volume of the right ventricle from the volume curves, and to reduce the right ventricular stroke volume to extremely low values. The right heart was kept free of blood by directing its outflow into a reservoir bottle placed at a level below the heart; this established a siphon and reduced the pulmonary artery pressure below atmospheric. The low-lying reservoir bottle was also used to drain the venae cavae, the blood being pumped mechanically to the left heart through the pulmonary arteries. This constituted method II. The volume curves presented in figures 3, 4 and 6 were obtained with this method.

RESULTS

Pressure and volume curves recorded from the left ventricle in a few experiments are presented and analyzed in order to illustrate the analyses enumerated above. It was necessary to estimate the changes occurring in early systole and early diastole due to movement of the heart into and out of the cardiometer, an error inherent in the method.

The effect of norepinephrine on a failing heart is shown in figure 1. Segment A is a tracing of simultaneous left ventricular pressure and volume curves obtained from a failing heart by method I. The systolic pressure was 44 mm. Hg, the stroke output 21 cc. and the heart rate 59 beats per minute. Cardiac output thus was 1240 cc per minute. Fifteen seconds later, after injection of 0.2 mg. of norepinephrine, segment B was obtained. Systolic blood pressure increased to 60 mm. Hg, stroke output rose to 24 cc. and the heart rate increased to 70 beats per minute, and the ejection time decreased from 0.18 to 0.16 second. Cardiac output rose to 1680 cc. per minute. End-diastolic volume decreased 12 cc., end-diastolic pressure fell 3 mm. Hg and the systolic residue decreased 15 cc. The cardiac output increase was temporary, returning to the control level soon after this. This transient rise of output was due in part to a decrease in systolic residual volume, in part to an increase in coronary flow...
Work diagrams constructed from the curves illustrated in figure 1 show the effects of norepinephrine on the heart's performance (fig. 2). The decrease in end-diastolic pressure and volume following norepinephrine is seen by comparing points A and A' in this figure. The work done by the heart in imparting pressure-energy to the blood is equal to the area under the curves of figure 2 during the ejection phase (ABC and A'B'C') using the end-diastolic pressure as the zero line. The work in the control curve was equal to 1.08 joules per beat, after infusion of norepinephrine it increased to 1.73 joules per beat. This represents a greater increase per minute (from 66 to 121 joules per minute) because of the increase of heart rate.

The kinetic work during ejection (ABC and A'B'C') for these two beats can be calculated in ergs from the formula: work = \( \frac{1}{2} mv^2 \), where \( m \) is the mass ejected in grams and \( v \) is the velocity of the blood passing into the aorta in cm. per second. The aortic cross-sectional area was approximately 3 cm.\(^2\). The velocity of 1 cc. of blood passing into the aorta in one second would thus be 0.33 cm. per second, discounting effects of stream-line flow and alterations in orifice size. In the control beat (fig. 1A) the first cc. of blood was ejected in \( \frac{1}{25} \) second so that the velocity of ejection of that cc. of blood was 8.3 cm. per second (25 \( \times \) 0.33 cm./sec.). The blood mass was approximately returning to the left heart, and in part to a decrease in the volume of the left atrium and pulmonary vascular bed.

Figure 3. Simultaneous curves of left ventricular pressure (above) and volume (below) illustrating effects of norepinephrine. Scales as in figure 1. A, control curve from a stable preparation; B, 30 seconds after rapid infusion of 27 uc. norepinephrine; C, 90 seconds after ending the infusion, 5'/4 minutes after it was started. Curves demonstrate an increase in left ventricular diastolic tone. Discussed in text.
one gram, so \( \frac{1}{2} \text{mv}^2 \) is equal to 34 ergs (\( \frac{1}{2} \times 1 \times 8.3 \times 8.3 \)). The second cc. was ejected twice as rapidly (\( \frac{1}{2} \) second), therefore, the work of ejection was four times as great. The total kinetic work of ejection thus calculated, was 0.05 joules in the control beat and 0.10 joules during infusion of norepinephrine.

A steeper rise of pressure during the latter part of diastole in D'A' than in DA (fig. 2) indicates that the impedance to diastolic filling was greater during infusion of norepinephrine.

A change in the diastolic tone of the ventricle is demonstrated either when end-diastolic volume or pressure changes with the other remaining constant, or when end-diastolic volume and pressure change in opposite directions. The same is true in determining changes in systolic tone. The effect of norepinephrine on the systolic tone of the left ventricle can be seen in figure 2 where an increase of end-systolic pressure is associated with a decrease of end-systolic volume. This represents an increase in systolic tone. The effect of norepinephrine on diastolic tone can be seen in figure 3. These volume curves were obtained with method II. Three successive records from a non-failing heart are presented showing conditions before and during rapid intravenous infusion of 2\( \gamma \)/cc. norepinephrine; the delivery of blood by the pump to the left heart being kept constant. The cyclical variation in the volume curves was related to the artificial respiration. End-diastolic volume decreased 3 to 4 cc. during the infusion of norepinephrine (when beats in the same part of the respiratory cycle were compared). However, end-diastolic pressure rose at first, from 8 to 9 mm. Hg, then returned to control level in spite of the continuing fall of volume.* Such a fall of end-diastolic volume

* The rise of end-diastolic pressure accompanied a temporary rise of left ventricular systolic pressure while heart rate and cardiac output remained constant.
Fig. 6. Simultaneous curves of left ventricular pressure (above) and volume (below) showing premature systoles which appeared during the early stages of asphyxia. Scales as in figure 1. Discussed in text.

represents an increase in ventricular diastolic tone.

A more striking increase in diastolic tone was seen during the development of asphyxia following cessation of artificial respiration. A progressive rise of end-diastolic pressure unaccompanied by a change in end-diastolic volume can be seen in figure 4. Thirty seconds after artificial respiration was stopped left ventricular end-diastolic pressure rose from 8 to 13 mm. Hg. Three minutes later, end-diastolic pressure rose to 20 mm. Hg, though end-diastolic volume had not changed. The three work diagrams in figure 5 were constructed from a cardiac cycle from each period in figure 4. In addition to the increase in ventricular diastolic tone, these curves demonstrate a progressive increase in both systolic tone and diastolic impedance.

Several premature beats occurred during early stages of asphyxia, two of which are shown in figure 6. The early diastolic volume curves of the premature beats were similar to those of the normal beats. However, part of the phase of diastasis was omitted in the former. The stroke volume of the premature beats was less because of both a smaller end-diastolic volume and a greater systolic residue. Similar changes were seen in sinus arrhythmia. Figure 7 is a work diagram constructed from the second, third and part of the fourth beat in figure 6B. The "control" beat preceding the premature beat appears as the larger loop, the premature beat as the small loop within this. The "compensatory" beat after the pause was graphed in part and demonstrates a larger end-diastolic pressure and volume. Its ejection took place at a higher pressure and volume than the "control" beat preceding the premature systole.

**DISCUSSION**

The results obtained with this intact preparation, like those in the unanesthetized mammal7,8 and the isolated mammalian heart,9 demonstrate that the physicochemical properties of the heart are subject to change. These studies, all based on the analysis of the pres-
sure-volume relationships of a single ventricle, have revealed that changes in the visco-elastic characteristics of the myocardium can not be ignored when considering the dynamics of cardiac function.

The curves relating pressure to volume in the fully-relaxed and fully-contracted ventricle reflect the visco-elastic properties of these two static states and are the limits within which the work diagram is inscribed. The latter represents the sequence of dynamic changes in the pressure-volume characteristics of the myocardium during the cardiac cycle.

The present results demonstrate that the static properties of the heart are subject to change. Alterations in both diastolic and systolic tone were found to occur in response to changes in the chemical environment of the heart.

The increase in the work of the heart which followed infusion of norepinephrine (fig. 2) was associated with an increase of systolic tone and diastolic impedance. It thus appears that norepinephrine “tightened” the molecular structure of the failing myocardium at the same time that it increased the rate and strength of the cardiac systole. A similar effect on a non-failing heart is seen in figure 3 where norepinephrine also caused an increase in ventricular diastolic tone. The mechanism by which this change is effected is at present a matter for speculation.

The effects of asphyxia were like those of norepinephrine; the amount of work performed increased at a constant end-diastolic volume, the rate of ejection increased and there was again an increase in diastolic impedance and in ventricular diastolic and systolic tone. Thus, it may be possible that these effects of asphyxia are mediated in part through the release of sympathomimetic amines.

It has been shown that the regulation of the heart beat by end-diastolic volume is not primary in the response of the intact animal’s heart to a maintained stress, such as exercise. Rather, this mechanism acts as a negative feedback, maintaining equilibrium in the face of beat to beat changes in the heart’s performance. This was demonstrated in the premature beats seen in these experiments. The end-diastolic volume of the compensatory beat following the weak premature beat was larger as a result of the increased systolic residue (figs. 6 and 7). Equilibrium tended to be restored through the increased strength of the compensatory beat. Thus, the maintenance of a steady output in the face of beat to beat changes can be considered to be an important physiologic role of this end-diastolic volume mechanism.

The data discussed in this report are not to be considered definitive. Rather they are hopefully presented in order to stimulate further investigation with this method.

SUMMARY

A method for recording volume curves of the left ventricle in an open-chested dog with an intact systemic circulation is described and two variations of the method are outlined. Examples of the types of analysis possible with this technic are presented and several lines of study indicated. The importance of changes in the ventricular diastolic and systolic tone are suggested. The addition of single ventricle volume curves to the data presently recorded with this preparation permits a more complete approach to analysis of the factors regulating the heart beat in the intact animal.

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