Left Ventricular Function Described in Physical Terms

By Dean L. Franklin, Robert L. Van Citters, M.D., and Robert F. Rushmer, M.D.

The first step in any physiological investigation is to define the problem. If this definition is ambiguous, the experimental results will most probably be inconclusive or may even prove irrelevant. To secure conclusive results, the investigator must select appropriate variables for measurement. Ideally, the terms comprising the definition of the problem should be sufficiently precise to enable him to identify these essential variables automatically. For example, if the problem centers around the work performed by the ventricular chamber, the variables to be measured are directly indicated by the physicists' definition of "work." On the other hand, a problem of cardiac function couched in terms of changes in "contractility" would be approached differently in different laboratories, according to the local interpretation of the term. Since "contractility" is variously employed to indicate "vigor" of contraction, rate of ejection, degree of ejection, rate of rise in ventricular pressure, or slope of a "function curve," what physical variables should be measured to determine whether this property has been altered under a specific experimental condition?

The significance of changes in the performance of the heart would be more clearly understood if they were described in precisely defined terms used by physical scientists and engineers. To this end, variations in the performance of the left ventricle in intact conscious dogs have been analyzed quantitatively by means of electronic computers in terms of variables selected on the basis of their appropriateness to a description of the left ventricle in its function as a pump. A functional description of any cyclical pump should include chamber pressure, rate of change of pressure, flow, average flow, power, average power, and stroke frequency. In a standard reciprocating pump with a fixed crankshaft, acceleration of the fluid, chamber dimensions, stroke duration, stroke volume, and stroke work would be redundant measurements. However, these measurements have been included in the present description since they may change independently during changes in cardiac performance.

Methods

Under aseptic conditions, a pulsed ultrasonic flowmeter transducer was fitted snugly over the ascending aorta in dogs (fig. 1, left). Two barium titanate disks, the transducers of a sonocardiometer, were sutured near the interventricular sulci on opposite sides of the left ventricle. Wires from both kinds of transducers were brought through the posterior thoracic wall for subsequent connection to recording apparatus. Finally, the flanged end of a polyethylene cannula (PE-320), plugged with a polyethylene stylus, was installed in the left atrium; the other end of the cannula was passed through the posterior thoracic wall between the scapulae.

After a dog had recovered from the surgical procedure (five to 20 days), experiments were begun. The stylus was removed from the cannula, and a fluid-filled polyethylene tube (PE-240) connected to a miniature differential transformer pressure gauge was inserted through the cannula, past the mitral valve, and into the ventricular cavity. The wires from the three transducers were connected to a terminal board, supported by a saddle strapped to the back of the animal. The terminals on the board were connected to the recording equipment by 30 feet of lightweight coaxial cable, supported from the ceiling.

As indicated at the left in figure 1, aortic flow...
and left ventricular pressure and diameter were recorded simultaneously on a four-channel Ampex tape recorder and a four-channel Sanborn strip chart recorder. These variables were measured under a variety of conditions, including spontaneous changes in position, eating, exercise, tilting, and administration of autonomic drugs. Later, the experimental data stored on the magnetic tape were fed through analogue computers to derive the variables illustrated at the right in figure 1.

The pulsed ultrasonic flowmeter measures the difference in the transit time of pulses transmitted alternately upstream and downstream, diagonally, through the moving blood. The resulting record shows the aortic flow (minus the coronary flow) as the instantaneous flow velocity (fig. 1, left). As the terminal event in the experiment, the flowmeter was calibrated directly in terms of the instantaneous rate of volume flow, i.e., cm²/sec. (fig. 1, right), by injecting known volumes through the flow section in situ. Stroke volume, cm³/stroke, could then be derived by integrating the instantaneous volume flow over each successive cycle, the electronic integrator being reset to zero at the end of each systole. The height of the deflection is equivalent to the area under the flow curve.

The values for cardiac output (in cm³/unit time) shown in figure 1 were obtained by integrating aortic flow over a fixed time interval, the integrator being reset to zero at the end of this time. The total amplitude of all steps in a trace reflects the combined effects of stroke volume and heart rate over the time period. Average volume flow calibrations for intervals of 2.5 seconds appear on the left of the record in figure 1. On the right side is a calibration in terms of cm³/minute, the more familiar unit of cardiac output. The values shown in figures 2 and 3 represent cardiac output computed by means of an integrator that continuously gives a mean value over an interval determined by the time constant of the RC circuit. This technique does not require resetting to zero.

Volume acceleration of the blood flowing out of the ventricle, in cm³/sec², was computed by differentiating the instantaneous volume flow. The deflection of the acceleration record continuously indicates the slope of the instantaneous flow record.

Ventricular pressure, which was measured directly through the indwelling cannula, is an expression of the tension developed by the myocardial fibers. This relationship is not a simple one, however. It is influenced by the dimensions of the chamber, in terms of the Laplace relationship (T = PR), and is complicated by the thickness of the ventricular walls and their complex geometry. The rate of change of pressure was derived by differentiating the pressure waveform. Both pressure records have been calibrated in dynes/em², as well as the mm Hg units familiar to biologists.

The duration of mechanical systole was also computed from the record of ventricular pressure. A linear ramp voltage was formed while the ventricular pressure was above a predetermined level (about 15 mm Hg), so that the peak voltage attained by the ramp indicated the duration of systole in seconds. To secure a record of heart rate, the abrupt rise in ventricular pressure at the beginning of systole was used to trigger a ratemeter. The voltage from the ratemeter varied linearly with the reciprocal of the time interval between the two most recent pressure pulses and thus was a measure of "instantaneous" heart rate. This rate is indicated in terms of the galvanometer level corresponding to the heart rate represented by the preceding cardiac cycle. Consequently, the prolonged systolic interval in figure 1 is followed rather than accompanied by an abrupt descent on the tracing for heart rate.

The instantaneous rate of effective energy conversion by the left ventricle (power in dyne-em./sec. or watts) was calculated by continuously multiplying the aortic flow (rate of change of ventricular volume) by the ventricular pressure. In an additional computation, the power waveform was integrated over each cycle to produce a peak galvanometer deflection representing the total effective work done by the left ventricle during that cycle (stroke work). The power waveform was also integrated over a fixed unit of time to indicate the effective work done within that time. This measure has the dimensions of average power (work/2.5 sec.) and reflects variations in both stroke work and heart rate.

A continuous measure of the volume of the pumping chamber would be pertinent to a complete analysis of a piston pump. Since we have no method for securing this information for the ventricular chamber, its diameter was recorded continuously, by means of the sonecardiometer crystals, to provide an indication of changes in size in at least one dimension.

**Results**

The aortic flow increases to a maximum during the first one-third of the ejection phase of systole, as indicated by both the instantaneous flow and the acceleration records. The flow decreases during the remainder of the systolic interval. A sharp retrograde surge of blood, marking the closure of the aortic valve, appears regularly at the transition be-
between systole and diastole in the aortic flow record. This phenomenon is indicated by a slight downward dip in the tracing for stroke volume and cardiac output. The record of aortic flow during diastole reveals slow fluctuations, presumably representing the oscillation of the blood within the elastic arterial system.

The acceleration record, which was obtained by differentiating the flow waveform, indicates the rate at which the flow was increasing or decreasing. Since the flowmeter samples the average flow velocity across the vascular lumen, a reliable value for the peak linear velocity cannot be derived unless the profile of the flow velocity is known. If the flow profile were flat across the stream, the maximal acceleration would be very high, e.g., \(3 \times 10^3\) cm./sec.\(^2\) during exercise. If the flow profile were parabolic, the axial stream would be accelerated even more rapidly—at about twice that rate. Since turbulence develops during peak flow velocities in the aorta, the true value for maximal linear acceleration probably is nearer the lower estimate.

The form of the ventricular pressure pulse is generally familiar, although attention is usually directed to the peak amplitude rather than to the details of the waveform. Tracings of the systolic pressure frequently exhibit a rounded dome shape, but the pressure may peak early in systole when ventricular ejection is exceptionally rapid and peripheral resistance is less than normal. In contrast, a marked increase in peripheral resistance may be accompanied by a progressively rising ventricular pressure during the systolic interval.

The rate of change of ventricular pressure, derived continuously by a differentiating circuit, is characterized by a sharp upward spike as the pressure rises and a sharp downward spike when the ventricular pressure falls at the end of systole. The amplitudes of these spikes reflect the maximum rates of rise or fall (slope) of the ventricular pressure pulses. These amplitudes are very labile, indicating that the rate at which the ventricular pressure changes is readily altered under such conditions as spontaneous changes in heart rate, exercise, sympathetic stimulation, and administration of catecholamines. The rate of change of pressure must be influenced by the degree of synchronization in the activation of the myocardial bundles and in the rate at which tension develops in these fibers.

In a mechanical pump, the duration of the stroke is determined by the r.p.m. of the crankshaft. Similarly, there is an inverse relationship between the duration of systole and the heart rate (fig. 1). This relationship tends to be preserved under many different conditions (see figs. 2 and 3), although the reasons are not so apparent in the heart as they are in a mechanical pump.

The effective power record indicates the rate at which the left ventricle performs work as the continuous product of aortic flow and ventricular pressure. This effective power is not a measure of the total rate of energy liberation because the viscous losses within the myocardium, which are probably not negligible, are not measured. Instead, the power record is interpreted as a measure of the rate at which energy is transferred from the left heart to the peripheral vasculature. Since peak outflow occurs early in systole when the pressure is achieving its maximum levels, power is also attaining its peak at this time.

The stroke work record, derived by the integration of the power record for each successive cycle, is a measure of the total energy transferred to the peripheral vasculature during the cardiac cycle. As the area under the power deflections increases, the stroke work deflections become higher. The work per unit time (average power) in combination with cardiac output yields an indication of variations in peripheral resistance. Commonly, average power varies directly with cardiac output during spontaneous activities. Exceptions are seen in figure 2, when the dog is tilted with head up, and in figure 3, in response to infusions of L-epinephrine and nor-epinephrine but not in response to isopropyl arternol.

As pointed out in the section on methods,
continuous measurement of one transventricular dimension is a poor substitute for a continuous record of absolute ventricular volume, but in default of a means of obtaining the latter values, it gives us our only clues to the direction of changes in the size of the chamber. The cyclical changes in ventricular diameter shown in figure 1 are typical of records obtained from sonocardiometer crystals mounted in the two interventricular sulci. The transition from late diastole to beginning systole is not marked by the sudden, spikelike deflections previously observed in records of other left ventricular dimensions. At this time, termed the period of isovolumic contraction, the internal length abruptly diminishes, and the external girth suddenly expands. However, this sudden change in shape has little effect on the specific dimension recorded by the sonocardiometer crystals located on opposite interventricular sulci. Unfortunately, this fact does not necessarily make this recorded dimension a more reliable index of ventricular volume than other dimensions of the chamber.

VENTRICULAR PERFORMANCE DURING SPONTANEOUS ACTIVITY

The responses of different dogs to the same stimulus have been very similar, varying primarily in magnitude rather than in pattern. The records in figures 2 and 3 were taken from one dog on one day and are typical of...
LEFT VENTRICULAR FUNCTION

the left ventricular responses of all 22 dogs of various sizes and breeds on which the effects of selected stimuli have been analyzed.

The response of the left ventricle to a sudden loud noise is indicated in figure 2. An abrupt increase in heart rate was accompanied by a transient reduction in ascending aortic flow, stroke volume, stroke work, and duration of systole. This brief reaction was followed by a peaking of all the variables except left ventricular diameter and the duration of systole. The typical reciprocal relationship between heart rate and duration of systole is indicated. The variables returned to control levels, changing rapidly at first and then at a gradual rate contrasting with the abrupt development of these alterations.

When the dog ran at 3 m.p.h. on a 12 per cent grade, the diameter of the ventricle did not change greatly at the end of systole or diastole. Peak ventricular pressure rose by about 50 per cent; peak rate of change of pressure (dp/dt) more than doubled during isovolumic contraction. Maximum rate of pressure drop increased by about 50 per cent during isovolumic relaxation. Both peak aortic flow and stroke volume increased by about 10 per cent, while cardiac output increased about 250 per cent of the resting value. The peak effective power more than doubled. The stroke work increased to about 1.7 times the resting level. Peak acceleration and deceleration increased simultaneously. Heart rate increased from 90 to 265 pulses per minute (p.p.m.) transiently, then fell gradually to a plateau at about 190 p.p.m. The duration of systole fell transiently to about half the resting level, then rose promptly to a plateau at about three-fourths of the resting level. During a second period of exercise at the same rate and grade, the changes in peak values and plateau levels were smaller in all variables except diameter. Such accommodation to exercise is very common in animals during successive bouts of similar activity.

When the dog was tilted, first head up and then head down, the responses were compatible with Starling's law of the heart: The end-diastolic diameter of the ventricle and stroke work varied together. When the dog spontaneously reclined, the end-diastolic diameter increased, and stroke work remained constant or decreased.

LEFT VENTRICULAR RESPONSES TO AUTONOMIC DRUGS

Selected drugs in saline solutions were infused intravenously through a superficial vein while the dog was reclining, quiet but alert. One dog's responses, illustrated in figure 3, are quite typical of responses of all the dogs, regardless of size or breed. The magnitude of the responses to each drug varied with dosage, but the response patterns were similar. A rapid intravenous infusion of acetylcholine (15 μg./Kg.) caused a transient bradycardia with dilation of the left ventricle, both lasting two to four seconds. The peak systolic pressure decreased, and the stroke volume increased, so that the stroke work was decreased or unchanged. A sustained tachycardia followed the transient bradycardia. During the tachycardia, ventricular pressure gradually rose above the control level. As the heart rate decreased again, the stroke work, peak power, and average power rose above control level.

Both norepinephrine and l-epinephrine caused a sustained increase in left ventricular pressure, a transient increase in peak aortic flow, and bradycardia. Stroke volume remained at the control level or slightly above. Peak instantaneous power, stroke work, and average power all increased markedly at first, then decreased quite slowly to control levels. Cardiac output and heart rate decreased. The duration of systole decreased transiently, increased markedly, and then declined slowly to control levels.

A constant infusion of 1 μg./Kg./min. of isopropyl artenerol caused marked increases

FIGURE 2
Changes in left ventricular performance in one dog, in terms of the variables derived by techniques illustrated in figure 1, during various forms of spontaneous activity, including startle, changes in posture, exercise, eating, and passive tilting.
in peak ventricular pressure, rate of change of pressure, average power, acceleration, cardiac output, and heart rate. Left ventricular diameter, stroke volume, stroke work, and the duration of systole all decreased. Peak aortic flow, cardiac output, and average power increased perceptibly. The differences between the responses to epinephrine and isopropyl arterenol cannot be attributed solely to differences in heart rate or duration of systole, since all of these variables can increase as heart rate increases and duration of systole decreases, e.g., during exercise.

Surgical anesthesia with pentobarbital sodium alters the baseline of ventricular performance perceptibly. If the heart rate is 120 p.p.m. or less, it is invariably increased. The normal sinus arrhythmia is eliminated, and the resultant elevated heart rate remains quite constant unless altered by some experimental manipulation.

LIMITATIONS OF METHODS

The experimental methods may be criticized on a number of counts. The dogs are considered to be "normal" only after they are capable of reasonable exercise, after their appetite returns, and when they display no outward signs of illness as a result of surgical implantation of the transducers. Each dog is autopsied to detect pathological effects of the implantation. In spite of such precautions, it is impossible to state with absolute certainty that the effects of the surgery on cardiac performance are inconsequential.

The catheter which is passed through the left atrial wall and the mitral valve to measure ventricular pressure is a potential source of interference with left ventricular performance, since it may impede the flow of blood through the mitral valve. Furthermore, suturing the indwelling catheter to the appendage could conceivably alter the effectiveness of atrial contraction. In similar experiments on a dog under local anesthesia, left ventricular pressure was measured by retrograde catheterization through the aortic valve from a superficial artery. No differences appeared in the patterns of the responses recorded by these two dissimilar methods.

The flow transducer is a bivalved plastic cylinder selected at surgery to fit about the artery in order to constrain the vessel and thus prevent pulsatile variations in its diameter. Such a transducer may be thought to interfere significantly with normal blood flow. However, the reduction in lumen diameter caused by the transducer is estimated to be less than 10 per cent. Spencer et al. have presented evidence that the instantaneous flow waveform is not significantly altered by a reduction of lumen diameter up to 15 per cent. When the transducer is too small, the aorta ruptures under the transducer, usually on the sixth to tenth day after surgery. If rupture does not occur within 10 days, the dog may be expected to live indefinitely. One dog (V-4), of which the research group became overly fond, is still living on a farm after three years with five flow transducers clamped about major abdominal and thoracic blood vessels, including the root of the aorta and coronary artery.

Each energy computation is based on the assumption that the product of the rate of change of volume of a chamber and the transmural pressure across the walls of the chamber is equal to the effective power generated by the pumping chamber. The pressure gauge is referred against atmospheric pressure. The power computation is in error, then, since intrathoracic pressure is disregarded. The actual effective power will be slightly higher than the recorded power, since the transmural pressure of the ventricle is higher than the measured pressure. Similarly, the computed stroke work and average power will be in error. Furthermore, the measured aortic root flow is assumed to equal the instantaneous rate of change of volume of the left ventricle. This assumption is valid only so long as the valves are competent. The assumption is in error by at least as much as the coronary flow, which the flowmeter does not measure.

There are errors in the computation of both volume acceleration and rate of change of pressure. The reading error is great in both records because the primary information was recorded on tape, which increases the noise level, and differentiation exaggerates this
Changes in left ventricular performance produced by the intravenous infusion of various autonomic drugs in the same dog, alert but lying quietly on a table. Similar changes were seen in other dogs receiving similar dosages.
noise. Furthermore, the computation is in error owing to the limitations of the frequency responses of both the electronic differentiator and the direct-writing recorder. These errors were minimized by carefully measuring the slope of the waveform which was differentiated and assigning this calibration to the simultaneous deflection of the galvanometer which was recording the derivative.

The flowmeter has been calibrated against a known volume flow in vitro only to 5 cycles per second; the higher frequency components of the flow waveform may be in error, which would result in an error primarily in the acceleration computation. The flowmeter measures an average flow velocity across the lumen of the flow transducer; where jets or asymmetrical velocity profiles occur during the cardiac cycle, the flow measurement may be in error.

The mean values of flow have been calibrated in vivo both by forcing known volumes through the exposed vessel in situ in a measured time and by preparing a heart-lung preparation from the experimental animal at the termination of the experiment. The pulsatile flow waveform obtained with the heart-lung preparation approximates the flow waveform in the normal dog and, in this way, serves as an approximation of an in vivo calibration.

Discussion

These experiments were designed specifically to provide a meaningful description of the integrated response of the intact cardiovascular system to spontaneously occurring and artificial stimuli. Such information is absolutely essential to test the validity of hypotheses regarding regulation of the cardiovascular system. For example, a hypothetical control mechanism may be demonstrably potent in an isolated heart, yet may not be detectable in an intact animal. This negative finding does not invalidate the concept. It demonstrates that the mechanism is not dominant but is commonly obscured by more potent mechanisms.

The recorded variables were selected on the basis of their meaningfulness. Each has a precise and accepted definition. For example, the term "power" is precisely defined in the most elementary texts of mechanics. The preciseness is to be contrasted with the connotations of such terms as "contractility," "vigor of contraction," "force of contraction," and "contractile efficiency." Their meanings are controversial, even among professional cardiovascular physiologists. If the concept of "contractility" is not included among these variables, it should have a specific definition. If the term is represented by one or more of these variables, it could well be discarded.

As biological sciences become less dependent on qualitative description and correlation in operational terms and more dependent on quantitative measurements of essential variables, poorly defined terms which impose semantic obstacles to understanding should be replaced by physical variables which have precise meaning and can be expressed quantitatively.

Summary

A description in standard physical terminology of the variations of the left ventricle in its role as a pump was derived. Left ventricular pressure, left ventricular outflow, and an external dimension of the left ventricle were measured in unanesthetized, active dogs during spontaneous activities and infusions of autonomic drugs. Secondary variables pertinent to a functional description of a pump were derived continuously from the primary variables by analogue computers. The derived variables included stroke volume, cardiac output, effective power, stroke work, average power, volume acceleration, rate of change of pressure, duration of systole, and heart rate.

These techniques allowed a detailed description in meaningful terminology of the integrated effects on the left ventricle of such stimuli as sleep, startle, exercise, postural variations, and infusions of autonomic drugs.

The descriptions of the variations in the characteristics of the left ventricle allow tests to be made of hypothetical cardiovascular control mechanisms. The use of standard, well-accepted, physical terminology allows...
LEFT VENTRICULAR FUNCTION

the descriptions to be evaluated in different laboratories by totally different measuring techniques. The terminology used was contrasted with operationally defined or ambiguous terms such as "contractility" or "vigor of contraction."

Acknowledgment

The contributions of Mr. Donald Baker, Mr. William Schlegel, Mr. Nolan Watson, Mr. Donald Harding, and Mr. Raymond Smith in the construction, maintenance, and operation of the electronic recording and computing systems are gratefully acknowledged.

References


Book Review

The Peripheral Circulation of Blood, Lymph and Tissular Fluid, Prof. Dr. C. D. De Langen. De Erven F. Bohn N. V., Haarlem, Holland, 1961, 165 pages, illustrated. $6.50.

The introduction starts as follows: "When in 1628 Harvey, in his classic work 'De Motu Cordis,' explained to the medical world the significance of the heart for the circulation of the blood, he compared the organ to the figure of his beloved sovereign Charles I. He put both on a level with the sun, the hub of the universe; to him, Charles was the centre of the earth, the heart the central organ around which everything in the human body revolved. However, Harvey lived to see King Charles lose his head on the scaffold; astronomers since have proved that the sun is by no means the centre of the universe, but only a star of the second or third rank. About three centuries after Harvey's time, several investigators have made serious attempts to dethrone the heart as the monarch of the body and to credit the peripheral circulation with a distinct and active part in the mechanism which governs the blood stream."

The author has proceeded to consider the problem of the peripheral circulation from a physiological point of view. Each chapter indicates some facts and possibilities which so far have not been recognized, or which have been interpreted in a different way. Some of such possibilities are as follows: "The function of an organ does not depend in the first place on the blood minute volume, as is usually assumed, but on the quantity of fluid of the right composition which leaves the blood stream and returns to it after having flown through the tissues and having freed it of all the metabolic products. For this reason the concept of the blood minute volume should be replaced by that of the tissular fluid minute volume."

Another group of concepts pertains to the existence of a double circulation, one of which feeds the organ, whereas the other provides for its functioning. The capillaries should be differentiated into two groups: the feeding capillaries and the functional capillaries. The old anatomists used to speak of the vasa privata and the vasa publica for the pulmonary and bronchial arteries, respectively. In most organs, the two kinds are found side by side.
Left Ventricular Function Described in Physical Terms
Dean L. Franklin, Robert L. van Citters and Robert F. Rushmer

_Circ Res._ 1962;11:702-711
doi: 10.1161/01.RES.11.4.702

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1962 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/11/4/702

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

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

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