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Quantitative Evaluation of Left Ventricular Relaxation by Apexcardiogram in Coronary Artery Disease.

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Abstract To assess non-invasively whether the location, extent and severity of left ventricular (LV) contraction abnormalities affect LV relaxation, we studied apexcardiogram (ACG) in 48 patients with coronary artery disease (CAD) of over 75% luminar stenosis and 16 control subjects under basal conditions within a week before cardiac catheterization.

Asynergy of LV wall motion was classified on the basis of AHA committee ventriculography reporting system. The patients consisted of control subjects〔Group Ⅰ; n=16〕 and the patients with CAD of one-vessel disease in right coronary artery or left circumflex coronary artery stenosis〔Group Ⅱ; n=16〕, of one-vessel disease in left anterior descending coronary artery stenosis〔Group Ⅲ; n=20〕 and of three-vessel disease associated with general hypokinesis〔Group Ⅳ; n=12〕. Δt was defined as the time interval between the aortic component of the second heart sound (A2) and the 50% height of ACG deflection from the end-systolic shoulder of the onset of A2 to the nadir of ACG (O-point), during isovolumic relaxation period.

Δt was significantly prolonged in Group Ⅲ (60 ± 12 msec, $P < 0.05$) and Group Ⅳ (73 ± 12 msec, $P < 0.001$) compared to in Group Ⅰ (51 ± 11 msec). There were good correlations between Δt and LV peak negative dP/dt ($r = -0.44$, $P < 0.001$) and between Δt and time constant of isovolumic LV pressure decay ($r = 0.54$, $P < 0.001$). Δt reflects the impairment of LV relaxation, and then the extent and/or severity rather than the locality of LV wall motion abnormalities increased Δt, probably due to a global impairment of LV relaxation.

Key words: LV relaxation, ACG, Ischemic heart disease

Introduction

Impairment of relaxation is an important component of left ventricular (LV) disorder, so that their non-invasive investigation may have appreciable clinical significance. We evaluated LV relaxation non-invasively using an apexcardiogram (ACG), because its method is one of the most conventional non-invasive methods and has the available merits of closely pattern resemblances and nearly nadir synchronisms of both the upstroke and the downstroke with LV pressure curve[1-3]

In the recent studies, experimental and clinical evaluation have shown that the impairment of LV relaxation have a close relationship with LV contraction abnormalities in myocardial ischemia[4-10] The purpose of this study is to assess non-invasively and quantitatively, whether the location, extent and severity of LV contraction abnormalities affect LV relaxation in patients with coronary artery disease (CAD) using the ACG.

Materials and Methods

We investigated sixteen control subjects and 48 patients with CAD. In all subjects, the diagnosis was confirmed by cardiac catheterization and coronary angiography, and all were in normal sinus rhythm. The patients with CAD had significant luminar stenosis of over 75% in one or more vessels. All of patients with CAD had previous myocardial infarction and five patients had recurrently, as demonstrated by typical electrocardiographic, enzymic changes and wall motion abnormalities of LV cineangiography. Patients with a history of hypertension (cuff blood pressure more than 160/100 mmHg), valvular heart disease, cor pulmonale, congenital heart disease, or bundle branch block were excluded in this study.

Apexcardiogram: Simultaneously ACG and Phonocardiogram (PCG) were recorded with standard lead II using an electrogram (Fukuda Electronics, MCM-8000) within a week before cardiac catheterization. PCG were recorded from the base of heart, where the aortic component of the second heart sound (A2) was most obvious using a medium or high frequency filter. The onset of A2 was identified from its relation to the dicrotic notch of the carotid pulse tracing. ACG were recorded using a transducer with a time constant of 5 seconds. The best record of ACG could be obtained by fixing a transducer hand-manually at the point of maximum impulse of the apex beat in the left lateral or semilateral position during mid-expiratory apnea. Records were made using an ink-jet recorder (Siemens-Elema, Mingograph) at a paper speed of 100 mm/sec.

The following measurements were made from ACG tracing, and five consecutive beats were measured and averaged (Fig. 1); Δt (msec): The time interval between the onset of A2 and the 50% height of the ACG deflection, which deflection is from the end-systolic shoulder at the onset of A2 to the nadir in the early diastolic downstroke of ACG (O-point). A2-O (msec): The time interval between the onset of A2 and O-point. Δt/A2-O: The ratio of Δt to A2-O interval[8].

Cardiac catheterization: All subjects underwent LV catheterization including coronary angiography and LV cineangiography approximately 30 minutes after premedication of 10 mg Diazepam. All other medications had been discontinued 24 hours before study. LV pressure was monitered from a high-fidelity micromanometer-tipped catheter (Millar, PC-471) and the rate of this change (dP/dt) was obtained using a differentiating amplifier (Electronics for Medicine, V-4202) with a high-frequency filter of 25 Hz and a linear response to 20 Hz by 20 dB/decade[4-8]. Micromanometer system was calibrated against a mercury column as reported elsewhere[7]. Hemodynamic variables were recorded on a multichannel recorder (Electronics for Medicine, VR-12) at a paper speed of 150 mm/sec. Time constant(T) of LV pressure decay during isovolumic relaxation period was computed every 5 msec by microcomputer system (NEC, PC-9801) according to the method of Weiss et al.[9]. LV cineangiogram was performed using the biplane right anterior oblique (RAO) and left anterior oblique (LAO) projections. LV volumes and ejection fraction were determined by the biplane area-length method[11]. LV wall motion score was determined by visual inspection on the basis of AHA commitee ventriculography reporting system at each segment as follows: normal=1, moderate hypokinesis=2, severe hypokinesis=3, akinesis=4, dyskinesis=5, anuerysm=6[12]. Abnormal contraction score (ACS) was defined as a total of each

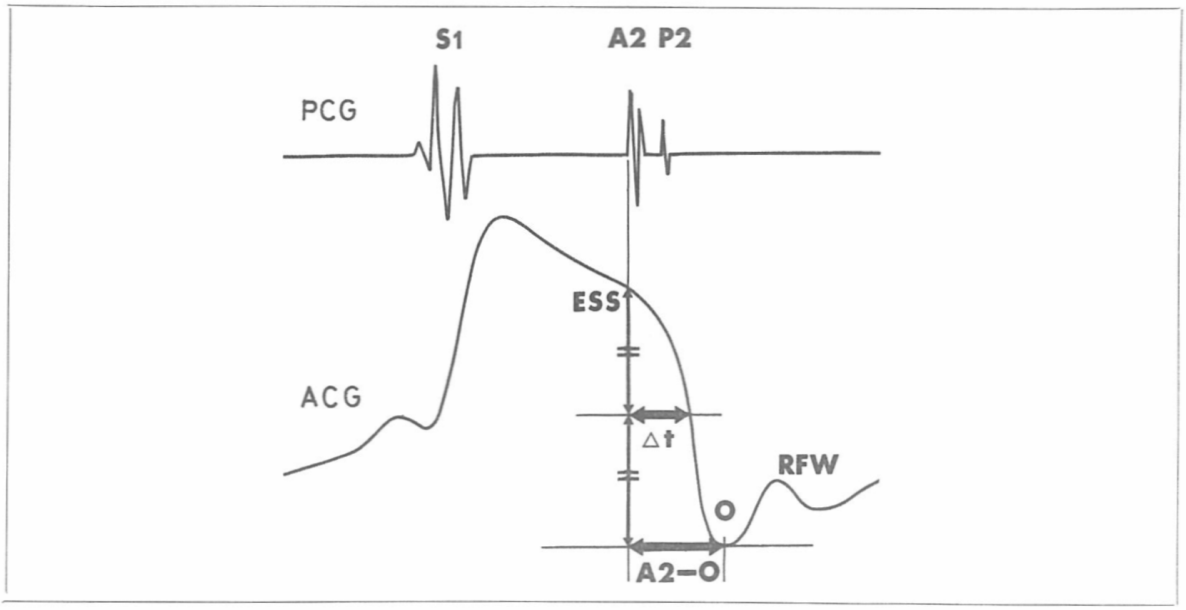

Fig. 1 Method of calculation of Δt. Δt(msec) is the time interval between the aortic component of the second heart sound (A2) and the 50% of the height from the onset of A2 to the nadir of the early diastolic downstroke of Apexcardiogram (O-point). A2-O (msec) is the time interval between A2 and O-point. Δt/A2-O is the ratio of Δt to A2-O interval.
Abbreviations: PCG=Phonocardiogram; S1=The first heart sound; A2=The aortic component of the second heart sound; P2=The pulmonary component of the second heart sound; ACG=Apexcardiogram; ESS=End-systolic shoulder; O=O-point; RFW=Rapid filling wave.

Table 1 Diagnosis and non-invasive parameters.

Patient Groups	n	Sex		Age	HR	BSP	Δt	A2-O	Δt/A2-O
		m	f	(y.o.)	(bts/min)	(mmHg)	(msec)	(msec)	ratio
Ⅰ) Normal control	16	13	3	49± 8	60±10	131±26	51±11	148±24	0.35±0.05
Ⅱ) One-vessel disease with RCA or LCX	16	15	1	52±11	54±11	133±23	55±12	156±27	0.35±0.09
Ⅲ) One-vessel disease with LAD	20	18	2	59±8**	64±13	113±21	60±12*	154±23	0.38±0.08
Ⅳ) Three-vessel disease with general hypokinesis	12	11	1	57±10**	62± 8	117±15	73±12***	181±31**	0.41±0.05**

Values: Mean±SD; *=0.05, **=0.01, ***=0.001, vs Group Ⅰ.
Abbreviations: m=Male; f=Female; y.o.=year old; HR=Heart rate at apexcardiogram examination; BSP=Brachial peak systemic pressure by cuff-method; RCA=Right coronary artery; LCX=Left circumflex coronary artery; LAD=Left anterior descending coronary artery; others see Fig. 1.

segmental score obtained by adding the values assigned to each segments from an analysis of the five segments and two segments from the ventriculograms in RAO, and LAO views, respectively. A score of 7 means normal wall motion of LV. A score of 21 or greater implies severely impaired LV wall motion[12),13)]. For each hemodynamic measurements, five consecutive beats were analyzed and

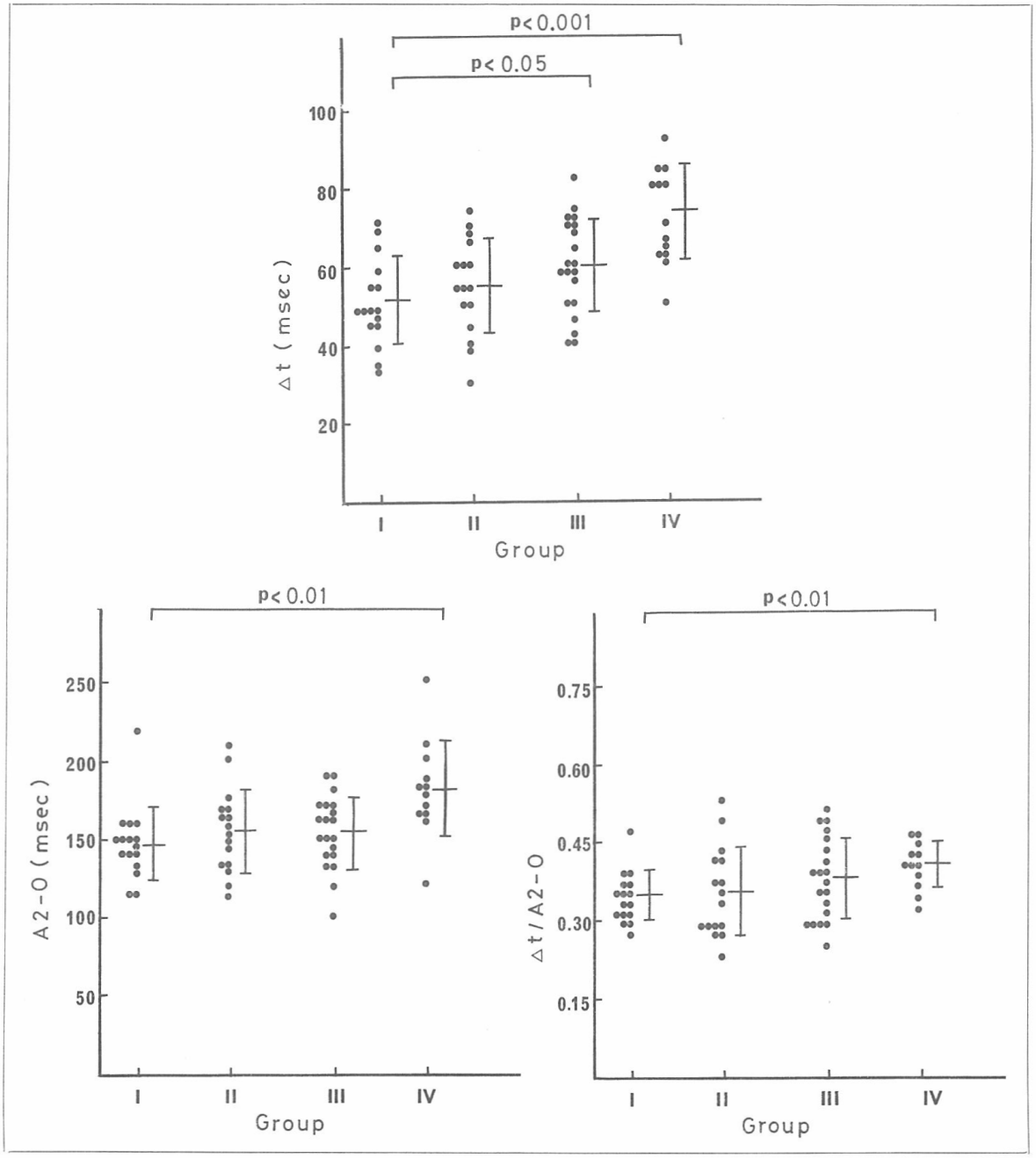

Fig. 2 Comparison of Δt(upper), A2-O(lower left), Δt/A2-O(lower right) among four groups of Group Ⅰ (n=16), Group Ⅱ (n=16), Group Ⅲ (n=20) and Group Ⅳ (n=12).
Abbreviations: Values: Mean±SD; *=0.05, **=0.01, ***=0.001, vs Group Ⅰ; others see Table 1 and a text in details.

averaged.

Patient groups: From the coronary angiographic and LV cineangiographic data, all subjects were classified as follows (Table 1);

Group Ⅰ: This group consisted of 16 patients (13 males and 3 females), ranged from 33 to 60

Table 2 Hemodynamic variables.

Groups	HR (bts/min)	LVPSP (mmHg)	LVEDP (mmHg)	Pea(+)dP/dt (mmHg/sec)	Peak(−)dp/dt (mmHg/sec)	T (msec)	EDVI (ml/m²)	EF (%)
Ⅰ)	64±10	134±13	9±3	1551±220	1896±198	37± 7	87±13	65± 5
Ⅱ)	69±12	140±22	12±4	1446±307	1661±263**	37±10	91±19	51± 7***
Ⅲ)	72±10	131±20	13±4**	1419±244	1497±493**	47± 7*	105±28*	43±10***
Ⅳ)	67±12	126±24	17±8*	1096±267***	1022±258***	54±7***	123±39*	30± 8***

Values: Mean±SD; *=0.05, **=0.01, ***=0.001, vs Group Ⅰ.
Abbreviations: HR=Heart rate; LVPSP=Left ventricular peak systolic pressure; LVEDP=Left ventricular end-diastolic pressure; Peak (+) dP/dt=Peak positive of the first derivatives of the left ventricular pressure; Peak (−) dP/dt=Peak negative of first derivatives of left ventricular pressure; T=Time constant of left ventricular pressure decay during isovolumic relaxation period; EDVI=End-diastolic volume index; EF=Ejection fraction; others see Table 1.

years old (49±8 years old) [mean±SD]. They had a history of atypical chest pain, but their hemodynamic parameters, left ventriculograms and coronary arteriograms were normal.

Group Ⅱ: This group consisted of 16 patients (15 males and 1 female), ranged from 29 to 65 years old (52±11 years old). They had one-vessel disease with significant stenosis of right coronary or left circumflex coronary artery.

Group Ⅲ: This group consisted of 20 patients (18 males and 2 females), range from 50 to 70 years old (59±8 years old). They had one-vessel disease with significant stenosis of left anterior descending coronary artery.

Group Ⅳ: This group consisted of 12 patients (11 males and 1 female), ranged from 50 to 71 years old (57±10 years old). They had three-vessel disease of coronary arteries associated with generalized hypokinesis of at least over 5 segments of abnormal contraction.

Statistics: Statistics analysis were performed using Student's paired t-test or Cochran-Cox non-paired test. The p value of less than 0.05 was considered significant. A linear regression was driven using a least squares method. All data are presented as a mean±SD.

Results

The patients diagnosis and profiles showed in Table 1. There was no significant difference in heart rate and brachial peak systemic pressure by cuff-method among each groups. Age was significantly higher in Group Ⅲ (59±8 years old, $P<0.01$) and Group Ⅳ (57±10 years old, $P<0.01$) than in Group Ⅰ (49±8 years old).

Δt, A2-O, Δt/A2-O: Variables measured from ACG were summarized in Table 1 and shown in Fig. 2. Δt was significantly prolonged in Group Ⅲ (60±12 msec, $P<0.05$) and Group Ⅳ (73±12 msec, $P<0.001$) than in Group Ⅰ (51±11 msec). However, Δt in Group Ⅱ (55±12 msec) was not significantly different from Group Ⅰ. A2-O was significantly prolonged in only Group Ⅳ (181±31 msec, $P<0.01$) compared to Group Ⅰ (148±24 msec). There was no significant difference of A2-O between Group Ⅰ and Group Ⅱ (156±27 msec) or Group Ⅲ (154±23 msec). The variations of A2-O was greater scatter than those of Δt. Moreover, Δt/A2-O was significantly greater in Group Ⅳ (0.41±0.05, $P<0.01$) than in Group Ⅰ (0.35±0.05). However, there was no significant difference of Δt/A2-O between Group Ⅰ and Group Ⅱ (0.35±0.09) or Group Ⅲ (0.38±0.08). The greater value of this ratio means the abnormal upward-convex pattern of ACG downstroke.

When we compared the timing of mitral valve opening with Δt by simultaneous tracing of ACG and mitral echocardiogram, Δt was shorter than IRT, ranged of Δt/IRT

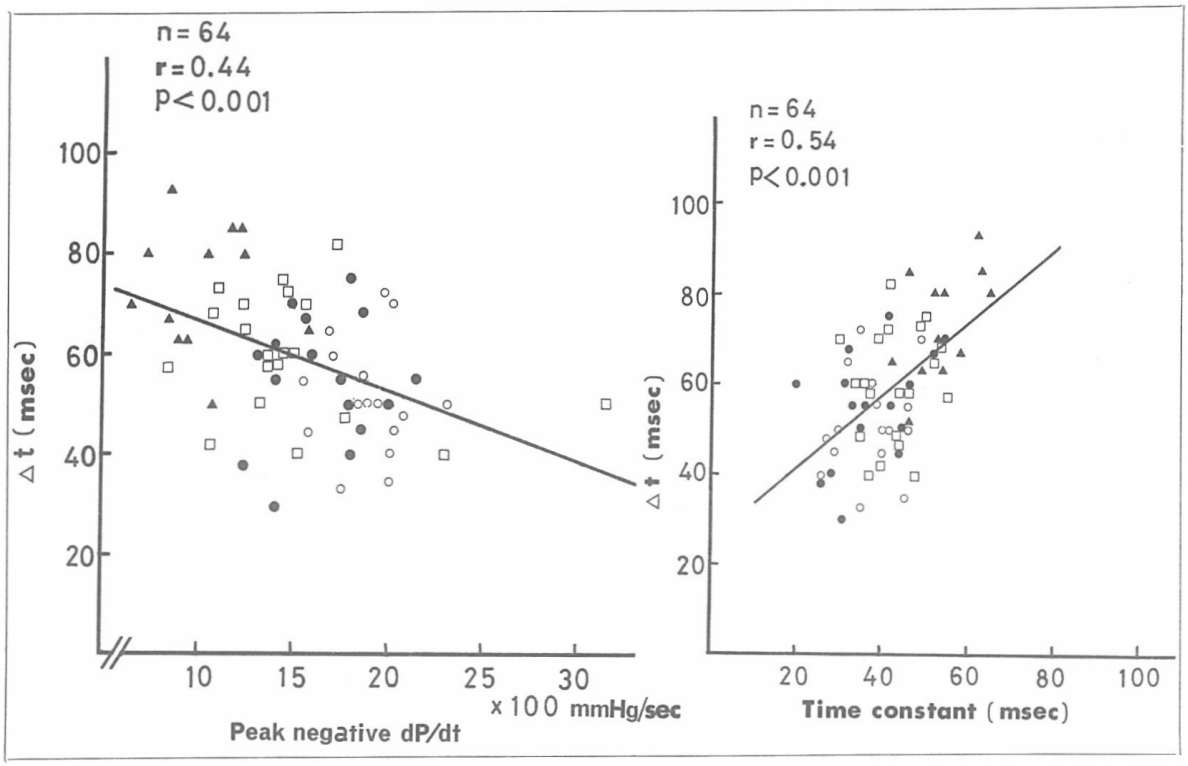

Fig. 3 Relation between Δt and LV relaxation indeces.Left: Δt vs peak (−) dP/dt ($r=0.44$, $Y=-0.01^{\times}X+80.33$, $P<0.001$); Right: Δt vs Time constant (T) ($r=0.54$, $Y=0.78^{\times}X+26.10$, $P<0.001$). Group I (n=16; open circle: ○); Group II (n=16; closed circle: ●); Group III (n=20; open square: □); Group IV (n=12; closed triangle: ▲). ; others see a text in details.

from 0.22 to 0.75, but there was no significant correlation ($r=0.14$, NS) between Δt and IRT. The interval of Δt was measured in early period during IRT.

Hemodynamics: Hemodynamic variables were summarized in Table 2. Heart rate and LV peak systolic pressure were not different among each groups. The left ventricular end-diastolic pressure (LVEDP) in Group III (13±4 mmHg, $P<0.01$) and Group IV (17±8 mmHg, $P<0.05$) were significantly elevated than in Group I (9±3 mmHg). The peak positive(+) dP/dt in Group IV (1096±267 mmHg/sec, $P<0.001$) was significantly reduced than in Group I (1551±220 mmHg/sec). The peak negative(−) dP/dt was significantly reduced in Group II (1661±263 mmHg/sec, $P<0.01$), Group III (1497±493 mmHg/sec, $P<0.01$) and Group IV (1022±258 mmHg/sec, $P<0.001$) compared to Group I (1896±198 mmHg/sec). The T in Group III (47±7 msec, $P<0.05$) and Group IV (54±7 msec, $P<0.001$) was significantly prolonged than in Group I (37±7 msec). The LV end-diastolic volume index in Group III (105±28 ml/m², $P<0.05$) and Group IV (123±39 ml/m², $P<0.05$) were significantly greater than in Group I (87±13 ml/m²). Ejection fraction was significantly smaller in Group II (51±7%, $P<0.001$), Group III (43±10%, $P<0.001$) and Group IV (30±8%, $P<0.001$) than in Group I (65±5%).

Correlations: The correlations between Δt and LV relaxation indices were shown in Fig. 3. There were a good inverse correlation between Δt and peak (−) dP/dt ($r=-0.44$, $P<0.001$), and a good correlation between Δt and T ($r=0.54$, $P<0.001$). A2-O was correlated to T ($r=0.56$, $P<0.001$), but not to peak (−) dP/dt ($r=-0.24$, NS).

Table 3 The number of patients classified by abnormal wall motion of left ventricles.

Patient Groups	A) Classification from a segment with the worst degree of wall motion abnormality			B) Classification by the amount of segment of abnormal wall motion								C) ACS
	Normal	Hypokinesis or akinesis	Dyskinesis or anuerysm	The number of abnormal segments 0	1	2	3	4	5	6	7	
Ⅰ)	16	0	0	16	–	–	–	–	–	–	–	7.0±0.0
Ⅱ)	0	16	0	–	5	6	5	–	–	–	–	12.0±2.9
Ⅲ)	0	6	14	–	–	8	10	2	–	–	–	16.1±3.2
Ⅳ)	0	12	0	–	–	–	–	–	5	2	5	21.9±5.2

A; The number of patients with normal or at least one abnormal left ventricular segment in LV cineangiograms classified by segment with the worst degree of contraction abnormality. B; The number of patients classified by the amount of segments of abnormal wall motion. C; Abnormal contraction score (ACS). This is a total of each segmental score obtained by adding the values assigned to each segment [mean±SD]; Others see Table 1 or 2 and see a text in details.

Thus, Δt had higher correlation with peak (−)dP/dt than A2-O, while Δt had nearly the same correlation with T as A2-O. To a certain level, Δt had significant correlations with both peak (−) dP/dt and T in the patients with CAD.

Wall motion: As shown in Table 3, the number of patients were classified by abnormal wall motion of LV. A segment with the worst degree of wall motion abnormality was normal in all of Group Ⅰ, hypo- or akinesis in all of Group Ⅱ, 6 of Group Ⅲ and all of Group Ⅳ, and dyskinesis or anuerysm in 14 of Group Ⅲ. On the other hand, the amount of segments with abnormal wall motion were zero segment in all of Group Ⅰ, 1 segment in 5 of Group Ⅱ, 2 segments in 6 of Group Ⅱ and 8 of Group Ⅲ, 3 segments in 5 of Group Ⅱ and 10 of Group Ⅲ, 4 segments in 2 of Group Ⅳ, 5 segments in 5 of Group Ⅳ, 6 segments in 2 of Group Ⅳ, and 7 segments in 5 of Group Ⅳ. The ACS were greater in Group Ⅲ (16.1±3.2), and more greater in Group Ⅳ (21.9±5.2) than in Group Ⅱ (12.0±2.9). The most severe abnormality with dyskinesis or anuerysm were present in 14 of 20 cases in Group Ⅲ. The amount of segments with abnormal wall motion were larger in Group Ⅲ, and more larger in extensive asynergic Group Ⅳ than in Group Ⅱ. Furthermore, ACS were the worst in Group Ⅳ, since the most extensive asynergy despite of hypo- or akinesis of abnormal wall motion.

Reproducibility: The interobserver and intraobserver variabilities for Δt were $r=0.92$, SEE=6.67, $P<0.001$ ($n=12$) and $r=0.82$, SEE=9.47, $P<0.001$ ($n=9$), respectively. The corresponding values for A2-O were $r=0.90$, SEE=11.51, $P<0.001$ ($n=12$) and $r=0.70$, SEE=25.35, $P<0.001$ ($n=9$), respectively. Reproducibilities for Δt was better than those for A2-O.

Discussion

Although an index of isovolumic relaxation time (IRT) had been used to evaluate LV relaxation, the duration of IRT was multifactorially determined by left atrial, aortic and LV pressures [14,15] In the last ten years, an index of T has been measured to assess LV relaxation as well as peak (−) dP/dt. In the present study, we reappraised the ACG to assess whether or how the ACG could predict LV pressure decay during IRT in normal subjects and even in patients with

regional LV wall motion abnormalities.

Firstly, Benchimol et al. and other previous investigators evaluated LV relaxation by means of A2-O by ACG in various heart diseases[14),16),17),18)]. Nevertheless, as indicated by Benchimol et al. and Gambel et al., A2-O was determined not only by the factors during the IRT, but also by the time interval from the mitral opening to the O-point of ACG. In our study, the variations of value of A2-O showed the same large scatter as those reported by Gambel et al.[14)].

To estimate LV relaxation more accurately and noninvasively, Doran and Gibson et al. made a model of the "Apex-Dimension loop" from the relation between ACG and LV intracavitary short axis dimension by M-mode echocardiography and reported that in CAD patients, the more the extent of LV contraction abnormalities appeared, the more the abnormal convex pattern of this loop was present during IRT[19)]. In addition, Manolas et al. has reported that the time interval between A2 and the peak negativity of the first derivatives of ACG has a closely inverse correlation with the value of LV peak (−) dP/dt[20)]. This paper was the first quantitative report for calculating the convex pattern of ACG to evaluate a correlation with LV relaxation indices. However, in some of control subjects of their data, the peak negativity of the first derivatives occurred preceding the A2, so that we thought this method had a somewhat limitation on predicting LV pressure decay during IRT. Compared to their methods, Δt was a simple and easy method for calculating the ACG downstroke and was a useful index for comparing between control subjects and diseased heart[8)]. Many various influencing factors, such as age, heart rate, preload, afterload and LV contractility, might be thought to affect LV relaxation[4-7,21,22)]. Regarding the age, Group Ⅲ and Ⅳ in the present study, were significantly higher than the other groups. Harrison et al. noted that LV relaxation may be prolonged in aged myocardium[21)]. However, Δt had no significant correlation with age in our control subjects. LVEDP was significantly elevated in proportion to severity of LV relaxation abnormalities. Weisfeld et al. reported that LV relaxation does not affect the compliance in late diastole[10)]. In the present study, we excluded the patients with CAD who might be influenced in both LV relaxation and the timing of A2 by abnormal variables such as heart rate, brachial peak systemic pressure and aortic or LV peak systolic pressure affecting on both LV relaxation and the timing of A2. In consequence, there was no significant difference of these variables between each group. Therefore, we thought that there was no need to correct Δt by age, heart rate, afterload and preload for comparison among each group, and that the timing of A2 might be an appropriate marker for the onset of rapid LV pressure decay[15)].

Although LV pressure fall during relaxation has been firstly reported to be mono-exponetial in intact heart[9)], Kumada documented that experimental acute myocardial ischemia disturbed mono-exponential nature of the isovolumic LV pressure fall[6)]. In the patients with CAD, Rausseau et al. reported that isovolumic LV pressure fall seemed to be fitted by bi-exponential curve better than by a monoexponential curve, and its initial portion of the bi-exponential curves, duration of which was 40 msec after peak (−) dP/dt, favored to reflect the LV relaxation impairment[22)]. We investigated simultaneously the ACG and LV pressure during cardiac catheterization in eight patients with CAD, and resulted to the same evidence that the downstroke of ACG simulates to that of LV pressure decay as reported by previous investigators[1-3)]. There were the closely resemblances of patterns and nearly coincidences of nadirs even in the patients with CAD. Therefore, Δt may be thought to reflect fairly the first exponential portion of the bi-

exponetial curves, because it was measured in early period during IRT.

Recently, Aubert and Kesteloot reported that the dimension change from the apex of the maximum impulse to the chest wall showed the curve of biphasic motion and simulated reciprocally to the pattern of ACG, using a laser beam method in dogs[23]. This report suggested that this dimensional change played an importent role to make a configuration of ACG throughout a cardiac cycle. Nevertheless, this dimension change may reflect not only the wall motion of apical region, but also the geometry and rotation of the whole heart. Therefore, this may be thought to be one of the most influencing factors to the genesis of ACG as proposed by Kesteloot[24]. The recent clinical studies have demonstrated that impaired relaxation was in association with contraction abnormalities, and that there were good correlations between relaxation indices and contraction indices such as peak (+) dP/dt, ejection fraction, end-systolic volume index and the percent extent of abnormal wa motion[4)5)7)]. In the present study, to assess whether the location, extent and/or severity of wall motion abnormalities affect the ACG downstroke, we classified all subjects into four groups according to the lesions supplied by the involved coronary arteries. As shown in Table 1 and 3, the local abnormalities of systolic wall motion in the anterolateral or apical regions where ACG was recorded, affected the convex pattern of ACG a little, while the extensive and/or severe abnormalities of wall motion affected the ACG downstroke more. The most affected pattern of ACG showed the most prolongation of Δt and the greatest values of Δt/A2-O in Group Ⅳ associated with the most severe impairment of relaxation indices. These results suggested that the more the extent and/or severity of systolic LV wall motion abnormalities occurred, the more the severe impairment of a global LV relaxation was present, associated with significant prolongation of Δt, rather than the influence of the location of the LV wall motion abnormality. As hypothesized by Waters et al., a global abnormality of LV relaxation may be the result of regional relaxation impairment related to regional systolic abnormalities, by dyssynchronous wall motion in the impaired zone during IRT[25]. We thought that the upward-convex pattern of ACG might reflect this mechanism of LV relaxation between a local asynergy and a global impairment of LV relaxation.

In an asynergic LV, regional outward movement during IRT occurred predominantly in normally contracting areas. Altieri et al. reported that the most frequent site of its phenomenon were in the anterolateral, anteroapical and apical wall, but that it occurred infrequently in the extensive asynergic ventricle[26]. In the present study, we could not documented the relationship between the convex pattern of ACG and wall motion abnormalities during IRT. Of course, we are unable to detect the direct affections of motion abnormalities of anterolateral or apical wall to the ACG pattern in our clinical study. As mensioned above, in spite of, we supposed that ACG pattern chiefly reflects the LV pressure fall because of the closely pattern resemblances and nearly nadir coincidences even in the patients with CAD.

Limitations: As a result, the correlations between Δt and LV relaxation indices were not so closely high, because of these narrower separations of the values of Δt among CAD patients and the exclusion of the more prolonged values in hypertrophic cardiomyopathy (HCM), as Okayama et al. reported in our institutes[8].

Conclusion: We concluded that [1] the extent and/or severity rather than the locality of LV wall motion abnormalities affected Δt, [2] The delay of a global isovolumic LV pressure fall may be a major determinant of the upward-convex pattern of the ACG

downstroke, [3] Δt was measured in early period of isovolumic LV relaxation. This might be favor to reflect fairly the initial exponential portion of bi-exponential fitting of isovolumic LV pressure fall, [4] Δt has a clinical usefullness to estimate non-invasively LV relaxation, because it can be measured simply, easily and quantitatively, and its variations were narrower than those of A2-O.

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