Evaluation of the Contractile State of the Human Heart from the First Derivative of the Apexcardiogram

By Attilio Reale, M.D.

SUMMARY

The first derivatives of the left ventricular pressure pulse \( (dp/dt \text{ LV}) \) and of the apexcardiogram \( (\Delta \text{ ACG}) \) were recorded 73 times in 45 subjects, and the time intervals from the peak of the R wave of the electrocardiogram to the peak of the derivatives \( (t-dp/dt \text{ LV} \) and \( t-\Delta \text{ ACG}) \) were determined under different circulatory conditions. These parameters express the duration of the development of maximum tension during isometric contraction of the ventricle. The values obtained from the left ventricular pressure pulse and from the ACG showed close correlation both at rest and after pharmacological interventions which enhanced or depressed the myocardial contractile state. During orciprenaline infusion, \( t-dp/dt \text{ LV} \) and \( t-\Delta \text{ ACG} \) were consistently shortened, while they increased in most cases after beta-adrenergic receptor blockade.

Determination of the time to peak derivative of the ACG, a parameter so far unexplored, is proposed as a simple method of detecting changes in the myocardial contractile state in the intact human being.

Additional Indexing Words:
Myocardial contractility Beta-adrenergic stimulation Beta-adrenergic blockade
First derivative

Changes in myocardial contractility have generally been interpreted as indicating changes in cardiac performance. Consequently, much effort has been devoted to the evaluation of the contractile state of the heart.

Among the different parameters used as indices of contractility, one of the more commonly employed methods relates to the analysis of the rate of pressure rise in the left ventricle, or first derivative of the ventricular pressure pulse.\(^1\)\(^2\) Its value, however, is limited by the fact that \( dp/dt \) is influenced by factors extraneous to contractility such as variations in ventricular preload and afterload.\(^3\)\(^4\)

To overcome the latter difficulty, Mason and associates\(^4\)\(^5\) proposed to determine the time interval from the onset of ventricular contraction to the peak of the first derivative, rather than only the magnitude of \( dp/dt \). The factor thus obtained \( (t-dp/dt) \) expresses the duration of the development of maximum tension in the ventricle. It varies inversely with the myocardial contractile state and is said to be uninfluenced by variations of ventricular load. The validity of this method was verified on canine heart, on human isolated papillary muscles, and in man under varying conditions of contractility and ventricular load. A shortening of \( t-dp/dt \) always corresponded to an increase, and a lengthening of it, to a decrease of the myocardial contractile state.\(^4\)\(^5\)

However, this, as well as other approaches to the analysis of the first derivative of the ventricular pressure pulse,\(^6\) obviously requires left heart catheterization. Hence, simpler yet reliable methods for the evaluation of myocardial contractility would be advantageous.
The recording of the low frequency displacement curves of the precordium overlying the apex of the heart yields a tracing, commonly known as the “apexcardiogram” (ACG), which has been extensively used in the study of the mechanical function of the heart in health and disease. A close correlation has been repeatedly demonstrated between the ACG and the hemodynamic events within the left heart.

This similarity suggested that it could be possible to substitute for the left ventricular pressure pulse the ACG, by analyzing the rate of ascent of the systolic phase of the ACG, as determined by the recording of its first derivative.

Owing to the difficulty in calibrating the sensing devices, and therefore, in assigning a unit of measurement to the first derivative of the ACG, the latter by itself appeared inadequate for the quantitative evaluation of ventricular function. An analysis of the ACG in terms of the time interval from the onset of contraction to the peak of its first derivative bypasses this difficulty, as it is expressed in time units, independently of the height of the derivative.

The purpose of the present study was to determine (1) whether correlation exists between the measurements, time to peak of the first derivative of the left ventricular pressure pulse (t-dp/dt LV) and time to peak of the first derivative of the apexcardiogram (t-Δ ACG), and (2) whether pharmacologically induced variations in the contractile state would cause parallel modifications of the above parameters.

**Methods**

In seven normal individuals and in 38 patients with acquired and congenital heart disease (table 1), the following data were obtained in the course of diagnostic cardiac catheterization: (1) left ventricular pressure through the transseptal or retrograde arterial route,* (2) brachial arterial pressure,* (3) apexcardiogram, (4) first derivative of the left ventricular pressure (dp/dt LV), and (5) first derivative of the apexcardiogram (Δ ACG).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>No heart disease</td>
<td>7</td>
</tr>
<tr>
<td>Mitral valvular disease</td>
<td>14</td>
</tr>
<tr>
<td>Aortic valvular disease</td>
<td>19</td>
</tr>
<tr>
<td>Patent ductus</td>
<td>2</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>1</td>
</tr>
<tr>
<td>Atrial septal defect (ostium primum)</td>
<td>1</td>
</tr>
<tr>
<td>Myocardiopathy</td>
<td>1</td>
</tr>
</tbody>
</table>

The apexcardiogram was recorded by means of a piezo-electric microphone† and an amplifier with the band-pass filter set to 0.1 cycles/sec for the lower limit and to 20 cycles/sec for the higher limit.† The microphone was held by hand at the point of maximal apical impulse with the patient in the supine position. The first derivatives of pressure and ACG were obtained by means of an RC differentiator with a time constant of 0.5 msec. The instrument has an output proportionately linear to input frequency within 5%, up to a maximum frequency of 75 cycles.† All tracings were recorded at 100 mm/sec paper speed with time lines at 0.05 sec.

In 11 patients the procedure was repeated in an exactly similar fashion during intravenous infusion of orciprenaline‡ and after intravenous injection of a beta-adrenergic receptor blocking agent.§ These different circulatory situations, the duration in milliseconds was measured from the peak of the R wave of the electrocardiogram to the peak of the first derivative of the left ventricular pressure (t-dp/dt LV) and from peak of R wave to peak derivative of the apexcardiogram (t-Δ ACG) on a minimum of five cardiac cycles and averaged. In the only two patients of the series with atrial fibrillation, the measurements were made on the beats with a preceding diastole of equal length.

**Results**

The time to peak of the first derivative of the left ventricular pressure and the time to peak of the first derivative of the ACG were identical in 23 of the 45 persons studied under basal conditions (from 40 to 92 msec.

*Statham P23 Db pressure transducers.

‡Dihydroxyphenyl-isopropylaminoethanol sulfate, registered name Alupent.
§Giba 39089-Ba.
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In 15 cases, t-dp/dt LV was longer, and in seven cases, shorter than t-Δ ACG. In both groups the maximum difference was 10 msec and the average difference was 7 msec. The same proportion of agreement and disagreement between t-dp/dt LV and t-Δ ACG was observed when the total number of 73 determinations obtained from the 45 subjects were considered, that is, under basal conditions, during orciprenaline infusion, and after beta blockade (fig. 1). Time to peak of first derivative of the left ventricular pressure and time to peak of the first derivative of the ACG were identical in 39 instances (from 25 to 92 msec; average, 57 msec). In 25 instances t-dp/dt LV was longer and in nine, shorter than t-Δ ACG. In both groups the maximum difference was 10 msec and the average difference was 6 msec. In the 11 patients submitted to intravenous infusion of orciprenaline, a drug which stimulates beta-adrenergic receptors, t-dp/dt LV showed decreases ranging from 5 to 30 msec (average,
Discussion

A statement of validity of the method proposed in the present investigation should be supported by an affirmative answer to the following questions: (1) Does the upstroke of the systolic phase of the apexcardiogram correspond to the isometric contraction of the left ventricle? (2) Does the parameter, time to peak derivative of the left ventricular pressure represent a reliable measurement of the myocardial contractile state? (3) Are variations of the time to peak derivative of the ACG comparable to those of the time to peak derivative of the left ventricle under different conditions of contractility?

Studies of simultaneous recordings of intracardiac pressures and of the apexcardiogram have repeatedly demonstrated that the rapid rising portion of the ACG comprised between the end of the a wave and the peak of the curve (E point) is inscribed during the ascending limb of the left ventricular pressure pulse and represents the period of isometric contraction. Our data confirmed these findings. Configuration and time relationships on the ACG corresponded closely to the pressure events in the left ventricle. According to Tavel and associates, corrections should be made on the time measurements for the different delay in conduction through the cardiac catheters and through the recording devices of the ACG, the difference being approximately a 3-msec lag of the pressure curve behind the ACG deflections. In our study, standard catheters and pressure transducers rather than catheter tip manometers were used for the recording of left ventricular pressure and its derivative. The main reason for this was that the left ventricle was entered by transseptal or retrograde arterial catheterization by the percutaneous Seldinger technique which does not permit the use of micromanometers. This technique may have introduced phase shifts and distorted to some extent time relationships as far as dp/dt LV is concerned. However, we were not interested in absolute values, but rather in changing measurements.
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Figure 4
Variations of \( t-dp/\text{dt} \) \( \text{LV} \) and \( t-\Delta \text{ACG} \) after beta-adrenergic receptor blockade. (a) At rest, (b) after beta-adrenergic blockade. Each pair of bars represents one patient.

Figure 5
(a) Simultaneous recordings of left ventricular pressure (LV), brachial arterial pressure (BA), ECG, apexcardiogram (ACG) and first derivative of left ventricular pressure (dp/dt LV); \( t-dt/dp \) \( \text{LV} = 45 \text{ msec} \). (a1) Same as a showing the first derivative of ACG (\( \Delta \text{ACG} \); \( t-\Delta \text{ACG} = 38 \text{ msec} \). (b1) Same tracings as in a1 but after \( \beta \)-adrenergic blockade; \( t-dp/\text{dt} \) \( \text{LV} = 60 \text{ msec} \). (b) Same tracings as in a, but after \( \beta \)-adrenergic blockade; \( t-\Delta \text{ACG} = 60 \text{ msec} \).
justified to use the first derivative of the ACG as a measure of the rate of development of tension that occurs during isometric contraction of the ventricle, and hence the interval, time to peak derivative of the ACG, should have the same significance as the interval, time to peak derivative of the left ventricular pressure, in expressing the duration of the development of maximum tension.\textsuperscript{5} Comparison of the absolute values for both parameters under control conditions seems to support the following statement: the time intervals were identical in most cases and deviated only slightly from each other in the remaining determinations. In other words, the duration of the development of maximum tension was similar whether determined from the left ventricular pressure or from the apexcardiogram. It is hardly believable that such a degree of correlation in a significant number of determinations could have been the result of coincidence.

The present study confirmed the findings of Mason and associates.\textsuperscript{4} When the myo-cardial contractile state was enhanced by orciprenaline infusion, there was an elevation of peak dp/dt accompanied by a decline in t-dp/dt. Conversely, when contractility was depressed by beta-adrenergic blockade, most patients showed a lower peak of dp/dt in the face of a prolonged t-dp/dt (fig. 6). There were only rare instances in which the height of dp/dt and t-dp/dt did not vary in the expected direction in respect to each other. For practical purposes, therefore, it appears from these data that t-dp/dt by itself may be used as an index of a changing contractile state without consideration of the variations in the size of the derivative. This observation was essential for the method described in the present study, as it is extremely difficult to calibrate the recording devices of the ACG and assign a unit of measurement to the derivative of the ACG. This was the fundamental rationale for choosing the parameter time to peak of the derivative in the attempt to utilize the ACG as an index of changes in the contractile state. It is well known that
the size of the ACG can change considerably depending on how the crystal is held to the chest wall. In our experiments reproducibility was the rule in repeated predrug determinations; when the sensing device was repositioned after pharmacological interventions which affected the hemodynamic situation, it was usually impossible to reproduce the same aspect of the ACG as before drug administration. The actual size of the derivative of the ACG changed too in the expected direction (figs. 3 and 5). Although no attempt was made at quantitating these changes because of the above-mentioned calibration problems, it is possible that technical refinements could lead to the inclusion of the size of Δ ACG in the evaluation of contractile state.

It is recognized that a change in heart rate and hence in total cycle length by itself may affect measurement of the time to peak derivative, since most time intervals tend to change in the direction in which cycle length is altered. In our experiments with drugs, no correction was made for changes in heart rate. However, when variations of time to peak derivative were expressed in percentage deviation from the predrug values and compared to the percentage changes in total cycle length, the following values were obtained. In 16 of the 20 instances in which drug administration affected the measurement of the time to peak derivative, this variation was definitely greater than the change in cycle length; in three, it was slightly less when marked changes in heart rate had occurred, and in one, it was equal to the change in cycle length. Thus, in most cases changes in cycle length could not be considered the sole responsible cause of shortening or lengthening of the parameter time to peak derivative. Furthermore, the duration of maximum tension as measured by this method was appreciably altered even in those instances in which drugs did not cause any significant change in heart rate and cycle length.

The results of this study clearly indicate that the time to peak derivative of the ACG followed consistently the behavior of the time to peak derivative of the left ventricular pressure whenever the latter deviated from its resting values by pharmacological interventions which enhanced or depressed the myocardial contractile state.

For the measurement of t-dp/dt LV and t-Δ ACG, the peak of the R wave of the electrocardiogram was arbitrarily chosen as a reference point rather than the onset of ventricular contraction. The inaccuracy which may have resulted from comparing two entirely different recording systems was outweighed by the much greater ease of defining the R wave than the beginning of contraction either from the ventricular pressure pulse or the ACG derivatives. It must be reemphasized that the method described does not in any way attempt to establish an absolute quantification of contractility between different individuals. The values for t-Δ ACG showed too wide a range even in normal subjects, and there was much overlapping between the figures for normal persons and for persons with the various diseases examined. The technique was merely designed as a means of detecting changes in the myocardial contractile state in the same patient. In this respect, regardless of possible imprecision, there was a closely similar behavior of the parameter being investigated and of that used as a reference measurement.

Some difficulties can be encountered in producing a good apexcardiogram and hence a reliable derivative of it. This occurs whenever the apex of the heart does not come close enough to the chest wall during ventricular contraction to produce an appreciable displacement, as in obese or emphysematous subjects, and the need for a more sensitive pickup device is recognized. The best tracings were obtained in the presence of hypertrophy or hyperactivity of the left ventricle, and the list of diseases in table 1 reflects these situations. Moreover, the configuration and size of the ACG can be changed considerably depending on how the crystal is held. This, of course, introduces the problem of reproducibility of the results. The technique used in the present study was
that generally followed for the recording of the ACG: the crystal was held by hand in the region of the apex and manipulated until a good quality tracing was obtained on the oscilloscope. Recognition of a satisfactory tracing was derived from previous experience with apexcardiography. Once the best position was defined, it was found that the same contour of the ACG could be reproduced at will in the same patient as long as the hemodynamic situation remained stable. Negation of the reproducibility of the ACG would invalidate most of the work accomplished in this field, especially that dealing with confrontation of ACG and intracardiac events. The most variable factor, depending on the amount of pressure applied by the hand holding the crystal, was the height of the ACG. This did affect the size of its derivative but not to any extent the time interval, peak of R wave to peak of derivative. The same observation applies to the particular contour of the ACG which is obtained in certain diseases such as aortic stenosis. In these cases the E point can be blurred and the ascent is broadened. Conventional interpretation of the ACG may thus be more difficult, but, in the present study, only the derivative was considered and therefore sharp definition of the E point seems relatively unimportant. Broadening of the ascent will be translated into a longer time for the derivative to reach its peak. This is believed to be a direct consequence of the hemodynamics of the diseased state which is apparent with the same characteristics on the left ventricular pressure pulse.

Knowledge of the configuration of the left ventricular pressure pulse and of its derivative while recording the ACG could have prompted the investigator to manipulate the crystal until both derivatives looked alike, thus invalidating the results. Because of the insufficient available number of adequate amplifiers, derivatives of pressure and ACG were recorded in succession so that the observer had no simultaneous confrontation with these curves while they were being inscribed. Attention was directed mainly at obtaining a good quality ACG, without consideration of its derivative. Several separate strips of recording were obtained for each determination after repositioning the crystal on the chest wall. In order to prevent biased interpretations of the tracings, $\Delta$ ACG was measured in every instance before $t-\Delta$ ACG LV, that is, without knowledge of the hemodynamic data. At any rate, the technique is designed to be used without the adjunct of left heart catheterization. The method is simple and safe and causes no inconvenience to the patient. It does not require complex or expensive equipment. Its limitations are mainly those of conventional apexcardiography. With this in mind, it is concluded that the time to peak derivative of the ACG, a parameter so far unexplored, does indicate changes in the myocardial contractile state with the same approximation as that yielded by the factor, time to peak derivative of the left ventricular pressure.

References

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To Perish by Silence

... What is needed, suggests Oppenheimer, is a harsh modesty, an affirmation that common men cannot, in fact, understand most things and that the realities of which even a highly trained intellect has cognizance are few and far between.

With respect to the sciences, this somber view seems unassailable. And perhaps it dooms most knowledge to fragmentation. But we should not readily accede to it in history, ethics, economics, or the analysis and formulation of social and political conduct. Here literacy must reaffirm its authority against jargon. I do not know whether this can be done; but the stakes are high. In our time, the language of politics has become infected with obscurity and madness. No lie is too gross for strenuous expression, no cruelty too abject to find apologia in the verbiage of historicism. Unless we can restore to the words in our newspapers, laws, and political acts some measure of clarity and stringency of meaning, our lives will draw yet nearer to chaos. There will then come to pass a new Dark Ages.—George Steiner: Language and Silence: Essays on Language, Literature, and the Inhuman. New York, Atheneum, 1967, p. 34.
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