THE FIRST DERIVATIVE OF APEX CARDIOMGRAM AND ITS UTILIZING FOR DETERMINING SOME SYSTOLIC AND DIASTOLIC TIME INTERVALS IN MAN

NIKOLAI KOLEV

SUMMARY

To determine the usefulness of the time intervals obtained from the first derivative of apex cardiogram (dA/dt) in assessing contraction and relaxation, 20 hemodynamically and angiographically investigated patients with coronary artery disease and 29 patients with hypertensive heart disease were studied. As a control group there were used 50 normal subjects. Since contraction and relaxation is dependent on preload and afterload, the time interval from R wave of electrocardiogram to the positive peak of dA/dt (R to dA/dt) and two relaxation parameters derived from negative peak dA/dt were investigated, early relaxation index (ERI) and total relaxation index (TRI). In patients with coronary artery disease all of these parameters were augmented (R to dA/dt: 121 ± 14 msec versus 76 ± 14 msec for controls; ERI: 13.1 ± 8 versus 4.3 ± 5 in controls; TRI: 149 ± 30 Versus

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71 \pm 18 for controls) and also patients with hypertensive heart disease showed similar changes (R to dA/dt: 115 \pm 15 msec; ERI: 9.5 \pm 6; TRI: 81 \pm 19). Significant correlations between these indexes and some internally parameters of myocardial performance were observed.

These findings indicate that systolic and diastolic time intervals measured from the first derivative of apex cardiogram may be used as a reliable indices for evaluation of contraction and relaxation independently of preload and afterload.

Measurement of systolic and diastolic time intervals for cardiac evaluation, such as isovolumetric contraction, preejection period, left ventricular ejection time and isovolumetric relaxation time has been emphasized by many authors. However, these intervals are influenced by factors extraneous to contractility and relaxation, such as variations in preload and afterload\textsuperscript{1,2}.

To overcome the latter difficulty, Reale\textsuperscript{3} proposed to determine the time interval from onset of ventricular depolarisation to the positive peak of the first derivative of left apex cardiogram (dA/dt), because he established the similarity in timing and contour between the first derivative of left ventricular pressure and dA/dt. In order to avoid the influence of afterload on relaxation, we divided as suggested by Manolas et al.\textsuperscript{4} time intervals derived from negative peak dA/dt by mean aortic pressure.

The first purpose of this study was to investigate

Key words: First derivative of apex cardiogram Systolic and diastolic time intervals Coronary artery disease Hypertensive heart disease
the average value of interval R to positive peak dA/dt and indices derived from negative peak dA/dt in patients with various cardiac disease and to compare the value obtained with those in a control group. The second purpose was to investigate in man the relationship between above mentioned parameters and some internal indexes obtained by heart catheterization.

SUBJECTS AND METHODS

This study covers 25 catheterized and angiographically investigated patients with arteriosclerotic coronary heart disease, cardiomyopathies, congenital heart disease and acquired valvular disease. The invasive studies were performed when clinically indication for diagnostic or therapeutic reasons, frequently before cardiac surgery.

Cardiac catheterization: Left ventricular pressure were recorded through well flushed 100 cm No 7 and No 8 catheters with Statham transducer (p23 Db) balanced at the mid-chest level on the multichannel recorder Electronics for Medicine using a paper speed of 100 mm/sec. The first derivative of the left ventricular pressure was obtained by means of resistance-capacitance circuit with time constant of 1 msec.

Angiography: Left ventricular biplane angiograms were filmed at a 6 frames/sec. Left ventricular volumes were calculated by the method of Dodge et al.* Clinical, hemodynamic and angiographic data of patients are given in the table I.

In the control group (50 normal subjects with an average age of 40 ± 12 years) no previous history of
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Table 1: Clinical characteristics and test results for patients with heart disease. ECG: electrocardiogram, CXR: chest X-ray.
Furthermore, twenty nine patients with hypertensive disease, from 34 to 58 years (medium age 41 ± 13 years) were also studied. The hypertensive patients were defined as subjects who had blood pressure persistently higher than 150/90 mm Hg, without secondary hypertension. When investigation were performed patients suffered from decompensation (NYHA I and II).

The polygraphic tracing was performed by rotating recumbent subjects 30 to 50° toward left lateral decubitus position. Apex cardiogram were recorded by means of a piezoelectric transducer Hellige (GFR) or RFT(GDR) with a time constant 0.1 sec. The first derivative of apex cardiogram was obtained by an unfiltered R-C circuit exhibiting a constant phase shift of 90° from 0 to 160 cycles/sec and a time constant 0.5 msec. In the catheterized patients polygraphic tracing were obtained within a week.

Analysis of the simultaneous tracings: (Fig. 1).
1. Interval from R wave of the electrocardiogram to the positive peak of the first derivative of the apex cardiogram (R to dA/dt).
2. Relaxation indexes derived from the negative peak of dA/dt. According to the Laplace's law there is a relationship between the minimal dP/dt and the rate in tension fall (negative dT/dt) during the isovolumetric relaxation phase. On the basis of the linear relationship between min dP/dt and the mean aortic pressure, the lateration in aortic pressure could be overlooked when using min dP/dt/mean aortic pressure. In the place of the min dP/dt we employed the time intervals obtained from min dA/dt, and mean aortic pressure was assessed by auscultatory Korotkoff's technique in the brachi-
Table II. The results of investigated interval R to positive peak dA/dt in msec and early apex cardiographic relaxation index (ERI) and total relaxation index (TRI). The value of P obtained when compared patients with control group.

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<th>Normal subjects</th>
<th>R to dA/dt</th>
<th>ERI</th>
<th>TRI</th>
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<td>n 50</td>
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<td>Ischemic heart</td>
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<td>13.1 ± 8</td>
<td>149 ± 32</td>
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<td>n 20</td>
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<td>Hypertensive</td>
<td>115 ± 15</td>
<td>9.5 ± 6</td>
<td>82 ± 19</td>
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<td>n 29</td>
<td>P 0.05</td>
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Table III. Correlations between parameters derived from the first derivative of apex cardiogram and internal indices of left ventricular performance. P value were for all correlations 0.001, except* P 0.01 and** NS. Abbreviations as in Table I.
Fig. 1. Simultaneous records of electrocardiogram (ECG), Phonocardiogram (PCG), and first derivative of apex cardiogram (dA/dt). 1 = interval R to dA/dt; 2a = interval early apex cardiographic relaxation time; 2b = total apex cardiographic relaxation time interval.
al artery.

A) Early relaxation index ERI = \frac{EART}{MAP} \times 100
where EART is the early apex cardiographic relaxation
time interval measured from the aortic component of
second heart sound A2 in the phonocardiogram to the ne-
gative peak of dA/dt, MAP is the mean arterial pressure
(MAP = diastolic pressure + 1/3 pulse pressure).

B) Total relaxation index TRI = \frac{TART}{MAP} \times 100
where TART is the total apex cardiographic relaxation
time elapsed from A2 to the protodiastolic nadir of the
apex tracing, the latter being defined more accurately
by determining the point where dA/dt after having reach-
ed its negative peak assumed and reached the zero; thus
provides more exact temporal measurement of the pro-
todiastolic nadir (0 point) of the apex tracing.

All intervals in examined group subjects are measured
in msec and corrected for heart rate by Bazett's formula
(corrected value = measured interval/\sqrt{R-R}. At least fi-
vie consecutive cardiac cycles were evaluated, and the re-
sults are presented as the average value. The overall
results from each group are reported as the mean ± stan-
dard deviation. Statistical analyses were performed us-
ing Student's t-test and standard least square linear regr-
ression method.

RESULTS

Table II lists the results for measurement of inter-
val R to positive peak dA/dt and indices derived from
negative peak dA/dt and mean arterial pressure in 2 gro-
ups of patients with ischemic heart disease and hyperte-
nsive disease. In these patients was established an elongation of the interval $R$ to $dA/dt$ and an increase of the relaxation indexes. Only in hypertensive disease the augmentation of TRI were statistically insignificant.

Table I contains clinical information, results of hemodynamic and angiographic data and measurement of $R$ to $dA/dt$, ERI and TRI in 25 patients subjected to cardiac catheterization. The significant correlation found when results of measurement of interval $R$ to $dA/dt$, ERI and TRI were compared with indexes derived from cardiac catheterization and angiographic data are listed in Table III.

**DISCUSSION**

Many investigators reported the similarity in timing and contour between the first derivative of left ventricular pressure and first derivative of left ventricular apex cardiogram. It was shown in the experimental study 7-8 and clinically$^9$ that correlation between the $dA/dt$ and $dP/dt$ during acute hemodynamic changes was fairly good. All those authors used calibrating device when measured the first derivative of apex cardiogram and expressed its value in different units - mmHg/sec$^7$-$^8$, $X/sec^9$ or grammes/sec$^{10}$.

The quantitation of the $dA/dt$ by use of amplitude have been rare because of difference among individual subjects in cardiac size and thoracic shape$^2$-$^3$,$^6$. In order to avoid the calibrating difficulties, and therefore in assessing a units of measurement of first derivative of apex cardiogram we examined the time intervals derived from positive and negative peaks of $dA/dt$. 
Measurement of conventional systolic and diastolic time intervals has been emphasized by many authors. However, most of these intervals are influenced by pre-and afterload. To overcome the latter difficulties we used a suggested by Reale interval R to peak dA/dt and introduced the EAI and TAI.

Mason and associates found that time from electrical stimulation to peak dP/dt was inversely related to contractile state in isolated muscle strips and that the interval was independent of pre-and afterload. In human catheterization studies they showed that time from ventricular depolarization to peak left ventricular dP/dt did not vary with load conditions. The same is valid for interval R to positive peak dA/dt. Vetter et al. established that no change in R to dA/dt in patients studied before and after valve replacement for severe aortic stenosis. Our data for elongation of interval R to dA/dt in coronary artery disease and close correlation with ejection fraction confirm the results of Vetter et al. and are in disagreement with those of Van de Werf et al.

Studies of cardiac muscle relaxation were performed by Parmley and Sonnenblick using isolated cat papillary muscles. Under afterloaded contractions, relaxation was divided into a rapid initial phase and a second slower exponential phase. The magnitude of the decline in tension during the rapid phase was greater at a higher afterloads. These data suggest that higher afterloads are associated with a more rapid fall in tension as well. It should be pointed out, however, that rate of fall of tension is proportional to the negative peak dP/dt.
A major difficulty in evaluating clinically left ventricular relaxation is establishing a suitable index of relaxation. In previous studies the negative peak dP/dt was used as an index of myocardial relaxation\textsuperscript{4,5,14}. But its appeared to be influenced by the mean aortic pressure\textsuperscript{4,5}. Similarily time intervals derived from negative peak dA/dt also is influenced by afterload\textsuperscript{15}. In this study using EAI and TAI it is possible (1) to determine a more accurate 0 point of the apex tracing\textsuperscript{3,16}, because conventional apex cardiographic A2-0 interval is not identical with isovolumetric relaxation time\textsuperscript{17,18} and (2) avoiding influence of afterload.

Our findings of increased relaxation indexes in ischemic heart disease with old myocardial infarction may be explained as follows. Loss of myocardium results in a decrease of left ventricular contractility, which is according to Cohn's study\textsuperscript{4} accompanied by a similar decrease of the relaxation ability. The second factor for the disturbed relaxation is considered to be the reduced interfascicular tension. Energy which is stored during contraction in the elastic wall elements of the left ventricle, is the sum of the energy stored in the infarcted and non-infarcted myocardium. Since the infarcted area is stiffer than the non-infarcted myocardium, it can be assumed that the energy stored there is less\textsuperscript{5}.

The mechanism of an impairment of relaxation in hypertensive disease is not known, but it may be related to a reduction in available energy during anaerobiosis in hypertrophied left ventricle. There is evidence to indicate that more energy is required for the process of calcium removal from contractile sites than for the steps that initiate muscle contraction\textsuperscript{19}. 
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* The invasive studies in this investigation were made in the Hemodynamic Laboratory of the National Hungarian Institute of Cardiology, Budapest and author express his thanks to Ass. Prof. T. Romoda for examination of the probands.