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Non-invasive Assessment of Left Ventricular End-diastolic Function. Usefulness of Apexcardiographic A-wave Peak Time (a New Parameter) in Correlation with Echocardiographic Indices

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ABSTRACT. An investigation was conducted on the relationships between A/E-O ratio (height of A-wave expressed as a percentage of total systolic deflection of the apexcardiogram) and A-wave peak time (time from onset to peak of A-wave on apexcardiogram) and echocardiographic left ventricular end-diastolic indices in various left ventricular diseases (hypertension, ischemic heart disease, hypertrophic cardiomyopathy and congestive cardiomyopathy).

Majority of patients with ischemic heart disease (myocardial infarction showing abnormal wall motion) and with congestive cardiomyopathy had a prolonged A-wave peak time (round A-wave) in addition to a high A/E-O ratio. In contrast, most of the patients with hypertrophic cardiomyopathy and those with hypertension had a normal A-wave peak time (peaked A-wave) and a high A/E-O ratio.

Therefore, a concomitant use of this new parameter (A-wave peak time) with conventional A/E-O ratio proved to be a valuable way of evaluating severity of hemodynamic alterations in left ventricular disorders.

An apexcardiographic parameter commonly employed in evaluating left ventricular hemodynamics is the A/E-O ratio[1-5]. It is, however, known that an elevation of left ventricular end-diastolic pressure may be present even though the A/E-O ratio is not increased, and that the A-wave amplitude may even decrease when the left ventricular disorder progresses to produce higher end-diastolic pressure[4-6]. There are reports that the pattern and duration of the A-wave may also bear a close relation to left ventricular function[7,8]. We have noted that in patients with left ventricular systolic overloads such as hypertension, aortic stenosis and hypertrophic cardiomyopathy both the total A-wave duration and the A-wave peak time (time from onset to peak of the A-wave) appeared to be shorter than in patients without systolic overloads but with left ventricular dysfunction due to congestive cardiomyopathy or ischemic heart disease[9]. The

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A-wave peak time showed a more distinct difference between hypertensive and ischemic heart disease groups (37.8±7.7 msec versus 60.4±14.7 msec, $p<0.01$) than did the A/E-O ratio (18.7±8.2% versus 15.7±11.8%, $p=0.1$)[10]. It seems, therefore, that the morphology of the A-wave is affected by the degree of ST-T abnormalities on electrocardiogram as well as by the presence of a pressure overload of the left ventricle[9,10].

In an attempt to elucidate the factors which cause the differences in A-wave patterns we used several echocardiographic indices of left ventricular end-diastolic hemodynamics ; (1) the end-diastolic step formation on descending limb of the mitral A-wave, (2) the left ventricular end-diastolic dimension, and (3) distensibility of the left ventricular end-diastolic phase (left ventricular end-diastolic expansion ratio).

SUBJECTS AND METHODS

We studied 41 patients with various left ventricular diseases. Eighteen patients had ischemic heart disease with old myocardial infarction and with abnormal left ventricular wall motion documented by electrocardiogram and coronary arteriography as well as left ventriculography. Three patients had congestive cardiomyopathy with an angiographic ejection fraction below the lower limit of normal in the absence of valvular, hypertensive, congenital or ischemic heart disease. Ten patients had hypertrophic non-obstructive cardiomyopathy with an ejection fraction of 60% or more established by echocardiogram and by left heart catheterization including coronary arteriography and left ventriculography. Another ten patients had hypertension with systolic blood pressure of 180 mmHg or more. The latter two groups of patients had no overt heart failure. All patients were in normal sinus rhythm and had a normal P-R interval on electrocardiogram. The male to female ratio was 32:9 with an average age of 48 years (Table 1).

TABLE 1: Classification of 41 Subjects Studied into Clinical Status, Number of Cases, Sex and Age.

Clinical Status	Number of Cases	Male : Female	Age (y-o)
Ischemic Heart Disease (old Myocardial Infarction)	18	15 : 3	55(24-78)
Congestive Cardiomyopathy	3	3 : 0	39(22-49)
Hypertrophic Non-obstructive Cardiomyopathy	10	8 : 2	36(26-47)
Hypertension	10	6 4	56(45-67)
Total	41	32 : 9	48(24-78)

The apexcardiogram was recorded at the site of the maximal left ventricular impulse with the patient in the supine, or if necessary, in the left recumbent position. The pulse transducer had a time constant of 4 seconds and was linear up to 50 Hz. The echocardiogram was simultaneously recorded using

Ekoline-20A interfaced by IREX Continutrace 101, and the echotransducer was placed over the 3rd or 4th left intercostal space. The recordings were made during normal expiratory apnea and with a paper speed of 50 or 100 mm per second.

The A/E-O ratio (normal value of 10.0% or less)[9] and the A-wave peak time (normal value of 36.3±13.9 msec)[10] were calculated from the apexcardiogram (Fig. 1a). From the echocardiogram the left ventricular end-diastolic dimension (Dd) and the left ventricular end-diastolic expansion ratio $\left(\frac{Dd-Dd'}{Dd}\right)$ were measured, where Dd' represents the echocardiographic dimension at the onset

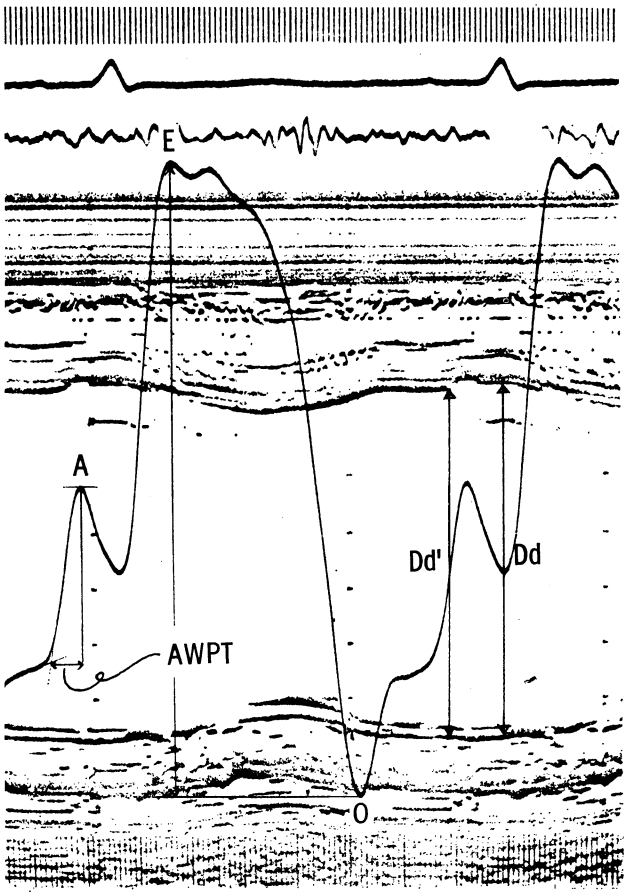


Fig. 1 a. The apexcardiogram and left ventricular echo from a 55-year-old male with an old myocardial infarction and ejection fraction of 42%. The A-wave peak time (AWPT) is measured from onset to peak of the A-wave in millisecond besides the measurement of A/E-O ratio. The high A/E-O ratio, the prolonged A-wave peak time and the small left ventricular end-diastolic expansion ratio.

of the left ventricular end-diastolic expansion caused by left atrial contraction[11] (Fig. 1b). The presence or the absence of the step formation on the anterior mitral echo (Fig. 1c) was also observed.

All data are expressed as a mean±standard deviation. Statistical correlations were carried out using the appropriate t test and a p-value <0.05 was considered significant.

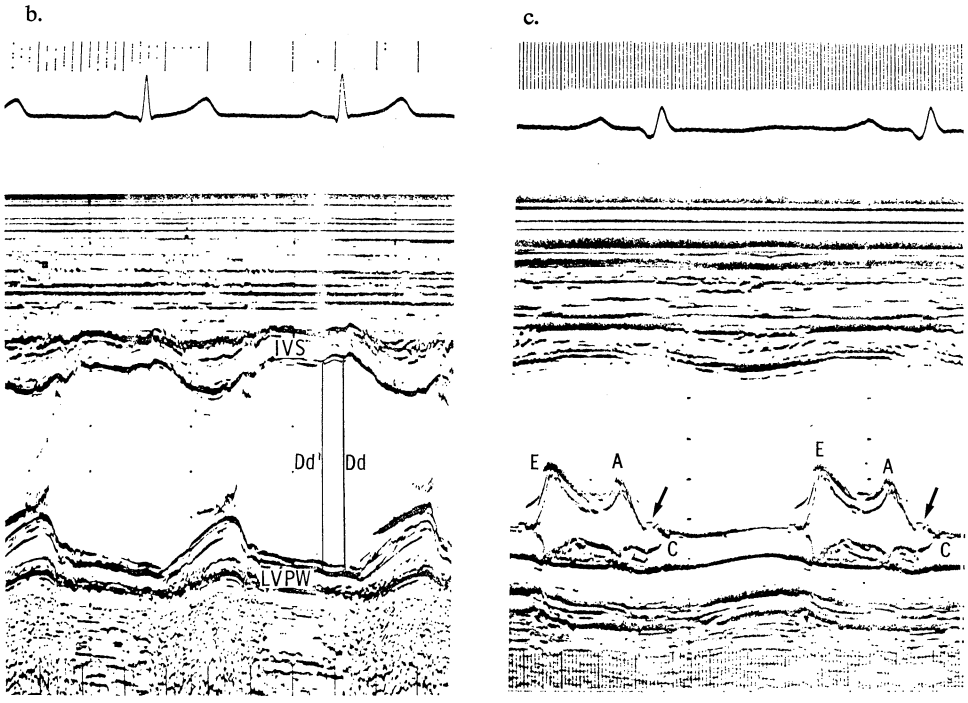


Fig. 1 b. The echocardiogram for measuring left ventricular end-diastolic dimension (Dd) at the peak of R-wave on electrocardiogram,and left ventricular end-diastolic expansion ratio$\left(\frac{Dd-Dd'}{Dd}\right)$, where Dd' represents a dimension at the onset of left ventricular end-diastolic expansion caused by left atrial contraction.

c. The mitral echo recorded from the same patient as la. The step formation (arrow) is clearly shown as an end-diastolic shoulder formation between A and C points on mitral echo.

RESULTS

1) The relation between the A/E-O ratio and echocardiographic parameters (Fig. 2a, b, c).

Figure 2a shows the relationship of the A/E-O ratio to the left ventricular end-diastolic dimension. Although no statistically significant correlation ($r=+0.38$, $p>0.01$) was found between the two parameters as a whole, end-diastolic dimension tended to be smaller in patients with hypertension and hypertrophic

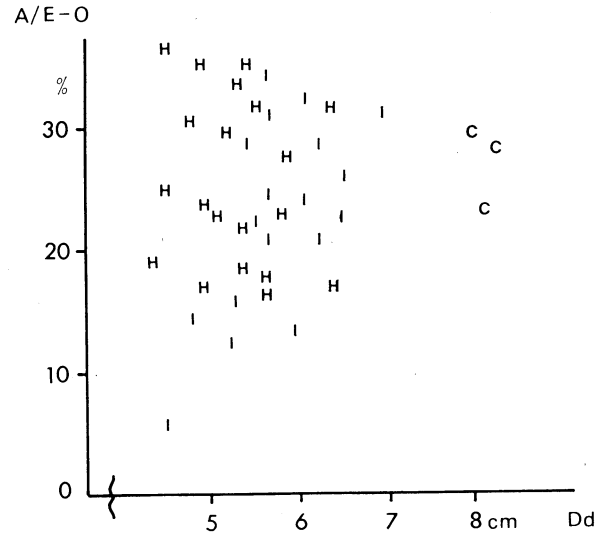
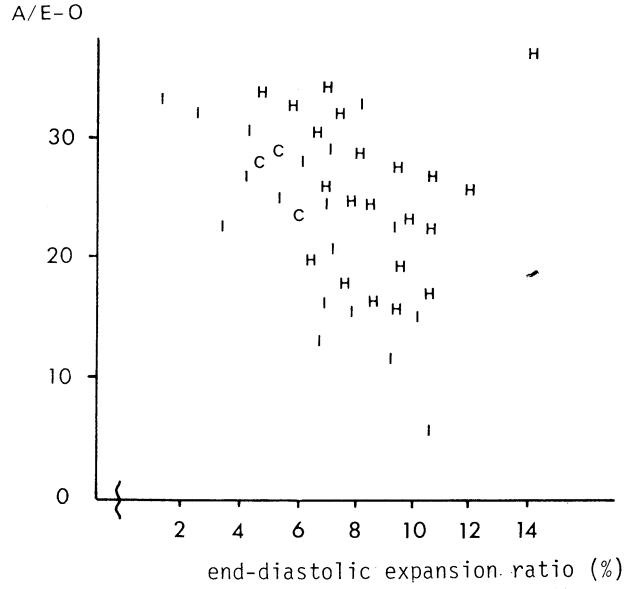
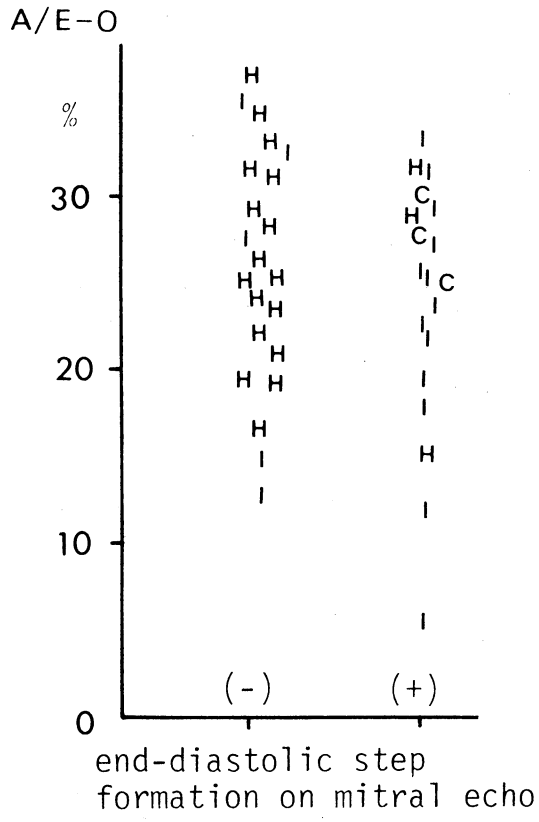


Fig. 2 a. The relationship of the A/E-O ratio (the Y-axis) to the left ventricular end-diastolic dimension (the X-axis). C=congestive cardiomyopathy ; H=hypertension and hypertrophic cardiomyopathy; I=ischemic heart disease (See text).



b. The relationship of the A/E-O ratio to the left ventricular end-diastolic expansion ratio (See text).



c. The relationship of the A/E-O ratio to the presence (+) or absence (−) of the step formation (See text).

cardiomyopathy, and larger in ischemic heart disease and congestive cardiomyopathy despite having equally high A/E-O ratio.

Figure 2b shows the relationship of the A/E-O ratio to the left ventricular end-diastolic expansion ratio. Although no statistically significant correlation ($r = -0.29$, $p > 0.01$) was again found between the two parameters as a whole, end-diastolic expansion ratio tended to be larger in patients with hypertension and hypertrophic cardiomyopathy, and smaller in ischemic heart disease and congestive cardiomyopathy despite having equally high A/E-O ratio.

Figure 2c shows the relationship of the A/E-O ratio to the presence or absence of end-diastolic step formation on mitral echo. Although no significant difference was found statistically between the two groups (with and without step formation) as a whole, most of the patients with ischemic heart disease and all with congestive cardiomyopathy who had a high A/E-O ratio had a step formation. Those with hypertension and hypertrophic cardiomyopathy, however, had no step formation despite a high A/E-O ratio.

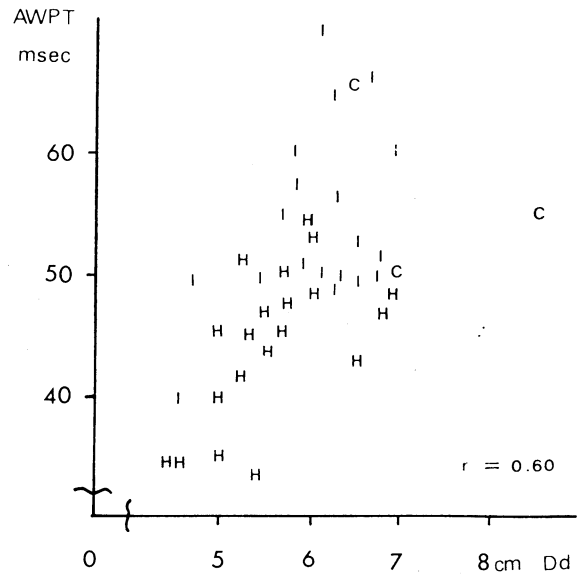
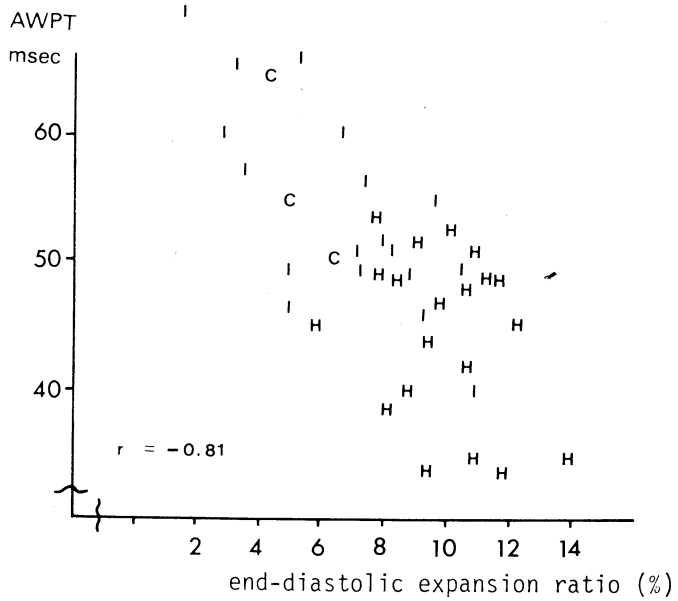
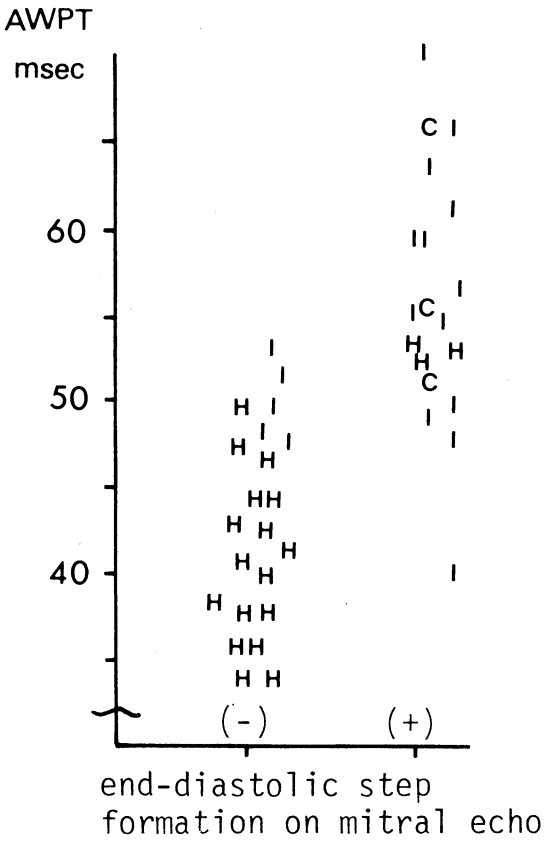


Fig. 3 a. The relationship of the A-wave peak time (AWPT) (the Y-axis) to the left ventricular end-diastolic dimension (the X-axis) (See text).



b. The relationship of the A-wave peak time (AWPT) to the left ventricular end-diastolic expansion ratio (See text).



c. The relationship of the A-wave peak time (AWPT) to the presence (+) or absence (−) of the step formation (See text).

2) The relationship of A-wave peak time to echocardiographic parameters (Fig. 3a, b, c).

Figure 3a shows the relationship between the A-wave peak time and the left ventricular end-diastolic dimension. In all disease group a longer A-wave peak time tended to be associated with a greater end-diastolic dimension, the correlation coefficient being $r = +0.60$ ($p<0.01$).

Figure 3b shows the relationship between the A-wave peak time and the left ventricular end-diastolic expansion ratio. It was found that the greater the A-wave peak time prolongation, the smaller was the end-diastolic expansion ratio with a highly inverse correlation coefficient of $r = -0.81$ ($p<0.01$).

Figure 3c shows the relationship between the A-wave peak time and the presence or absence of end-diastolic step formation on mitral echo. There was a statistically significant difference ($p<0.01$) between the two groups. No patient with hypertension or hypertrophic cardiomyopathy whose A-wave peak

time was in the normal range had a step formation. Most of the patients with prolonged A-wave peak time of 50 msec or more had a step formation.

Two individual cases follow that exemplify our results.

Case 1 : A 55-year-old male with an old myocardial infarction and with ejection fraction of 42% died of congestive heart failure 5 months after our studies revealed the characteristic findings shown in Fig. 1a, c. The A/E-O ratio was high, the peak time was prolonged to 70 msec, and the left ventricular end-diastolic expansion ratio was small (1.9% as against our normal value of 4.5±1.2%) (Fig. 1a), and there was a remarkable step formation on mitral echo (Fig. 1c).

Case 2 : A 36-year-old male with a hypertrophic cardiomyopathy whose ejection fraction was 75% showed the tracings seen in Fig. 4a, b. The A/E-O ratio was high but the peak time was normal (35 msec), and the mitral echo showed a sharp A-wave with no step formation (Fig. 4a). The left ventricular end-diastolic expansion ratio was well preserved (6.5%) (Fig. 4b).

On the basis of our findings we were able to divide our patients into two

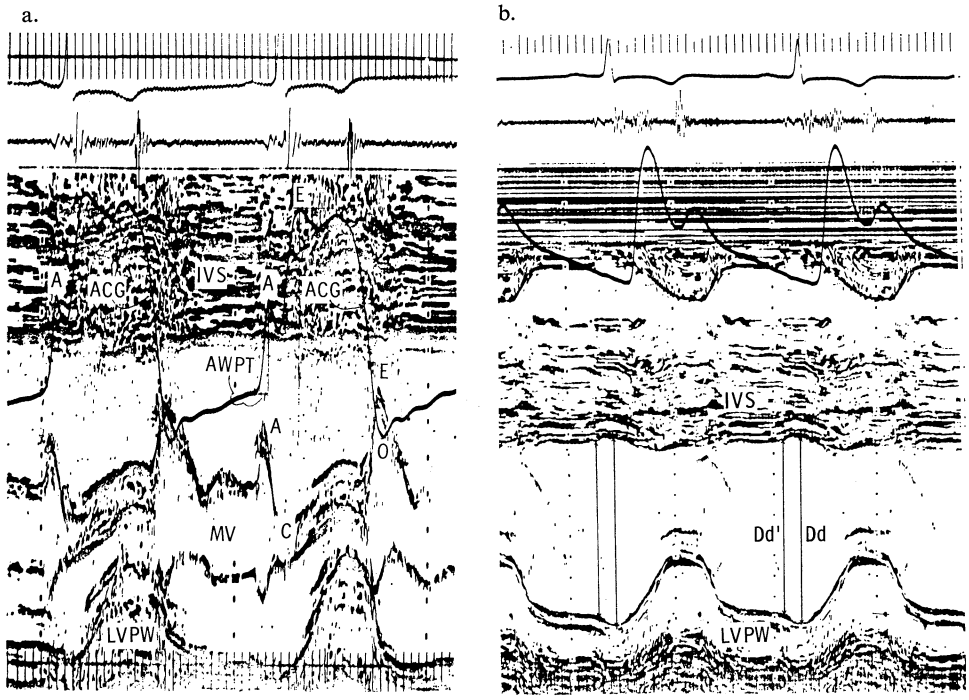


Fig. 4. The apexcardiogram and left ventricular echo from a 36-year-old male with a hypertrophic cardiomyopathy whose ejection fraction was 75%. a. The high A/E-O ratio, the normal A-wave peak time and no step formation on mitral echo are seen. b. The left ventricular end-diastolic expansion ratio is well preserved.

groups (Fig. 5). Group 1 patients were those with high A-wave but normal peak time on apexcardiogram, and normal left ventricular end-diastolic dimension with larger left ventricular end-diastolic expansion ratio and with no step formation on mitral echogram. Many of these were patients with marked left ventricular hypertrophy (systolic overload) but no failure. Group 2 patients were those with prolonged A-wave peak time in addition to high A/E-O ratio on apexcardiogram, and larger left ventricular end-diastolic dimension with smaller left ventricular end-diastolic expansion ratio and with step formation on mitral echogram. Many of these were patients with congestive cardiomyopathy and ischemic heart disease.

Table 2 discloses directly measured hemodynamic data including left ventricular end-diastolic pressure, end-diastolic volume and ejection fraction in two groups described above. The left ventricular end-diastolic pressure was equally elevated in both groups. However, there were distinct differences in other two parameters ; group 2 patients had a significantly ($p<0.05$) larger end-diastolic

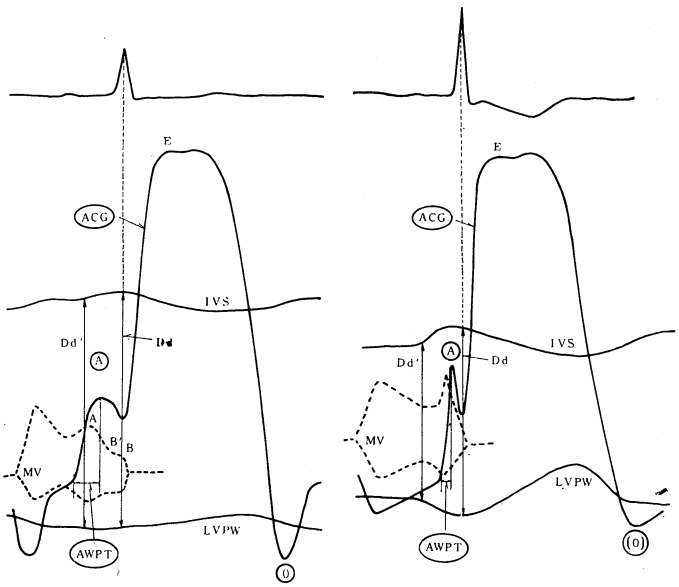


Fig. 5. Apexcardiographic and echocardiographic features of the patients divided into 2 groups in this study (See Table 2) are shown in this schematic illustrations. Group 1 patients generally showed a normal A-wave peak time in addition to a high A/E-O ratio on apexcardiogram, and smaller left ventricular end-diastolic dimension with larger left ventricular end-diastolic expansion ratio and lack of step formation on mitral echogram (right panel), whereas the majority of group 2 patients showed a prolonged A-wave peak time in addition to a high A/E-O ratio on apexcardiogram, and larger left ventricular end-diastolic dimension with smaller left ventricular end-diastolic expansion ratio and step formation on mitral echogram (left panel).

volume and a significantly ($p<0.05$) smaller ejection fraction as compared to group 1 patients.

TABLE 2. Hemodynamic Data in Groups 1 and 2

	Group 1 (N=20)	Group 2 (N=21)	p value
End-diastolic Pressure (mmHg)	24.5± 2.5	28.8± 3.6	NS
End-diastolic Volume (ml/m^2)	57.8±10.9	89.8±18.2	<0.01
Ejection Fraction (%)	71.3± 9.8	49.8±13.9	<0.01

Abbreviations : N=Number of Cases ; NS=Non-significant ; ±=1 Standard Deviation.

DISCUSSION

1) A-wave peak time :

We have noted that the A-wave peak time is often prolonged in ischemic heart disease, but it is not prolonged in most patients of hypertension unless there is concomitant congestive heart failure or marked ST-T wave changes on electrocardiogram[10]. This suggests that the A-wave peak time is not prolonged by pressure overloads of the left ventricle but by a decrease in cardiac function[9,10].

Since the A-wave peak time may be normal or prolonged in patients with equally high left ventricular end-diastolic pressures, the differences in the A-wave peak time may be due to the distensibility of the left ventricle as well as the contractility of the left atrium. The fact that the contractility of the left atrium may also be one of factors to control the A-wave peak time is suggested by the findings that in patients with prolonged A-wave of the left ventricle on the impedance cardiogram the left atrial ejection fraction is decreased[12].

Recently Denef and his associates found the following evidence using the calibrated apexcardiographic A-wave[13] : in patients with a noncompliant hypertrophic left ventricle, as in severe aortic or subaortic stenosis, the rate of the A-wave is frequently high ; in congestive or ischemic cardiomyopathy, the rate of rise is low. Their previous experimental studies in the dog have also shown that the first derivative of the apical A-wave correlated significantly with the rate of left ventricular pressure rise during atrial systole[14]. Their results, therefore, indicate that analyzing the calibrated apical A-wave in terms of total amplitude and velocity enhances the assessment of left atrial and left ventricular diastolic functions[13].

Instead of using the calibrated apexcardiogram which is a rather complicated technique, we considered it adequate for clinical practice to measure the A-wave peak time, in addition to the A/E-O ratio, for the evaluation of the left ventricular and atrial functions.

Although the total duration of the apexcardiographic A-wave has been found to be significantly prolonged in ischemic heart disease[8], this parameter,

in our experience, was found to be affected by electrocardiographic P-R interval. On the other hand, A-wave peak time was not dependent on P-R interval, which was confirmed by a patient with Wenckebach type of atrioventricular block where P-R intervals varied from beat to beat.

2) Apexcardiographic versus echocardiographic parameters :

In most patients in group 1, that is, with an abnormally high A-wave but normal A-wave peak time, there was no step formation but a greater atrial contribution to left ventricular filling. This was the group with marked left ventricular hypertrophy but no congestive failure. On the other hand, in most patients in group 2, that is, with a prolonged A-wave peak time as in congestive cardiomyopathy or ischemic heart disease, there was a step formation as well as a smaller atrial contribution to left ventricular filling.

Ambrose et al.[15,16] have recently proved that majority of patients with advanced left ventricular dysfunction and markedly increased chamber stiffness measured by left ventricular pressure and volume showed a large step formation on the anterior mitral echo as well as a small atrial contribution to left ventricular filling. Since we have found that the A-wave peak time, as compared to the A/E-O ratio, correlates more significantly with echocardiographic differences of left ventricular end-diastolic parameters in our 2 groups of patients, a concomitant use of this new parameter with the A/E-O ratio would be clinically useful in evaluating severity of left ventricular disorders with totaly non-invasive procedure. This may also suggest a possible non-invasive follow-up indicator of left ventricular dysfunction.

Further investigations have been scheduled on the A-wave peak time with simultaneous recordings of left ventricular pressure trace and apexcardiogram, and in the clinical course of the various groups of patients as determined from longitudinal observations.

3) Problems on the measurement of the apexcardiographic A-wave :

The A/E-O ratio is represented as the relative value of A-wave height to total amplitude. Consequently, the A/E-O ratio has the disadvantage of being altered by the amplitude of the systolic wave. Although an abnormal increase of the A/E-O ratio has been found in various types of left ventricular disorders[3,17,18], some patients do not have large A-wave despite severe heart disease, and normal A/E-O ratio has been reported in patients with critical aortic stenosis[19]. The reason for this discrepancy is obvious, and may be related to a significant increase in the amplitude of the systolic wave as well as the A-wave of the apexcardiogram in patients with systolic and diastolic overloads of the left ventricle[20–22]. The presence of an abnormal systolic wave (for example a systolic bulge) may also affect its amplitude.

The A-wave peak time, on the other hand, can usually be determined accurately if the recording is taken at high enough amplitude to eliminate much of the systolic wave.

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