Ventricular Function

I. Starling’s Law of the Heart Studied by Means of Simultaneous Right and Left Ventricular Function Curves in the Dog

By Stanley J. Sarnoff, M.D., and Erik Berglund, M.D.

Starling’s law of the heart has been studied in the dog with a complete circulation with the continuous registration of cardiac output, and atrial and arterial pressures. From this data ventricular function curves were constructed. In any given physiologic state there was a consistent and reproducible correlation between atrial pressure and ventricular stroke work on the same side. The classically conceived descending limb did not occur in the normal heart. The concept of a family of Starling or ventricular function curves adds a third dimension to the adaptive capacity of the heart as put forth by Frank and Starling.

STARLING’S LAW of the heart states "that the energy of contraction, however measured, is a function of the length of the muscle fibers" prior to contraction. Starling deduced this law from his own and also from the prior studies of Frank on isolated heart and heart-lung preparations. Both its validity and significance in the presence of an intact circulation have been questioned. Many investigations of this matter in the presence of a complete circulation have been either inadequate or misleading largely because of the following: (1) stroke volume or cardiac output and not stroke work has been used as the measure of the "energy of contraction"; (2) attempts have been made to correlate right sided filling pressure with left ventricular stroke work; (3) attempts have been made to correlate filling pressure with ventricular work per minute instead of per stroke, and (4) perhaps most important, it has not been generally appreciated that a single Starling curve cannot always satisfactorily explain the observed phenomena; for any given heart there is a series or family of curves.

Further, the views of Starling and subsequent workers 1-4, 12, 13, 41 led to the firmly entrenched concept that there is a significant descending limb of the curve at high filling pressures. Data will be presented below which support the interpretation that a descending limb occurs when the function of the myocardium is compromised but not in the normal heart.

An investigation has been started in this laboratory to evaluate more completely the law of the heart and the physical determinants of ventricular work in the living animal with a complete circulation. The objectives of this communication will be (1) to describe a method by means of which myocardial contractility can be quantitated in the dog with a complete circulation and the effect of any given physiologic or pharmacologic intervention can be more precisely appreciated; (2) to present data concerning the relationship between filling pressure and ventricular stroke work under a variety of physiologic circumstances and to examine these data in relation to the validity of Starling's law of the heart; and (3) to present data in support of a unifying concept, the family of Starling or ventricular function curves, which may help to reconcile previously conflicting views.

The data will be presented as right and left ventricular function curves. These curves are obtained by plotting the ventricular work in grammeters per stroke against the mean atrial
pressure on the same side. That aspect of Starling’s law which deals with myocardial oxygen consumption will not be dealt with in this communication.

**Method**

Mongrel dogs weighing 12 to 28 Kg. but generally over 16 Kg. were anesthetized with morphine sulfate, 4 mg. per kilogram and 20 minutes later chloralose, 48 mg. per kilogram, and urethane, 480 mg. per kilogram. After starting positive pressure breathing, the chest was opened with the dog in the right oblique position and the left ribs 3, 4 and 5 and sometimes 2 were removed. Systemic blood flow (cardiac output minus coronary flow) was continuously recorded with a Potter Electro-turbidometer.* The performance characteristics of this flowmeter and its application to the measurement of systemic blood flow have been described. In some experiments left main coronary artery flow was also recorded with the rotameter of Shipley and Wilson. Full pulse pressures and electrically integrated mean pressures were measured with Sanborn Electromanometers. These were obtained from a catheter in the right atrium through the left femoral vein, one in a lobular branch of the left pulmonary artery, one in the left atrium through a lobular pulmonary vein, and one in the aortic arch. All data were continuously recorded on a four channel direct-writing oscillograph. An electronic switching device (Sanborn Triplexer) made it possible to record five or six simultaneous events on four channels. The midlevel of the tricuspid valve was used as the zero reference for right atrium and pulmonary artery pressures. The midlevel of the mitral valve was used as the baseline for left atrial and aortic pressures.

A cannula was inserted into either the right or left atrium through a small opening in the pericardium. This communicated with a heated reservoir by means of Tygon tubing. The reservoir contained 6 per cent Dextran† in 0.9 per cent sodium chloride which was thoroughly mixed with the dog’s blood prior to obtaining the ventricular function curves. Lowering of the hematocrit by Dextran does not alter the ventricular function curve until anemia becomes marked. In the more recent experiments, blood from a donor dog was used in the reservoir instead of Dextran. This was then thoroughly mixed with the blood of the experimental dog.

By changing the height of the reservoir, the pressures in both atria could be varied over wide ranges just as by infusing or bleeding the dog through a femoral vein; the latter route has been used in more recent experiments. The pericardium either remained intact except for the small opening through which the reservoir tubing passed or was widely opened.

The blood was rendered incoagulable with Treburon.* An attempt was made to maintain body temperature by means of a heating pad under the dog. High bilateral cervical vagotomy was done in some experiments, usually at the beginning of the experiment.

For simultaneous right and left ventricular function curves were obtained in the following manner. The reservoir was lowered until the aortic pressure came down to 50 to 90 mm. Hg and then elevated in steps of 2 to 5 cm. at 30-second intervals until the left atrial pressure was 35 to 50 cm. H2O. At this point high speed, full pressure tracings (50 mm. per second) were taken from both atria so as to ascertain whether obvious mitral or tricuspid regurgitation was present. Data for full ventricular function curves were obtained in 4 to 5 minutes and could be repeated frequently. Pressure and flow values were taken from the tracing at a point 30 seconds after each elevation of the reservoir. The stroke work of each ventricle in gram-meters was calculated according to the following formula:

\[
\frac{(cm.\ H_2O \text{ mean arterial pressure} - \text{cm.}\ H_2O)}{\text{mean atrial pressure}} \times \text{stroke volume} = \frac{1}{100}
\]

Stroke volume in cubic centimeters was obtained by dividing systemic blood flow per minute by the heart rate. When either marked cardiac arrhythmias or regurgitation were found, the values were not used for the comparison of ventricular function curves.

Figure 1A shows a representative tracing of values obtained during a ventricular function run and the calculated right and left ventricular stroke work for each level of atrial pressure. Figure 1B shows the right and left ventricular function curves constructed from the data in figure 1A.

When the effect of a physiologic or pharmacologic intervention on myocardial contractility was studied, a control curve was obtained before the intervention and also after the removal of the intervention (figs. 4 and 5).

**Evaluation of Method**

1. **The Use of Mean Atrial Pressure as an Index of Ventricular End Diastolic Pressures.** (a) It is the authors’ opinion that, at high heart rates, the precise determination of ventricular end-diastolic pressures is difficult to obtain consistently with the catheter technique. (b) The use of mean atrial

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pressures yields consistently reproducible ventricular function curves. (c) The correlation between mean atrial pressures and end-diastolic ventricular pressures was satisfactorily close in the low and medium ranges. The errors encountered at high filling pressures do not change the shape of the curve appreciably since in that range a moderate change in filling pressure does not significantly alter stroke work (figs. 1, 2, 4, 5, 6). (d) Another advantage of atrial over ventricular pressure recording is that, by the use of full atrial pulse contours, the presence of obvious tricuspid or mitral regurgitation may be detected. Ventricular recording does not afford this opportunity.

2. Accuracy of Flowmeter. The Electroturbinometer baseline is steady and its calibration is not affected by wide variations of blood viscosity or temperature. The correlation factor on blood calibrations with pulsating flow is 0.99. The meter was calibrated after each experiment even though its calibration remained the same from month to month.

3. The Acceleration Fraction of Ventricular Stroke Work. In three experiments the kinetic component of the left ventricle stroke work was calculated during a ventricular function run. The following formula was used: \[ W_a = \frac{MV^2}{2g} \], in which \( W_a \) is acceleration.
work expressed in gram-meters, \( M \) is mass of blood per stroke in grams, and \( g \) is 9.81 M. per second\(^2\). \( V \) is the mean ejection velocity in meters per second, and is calculated from the formula:

\[
V = \frac{\text{stroke volume in } cc.}{\text{cross sectional area of root of aorta} \times (E) \times 100}
\]

\( (E) \) is the systolic ejection time obtained from high speed aortic pressure tracings. The aortic cross-sectional area values were calculated from measured aortic circumferences obtained post mortem over the range of intra-aortic pressures encountered during the ventricular function run.

It was found that the acceleration component of left ventricular work during the entire ventricular function curve was less than 1 per cent of the total stroke work values obtained under the conditions of our experiment. This is in agreement with Remington and Hamilton.\(^2\) The acceleration component of ventricular stroke work was disregarded in the calculation of the curves presented in this communication.

4. The Coronary Flow Fraction of Cardiac Output. Utilizing techniques described in detail in other communications,\(^17,18\) the left main coronary artery flow was also measured while obtaining ventricular function curves in some experiments. Figure 2A shows the similarity of the shape and the minor difference in height of the function curves obtained (a) with the coronary flow included in the stroke volume values, and (b) without the coronary flow included. The subsequent ventricular curves shown do not include coronary flow in the calculation of stroke volume except for the curves shown in figure 4.

5. Equilibrium State. In order to ascertain whether equilibrium had been achieved 30 seconds after each elevation of the reservoir, two experiments were performed in which the atrial reservoir was raised at two-minute intervals instead of the usual 30-second intervals. Stroke work values were calculated and plotted against atrial pressure values at one-half minute, one minute and two minutes after each elevation of the reservoir. The result, shown in figure 2B, demonstrates that 30 seconds after any given elevation of the atrial reservoir, ventricular stroke work has reached its new level.

Results

More than 300 simultaneous right and left ventricular function curves have been obtained. Figure 1B shows ventricular function curves constructed from the data in figure 1A. It should be emphasized that left ventricle stroke work values are plotted against left atrial mean pressures, and right ventricle stroke work values against right atrial mean pressures.

1. The Shape of the Ventricular Function Curves

The curves showed an initial steep rise at low filling pressures and then flattened off to a plateau with little or no decline even at high filling pressures. In our experiments this plateau always appeared in the left ventricular work curve. On the right, the shape of the curve was often as shown in figures 1B and 4, but not infrequently it was as shown in figures 2B and 6.

A descending limb, that is, a fall in stroke work at high filling pressures (50 cm. H\(_2\)O), did not occur in a normal heart with an intact pericardium. This is at variance with the classically conceived Starling curve which involves a pronounced descending limb at higher rates of "venous inflow."\(^7,12,13,41\)
2. The Importance of Homolateral Correlation

It is seen in figure 1 that while right atrial pressure rose only 9 cm. H$_2$O throughout this function run, the left atrial pressure increased 28 cm. H$_2$O. This emphasizes the importance of relating right atrial pressure to right ventricle stroke work and left atrial pressure to left ventricle stroke work. Moreover, a change of pressure in one atrium is not always accompanied by a similar directional change in the other atrium. One such circumstance is illustrated in figure 3. A stepwise screw clamp constriction of the descending aorta was accompanied by stepwise increases of left atrial pressure from 9 to 17 cm. H$_2$O, while the right atrial pressure did not change significantly. The increases in left atrial pressures were accompanied by increases of left ventricle stroke work, while there was no significant change in right ventricle stroke work. It is apparent that attempts to correlate right atrial pressure and left ventricle stroke work under these circumstances may be misleading. 

3. The Importance of Correlating Filling Pressures with Work Instead of Stroke Volume or Cardiac Output

In figure 3 the stepwise increases in left atrial pressure were accompanied by step-wise increases of left ventricle stroke work,
whereas stroke and minute output did not rise. It is obvious that the often used practice of correlating filling pressure with output\textsuperscript{6-10}, 12, 13, 25 may also be misleading.

Another physiologic circumstance under which the correlation between filling pressure and stroke volume may be misleading is shown in figure 4. After one set of control function curves was obtained (C, dots), the flow through the left main coronary artery was restricted by tightening a screw clamp on the tube feeding the coronary cannula. Ventricular function curves were obtained during mild (0) and moderate (0') restriction of left coronary artery flow, and again after removal of the clamp (C, open circles). While the left ventricle was changing from the control to a depressed or "failure" curve, the right ventricle was unaffected, that is, did not show a depressed function curve. However, the plot of right atrial pressure against right ventricular stroke volume would give the impression that not only was the function of the right ventricle impaired but even that a descending limb was present. That such was not the case is clear from the right ventricle work plot. It was still doing as much work per unit of filling pressure, but more of this work was absorbed by the higher pulmonary artery pressures present.\textsuperscript{17, 18}

Fig. 4. Exper. 72. The effect of restriction of left main coronary artery flow on right and left ventricular function curves. Dog weight: 16.8 Kg. Heart weight: 130 Gm. Pericardium open. Vagotomized. Reservoir connected to right atrium. Curve C = mean of control curves obtained before (dots) and after (circles) restriction of the left main coronary artery flow. Curve 0 = curve obtained during mild restriction of coronary flow. Curve 0' = curve obtained during further restriction of flow. Note that during restriction of left main coronary artery flow there was: a) depression of the left ventricle function curve together with b) the appearance of a descending limb c) the occurrence of unilateral ventricular failure d) a misleading correlation between right atrial pressure and right ventricular stroke volume: i.e. right ventricular function was not depressed.

Fig. 5. Exper. 53. Same dog and symbols as shown in figure 1 after the myocardium was in failure. (Upper figure) Hemodynamic effects of a single intravenous injection of 1.17 µg per kilogram synthetic epinephrine (Suprarenin), made immediately after A. B is one-half minute later. Note the lower filling pressures and increased stroke work of both ventricles in B. (Lower figure) Comparison of simultaneously obtained left and right ventricular function curves before, during and 12 minutes after continuous infusion of the same agent.

Note that the effect of the single injection in the upper figure was simply to shift the ventricular performance from a point on the depressed function curve to a higher one as shown by the arrows. Figure 1 shows this dog's function curves before the heart went into failure.
The plot of right atrial pressure against cardiac output was similar to that shown for stroke volume since pulse rates were close to the same. The demonstrated occurrence of unilateral depression of left ventricular function (fig. 4) further emphasizes the importance of interpreting the function of each ventricle in terms of its own filling pressure.

4. The Importance of Distinguishing Between Apparent and Effective Filling Pressures

When the pressure around the ventricles was increased by the production of cardiac tamponade, the ventricular stroke work of both ventricles fell in spite of increased atrial pressures and thus the ventricular function curves during tamponade showed an apparent suppression.²⁶ ²⁷ If, however, the effective filling pressure (pericardial pressure minus atrial pressure) was plotted against stroke work, no suppression of the ventricular function curves was observed. This is in accord with the view that the work of the ventricle is a function of diastolic fiber length¹ ²⁸ and that this in turn is determined largely by the effective filling pressure.²⁹

5. Family of Ventricular Function Curves

In the same dog, reproducible ventricular function curves were obtained while those factors which govern the response of the myocardium and vascular resistance remained constant. However, when these were significantly altered, many different types of curves could be obtained. Examples of such families of related curves are shown below.

A. Effect of Epinephrine on the Ventricular Function Curve. The upper part of figure 5 shows the hemodynamic effects of a single injection of synthetic epinephrine tartrate (Suprarenin). Prior to the injection (A) this dog exhibited evidence of myocardial failure, that is relatively little ventricular stroke work at elevated filling pressures. Thirty seconds after the injection of epinephrine (B), the stroke work of both ventricles was higher even though their filling pressures were lower. This apparent negation of the Starling relationship is clarified by the curves in the lower part of figure 5; that is, ventricular function curves before, during and after a continuous infusion of epinephrine. The curve during the epinephrine infusion is markedly higher than the curves obtained before and after it. The effect of the prior single injection of epinephrine was simply to shift the work performance of the ventricles from a point on the control function curve to a point on the epinephrine curve as indicated by the arrows. Another sympathomimetic amine, Aramine, * was similarly found to increase ventricular stroke work per unit of filling pressure.³⁰

B. Effect of Restricting Coronary Flow. The restriction of left main coronary artery flow yielded progressively depressed left ventricular function curves the degree of which was a function of the restriction imposed (fig. 4).

C. The Effect of Severe Anemia. Moderate degrees of anemia did not lower the ventricular function curves significantly because of an observed increase in coronary flow. However, when the anemia became so severe that coronary vasodilation could no longer compensate for the lowered oxygen transport capacity of the blood, depression of the ventricular function curves occurred.³⁰ These were similar to those obtained by partial coronary occlusion seen in figure 4.

* Supplied through the courtesy of Dr. Karl Beyer, Sharp & Dohme, West Point, Pa.
D. The Effect of Aortic Constriction. After obtaining a control curve, aortic resistance was increased by constriction of the aortic tubing. Figure 6 shows that during the curve with a high aortic resistance, the left ventricle produced less external stroke work at any given filling pressure. After removal of the aortic clamp, the curve was similar to the control. It will be noted that in this dog, with the pericardium intact, the right ventricle function curve was also suppressed when the aortic constriction was in place. This reflected or apparent lowering of the right ventricle curve shown in figure 6 did not occur in this dog after the removal of the pericardium, whereas the suppression on the left remained. The influence of the pericardium on cardiovascular hemodynamics is treated more fully in other communications.34, 35

The families of curves shown above demonstrate that certain factors which influence myocardial contractility and vascular resistance can alter the ventricular function curve of any given heart. However, if the full range of ventricular performance is again examined under the new conditions, a relationship between filling pressure and stroke work never fails to obtain.

DISCUSSION

The examination of the relation between the “fiber length” in diastole and the “energy of contraction” presents two major technical problems in the mammalian heart. For, although the methods available at present allow a reasonably precise measurement of the external mechanical work performed by each ventricle, they do not measure the total energy liberated while doing this work. For example, it is likely that an appreciable portion of this energy is spent on isometric contraction, but that portion is not measurable as work in the physical sense. The relationship between myocardial oxygen consumption and ventricular work may vary significantly and therefore the former may not accurately represent the force of contraction.32, 33

Further, ventricular diastolic fiber length, to which the energy of contraction is apparently related, is also a determination which is extremely difficult to achieve in the in vivo mammalian heart. And, although the authors subscribe to this relationship as put forth by Starling,1 neither he nor subsequent investigators achieved those measurements required to fully substantiate it. The cardio-oncometer does indicate changes in diastolic ventricular volumes and these do vary with diastolic fiber length. But this instrument measures the sum of right and left ventricular volumes and therefore cannot be used to determine the volume of either ventricle alone.9 Disagreement has existed regarding whether it is the volume of the ventricle or the pressure in it which regulates the strength of the subsequent ventricular contraction.1, 14, 28, 16, 47 For example, Starling's group came to the conclusion that it is the diastolic volume and not the filling pressure.4 For, when they increased the outflow resistance to the left ventricle, its volume and thus the sum of the ventricular volumes increased, but, as might be expected, the right atrial pressure remained the same.4 (See fig. 3). It seems to the authors that much of this debate is artificial. For, in any hollow viscus, an increase in its volume is accompanied by an increase in pressure, and these interdependent variables bear a constant relationship to each other unless a change in elasticity or tone occurs.

With these reasons in mind the form of analysis presented above was chosen; that is, the correlation of filling pressure with the external work produced. For, notwithstanding the basic limitations as regards energy measurements, this method does provide a rapid means of quantitating ventricular performance in terms of physiologically significant work. Thus, normal function, the deterioration of ventricular function and the effect of therapeutic maneuvers can be satisfactorily measured. Lastly, the data were gathered in terms of pressures and flows, determinations which are readily achieved in man. The measurement of ventricular volume in man is at present an uncertain one.

In this preparation it was frequently possible to make continuous output and work determinations and to obtain 20 simultaneous right and left ventricular function curves in a
STARLING'S LAW OF THE HEART

single experimental animal. The work values in our preparation compare well with work values obtained in closed chest anesthetized dogs.34 Unlike heart-lung preparations which are probably failing, this preparation still has normal or near normal metabolic support. The open-chest preparation has the advantage of avoiding the vagaries of intrapleural pressure measurements35 and the consequent difficulty of precisely determining effective filling pressure. Attempts are being made, however, to achieve the type of measurements presented above in the unanesthetized, closed-chest dog for the purpose of other studies.*

Shape of the Ventricular Function Curves. As noted above, the ventricular function curve shows a steep initial rise which then flattens off to a plateau. The only available determinations of the pressure-volume relationship of the ventricle in the mammalian heart are approximate because they were not done in the beating heart.34 Nevertheless they reveal that in the low range, large volume (fiber length) increments produce only small increases in pressure. In the upper range, small volume increments produce large pressure increases. Considering this shape of the ventricular pressure-volume curve together with the shape of the ventricular function curves shown, it becomes likely that a plot of work against volume (or fiber length) would be closer to a straight line than either the ventricular function or the pressure-volume curves.37

The initial steep rise of the curve is of considerable importance. A rise of 1 cm. H2O in atrial pressure may increase ventricular work by as much as 300 per cent. This emphasizes the necessity for precise measurements of the changes in effective filling pressure, especially in the normal heart.

The Absence of a Descending Limb on the Normal Ventricular Function Curve. The normal ventricular function curves presented above (with filling pressures as high as 55 cm. H2O) differ from the classically conceived curves1, 8, 12, 13, 38, 41 in that they show little or no descending limb. With the pericardium wide open, the stroke work values sometimes decreased at high filling pressures, but this phenomenon was attributable to regurgitation through the distended atrioventricular valves and not to a decrease of myocardial contractility. Frank observed this phenomenon in the frog heart and stressed its importance.3 It has been demonstrated that the pericardium restrains extreme dilation of the heart24, 31, 38, 39 and probably also prevents valvular regurgitation.34 The classic Starling curve with a descending limb was obtained in heart-lung preparations with the pericardium removed. But even in such a preparation, left atrial pressures of 40 cm. H2O were occasionally reached without a fall in stroke work.3 The findings of Lundin, namely, the extent to which a ventricular muscle strip can be stretched without a decrease in the force of contraction,49 suggest the magnitude of increase in ventricular volume that would be required to produce a descending limb. And, as demonstrated above, a descending limb was not encountered in the normal heart even when the left ventricle was severely challenged by a high aortic resistance (fig. 6). A descending limb did occur when the metabolic support of the myocardium was compromised (fig. 4).17, 18, 20

Myocardial Failure. The shape of the normal ventricular function curve does not confirm the interpretation that cardiac failure may result merely from stretching the muscle fibers beyond that point where an increased filling pressure causes a decrease in cardiac work.41, 42 We consider myocardial failure to be an alteration of the contractility of the myocardial fibers, resulting in a shift of the ventricle from a normal function curve to a depressed one. The increased filling pressures are thus not the cause of failure but a consequence of decreased myocardial contractility.

In regard to this general area McMichael, in 1952, stated "In the very near future we shall possibly abandon the vague term 'cardiac failure' and analyze all our cardiacs in terms of their altered dynamics."34 With the exception of heart disease involving valvular insufficiency, it would appear that the use of ventricular function curves or portions thereof may bring this goal within reach.

Family of Ventricular Function Curves. In
order to uphold the view of Frank and Starling it has been necessary to broaden this view with a spectrum or family of curves so as to have it encompass the observed phenomena. The idea of a family of Starling curves was first suggested to us by Dow in 1949.4 In 1952 Mc-Michael drew three theoretical plots of cardiac work against filling pressure representing the normal, the hypodynamic and the hypertrophied heart.13 The theoretic curves presented by Youmans and Huckins15 and by Lewis and coworkers23 unfortunately plotted cardiac output or stroke volume against filling pressure. The data presented above and elsewhere17, 19, 20, 26, 27, 30, 31 substantially strengthen the view that a ventricle may describe many different ventricular function curves. These data also furnish examples of certain ways in which the curves may be altered (figs. 4, 5, 6).

A change in filling pressure in one direction accompanied by a change of ventricular work in the opposite direction (fig. 5) does not mean that the Frank-Starling relationship no longer obtains. It is still present but is shifted to another scale. This concept is helpful in understanding certain phenomena (for example, exercise, epinephrine) which, on the surface, are not in accord with Starling's law.

It is the view of Richards8 and Hamilton9 that the heart "has fallen back upon the Starling mechanism" only when other mechanisms for the regulation of "cardiac output" fail; that is, only the failing heart obeys Starling's Law. This interpretation overlooks the above demonstrated ability of the heart to operate on widely different Starling curves. The above data are consonant with the view of Youmans and Huckins: "It is an unfortunate choice of words to say that Starling's law is not operating when an increased cardiac output is associated with a decreased venous pressure... In such cases the cardiac output is certainly less than it would be if the venous pressure were maintained..."13

The question has reasonably been asked as to where the family of curves fits into our thinking about the circulation. For even if it is agreed that the Frank-Starling relationship does obtain in the intact mammalian organism, "of what use is this information if the myo-cardium can blithely skip from curve to curve?" Obviously, it is less convenient to have to deal with a family of curves rather than with a single curve. But it is much more convenient to deal with a family of curves than with a miscellaneous group of random values which do not fit any pattern at all. Further it is clear from the above that the ventricles do not "blithely skip from curve to curve" unless some influence of physiologic importance intervenes. This family of curves may therefore be helpful in understanding the nature of certain pathologic processes and, by the experimental use of such curves, factors which alter myocardial contractility may be more precisely determined.17, 18, 20, 26, 27, 30, 49

As expressed by Starling "the heart possesses in a high degree the power of adaptation to changed conditions which is the essential characteristic of living organisms."72 In the authors' view the concept of a family of curves adds a third dimension to the Frank-Starling mechanism. This third dimensional adaptation is of importance not only in the responses of the normal organism but also in compensating for physiologic adversity.

The most important missing link in the chain of information derives from our present inability to determine changes in the pressure-volume relationship of each ventricle in diastole; that is, changes, if any, in ventricular tone or elasticity. If it were possible to correlate the family of ventricular function curves under varying conditions with simultaneously obtained ventricular pressure-volume curves, a comprehensive view of the physical determinants of cardiac action would be at hand.

As both Starling1 and Frank2 indicated, the law of the heart is little more than the application to cardiac muscle of what was already known about skeletal muscle by Blix in 189550 and Fick in 1882.51 These four workers were, in one sense, anticipated by A. Waller in 1878 who grasped this matter when he stated that "... whenever the left ventricle is forced to work against a higher pressure it has to be filled abundantly and under higher pressure; this condition is fulfilled only if the blood runs in from the distended pulmonary veins at a higher pressure."52

* Author's translation.
Conclusions

1. A preparation is described whereby it is possible to examine in the dog with a complete circulation the relationship between atrial pressures and external stroke work for the left and right ventricles simultaneously. Twenty combined ventricular function curves can frequently be obtained in one experiment.

2. In any given circulatory state there is a consistent relationship between atrial pressure and ventricular stroke work.

3. The ventricular function curve shows an initial steep rise, during which a 1 cm. H₂O increase in atrial pressure may increase the ventricular stroke work as much as 300 per cent. At high filling pressures the curve flattens off to a plateau.

4. A descending limb (decrease of ventricular work with increased effective filling pressure) does not occur in the normal dog heart but may occur in the heart with a compromised myocardium.

5. The above data confirm the opinion of Starr and his colleagues specifically, that stroke work is the proper value to consider in the analysis of ventricular performance. Whereas a consistent relationship was found between atrial pressure and the stroke work of the ventricle on the same side, such a relationship was not consistently found (a) between right atrial pressure and left ventricle stroke work, or vice versa; (b) between atrial pressure and stroke volume; or (c) between atrial pressure and cardiac output.

6. A significant alteration in the circulatory state (such as the injection of epinephrine, coronary artery constriction, severe anemia and increased aortic resistance) produced different ventricular function curves; in this new circulatory state, however, the relationship between atrial pressure and ventricular stroke work was again a consistent one.

7. It is felt that previous investigations which challenge the validity of the Frank-Starling relationship have been based on either (a) improperly attempted or misleading correlations, (b) failure to appreciate the steepness of the ventricular function curve in its lower ranges, and the importance of determining effective filling pressures, or (c) failure to appreciate that no single curve can adequately express the patterns of ventricular performance elicited when certain parameters of its work conditions are altered.

8. The demonstration of the family of Starling or ventricular function curves makes available a unifying concept on the basis of which changes in ventricular function can be more completely appreciated.

Sumario Español

1. Se describe una preparación en la cual es posible examinar en el perro con circulación completa la relación entre presión atrial y el trabajo externo por contracción cardíaca para el ventrículo izquierdo y derecho simultáneamente. Veinte curvas combinadas de función ventricular pueden frecuentemente ser obtenidas en un experimento.

2. En cualquier estado circulatorio dado hay una relación constante entre la presión atrial y el trabajo por contracción ventricular.

3. La curva de función ventricular muestra un ascenso rápido, durante el cual un aumento en presión atrial de 1 cm. de H₂O puede aumentar el trabajo por contracción ventricular por tanto como un 300 por ciento. A presiones de henchimiento altas la curva se aplanita hasta formar una meseta.

4. Una porción descendente (decremento de trabajo ventricular con incremento en presión efectiva de henchimiento) no ocurre en el corazón del perro normal pero puede ocurrir en el corazón con un miocardio averiado.

5. Los datos arriba mencionados confirman la opinión de Starr y sus colegas, o sea, que el trabajo por contracción ventricular es el valor apropiado para considerar el análisis del funcionamiento ventricular. Aunque una relación consistente se encontró entre la presión atrial y el trabajo por contracción ventricular en el mismo lado, tal relación no fue consistentemente encontrada, (a) entre presión atrial derecha y trabajo por contracción ventricular izquierda, o vice versa; (b) entre presión atrial y volumen por contracción; o (c) entre presión atrial y producción cardíaca total.

6. Una alteración significativa en el estado circulatorio (como inyección de epinefrina, constricción coronaria, anemia severa y resis-
encia aórtica aumentada) produjo curvas de función ventricular diferentes; en este nuevo estado circulatorio, sin embargo, la relación entre presión atrial y trabajo por contracción fue una vez más consistente.

7. Se cree que previas investigaciones que dudaban la validez de la relación de Frank-Starling habían sido basadas en una u otra de las siguientes razones; (a) correlaciones erróneas o impropiamente atentadas, (b) falta de apreciación del empinado de la curva de función ventricular en su esfera de actividad baja, y la importancia de la determinación de presiones de henchimiento, o (c) falta de apreciar el que una curva sencilla pueda expresar los patrones de funcionamiento ventricular producidos cuando ciertos parámetros de sus condiciones de trabajo son alterados.

8. La demostración de la familia de curvas de Starling o de funcionamiento ventricular hace posible un concepto unificado a base de que cambios en función ventricular puedan ser más completamente apreciados.

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STANLEY J. SARNOFF and ERIK BERGLUND

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