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Systolic time intervals in coronary artery disease as indices of left ventricular function: fact or fancy?

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Characteristic changes in systolic time intervals have been described in left ventricular failure, and it has been held that patients with coronary artery disease have similar abnormalities in pre-ejection and ejection times as well as in the length of total electromechanical systole. In order to assess the contribution of systolic time intervals to the clinical evaluation of patients with coronary artery disease, correlative studies were made between systolic time intervals and the standard variables of contractility and performance obtained at cardiac catheterization.

A wide spectrum of left ventricular functional disturbance was present in 36 male patients with electrocardiographically and angiographically demonstrable coronary artery disease. While excellent correlations were shown between contractility indices, especially dp/dt max, and ejection fraction and extent of asynergy, systolic time intervals were not reliable indices of ventricular function. It is doubtful whether systolic time intervals are of value in the clinical assessment of coronary artery disease.

The haemodynamic changes in coronary heart disease have been the subject of numerous investigations. It is generally agreed that the first derivative of the pressure pulse (dp/dt) in man, despite its dependence on multiple variables, can be taken as an index of the contractile state in health and in disease (Mason, 1969). This, however, as well as other factors relating to left ventricular function – ejection fraction (EF), max. systolic ejection rate (MSER), end-diastolic volume (EDV) – is obtainable only through an invasive procedure and therefore not available to general clinical assessment. It would be useful if within the classical approach of Osler – observation, palpation, auscultation, contemplation – an easily and externally measured variable could be shown to correlate well with the more definitive intracardiac measurements of ventricular performance.

It has been suggested that one such variable in coronary artery disease might be obtained by the determination of systolic time intervals through recording of the carotid pressure pulse simultaneously with the phonocardiogram and apex cardiogram (McConahay, Martin, and Cheitlin, 1972; Garrard, Weissler, and Dodge, 1970; Aronow, Bowyer, and Kaplan, 1971). That changes in cardiac contraction influence the length of mechanical systole is known (Metzger *et al.*, 1970). At what point and through what mechanisms this influence is exerted remains largely unexplained. Similarly the role of relaxation, especially its relation to the factors determining the duration of systole, is not clear.

A group of patients with known coronary artery disease and presenting with a wide spectrum of left ventricular functional disturbance at the time of routine and preoperative evaluation through cardiac catheterization offers an opportunity for correlative observations in this regard. The purpose of this study was to compare velocity-related indices of left ventricular function with ventricular performance as defined angiographically and to examine the relation of these variables to systolic time intervals in ischaemic heart disease. These alterations as determined at catheterization will be discussed with respect to one another and with regard to their extension to bedside examination in coronary heart disease.

Subjects and methods

Thirty-six male patients with coronary heart disease as defined clinically by classical angina pectoris and electrocardiographically by the presence of changes consistent

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with either previous myocardial infarction or stress-induced ischaemia were studied by right and left heart catheterization with selective coronary and left ventricular angiography. Their ages ranged from 35 to 62, with a mean of 52 years. A total of 33 infarcts was documented, 7 patients having more than 1 (5 patients in this group having double and 2 patients triple lesions). Sixteen posterior wall, 13 anterior, and 4 mixed infarctions were electrocardiographically present. Twelve patients had severe angina pectoris but no infarction. Patients with manifest left ventricular insufficiency, auscultatory evidence of mitral regurgitation, or radiographically demonstrable aneurysm were excluded from the study, since in these cases the isovolumetric requirements for evaluation of contractility by means of velocity related indices are not fulfilled. All patients were in sinus rhythm. One case of left bundle-branch block and three of incomplete right bundle-branch block were observed, the velocity indices in none of these cases significantly influencing the mean findings for the group as a whole. The therapeutic regimen for each patient, consisting primarily of nitroglycerin preparations, was continued for up to 24 hours before the study. Propranolol and related drugs, where chronically used, were discontinued for at least 7 days preceding catheterization. It should be noted that a ventricular diastolic gallop had been noted in 16 patients at varying times during precatheterization examination. While not interpreted as overt insufficiency or accompanied by other objective evidence of decompensation (neck vein distension, *x*-ray abnormalities), this had led in some cases to the administration of digitalis, which was continued for up to 24 hours before the procedure. It is important to mention that blood volume, changes in which may have occurred under digitalis and diuresis, was not measured at the time of catheterization.

Intracardiac pressures were measured with the Statham micromanometer SF 1 or P 866 with simultaneous recording on the Hellige multichannel console of the electrocardiogram, the left ventricular pressure pulse, and, through an electronic differentiating circuit, its first derivative (dp/dt). Measurements of left ventricular end-diastolic pressure, dp/dt max, and related contractile indices were taken from high speed (200 mm/sec) photographic paper recordings of left ventricular pressure. In each case calculations were made from at least five separate systolic contractions during the post-expiratory resting phase of respiration.

Systolic time intervals were measured, in all cases before angiography, from simultaneous recordings of the electrocardiogram and the aortic pressure pulse as registered by the catheter tip micromanometer. The following phases of the cardiac cycle were measured directly: (1) total electromechanical systole (QA2) from the onset of the QRS complex to the trough of the incisura of the aortic pulse; (2) left ventricular ejection time (LVET) from the beginning of the aortic upstroke to the incisura; and (3) the pre-ejection period (PEP), taken as the difference between the QA2 interval and LVET (Fig. 1). Heart rate was calculated by dividing the average RR interval on 5 consecutive cycles with regular rhythm, each read to the nearest millisecond, into 60. The regression equation relating heart rate to systolic

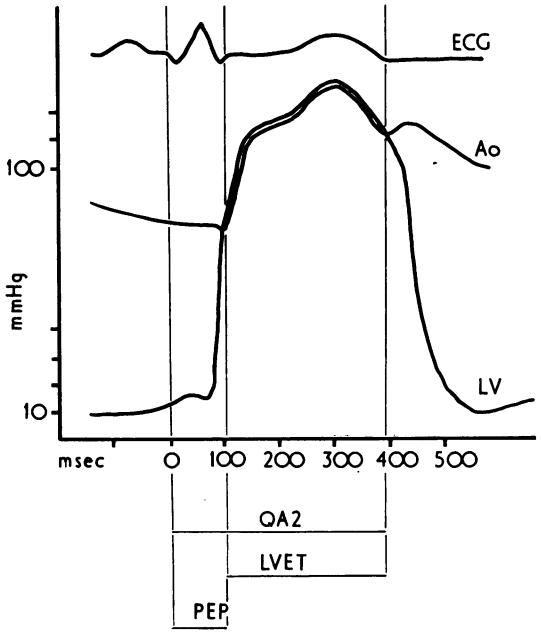


FIG. 1 *High-fidelity intracardiac pressure curves obtained from the left ventricle and aorta with the micromanometer, showing measurement of systolic time intervals.*

time intervals has been derived by Weissler, Harris, and Schoenfeld (1968). In addition to expression of the absolute values for each interval, the magnitude of change in the variables PEP, LVET, and QA2 was obtained by subtracting the observed value from the mean normal value at the same heart rate and expressed as an increase or decrease from zero in milliseconds.

From extrapolation to the left ventricular pressure curve with simultaneous registration of the first derivative of the pressure pulse (dp/dt) the following additional measurements were made: (1) isovolumic contraction time (ICT) derived as the difference between the PEP and the time from the onset of the QRS complex to the upstroke of both the left ventricular pressure pulse and its electronically differentiated first derivative; (2) Q–dp/dt max and Q–dp/dt relax; (3) from the above data the quotients LVET/PEP and LVET/ICT were derived. Care was taken to ensure that the heart rate was the same as that registered during the aortic pulse recording; in most cases this was obtained by virtue of the left ventricle–aorta pullback manoeuvre.

Ventricular injection for angiocardiography was made in the right anterior oblique (RAO) projection with the patient at 30° rotation or that which ensured projection of the longest axis of the left ventricle. After injection of 40 to 70 ml of Angiografin single-plane cineangiograms were made at 80 frames per second. In 23 of the 36 patients ejection fraction (EF) could be calculated from

the angiographic series according to the methods of Dodge *et al.* (1960). For this group asynergy was derived from the single plane angiocardiograms as a percentage estimate of that portion of the ventricular surface which did not contribute to contraction,.

Selective right and left coronary angiography followed, using the techniques of Sones and/or Judkins, with hand injection of 5 to 10 ml of Angiografin and 35 mm cine-angiography at 64 frames per second.

Results

Left ventricular function as determined by isovolumic velocity-related contractility indices and quantitative angiographic variables were used as a gauge with which to compare systolic time intervals.

The haemodynamic variables and contractility data are presented in Table 1, including ejection fraction (EF) and percentage asynergy, as derived angiographically.

Contractility

The mean values for dp/dt max and dp/dt relax did not show significant deviations from the norm as calculated for the group as a whole. Extreme variations

TABLE 1 *Haemodynamic and contractility variables*

Case No.	*HR*	*Ao (mmHg)* s	d	m	*LVEDP (mmHg)*	*dp/dt max (mmHg/sec)*	*dp/dt relax (mmHg/sec)*	*t-dp/dt max (msec)*	*dp/dt max/IP (sec^{-1})*	*EF*	*Asyn. (%)*	*MSER (ml/sec)*
1	78	175	90	120	13·0	1430	1215	70	23·8	10·34	50	125
2	70*	108	67	83	6·5	1400	1750	110	23·0			254
3	79	120	70	95	12·0	1440	1248	76	23·1			189
4	96	95	60	72	12·0	910	700	75	25·3	12·44	60	184
5	77	93	63	76	29·0	830	934	70	28·6	11·36	10	143
6	92	108	74	83	26·0	1030	772	70	32·2			79
7	81	110	70	93	19·0	1330	1240	70	27·8	13·80	70	123
8	62	138	78	100	21·0	1160	730	38	20·0	22·24	35	190
9	68	120	70	85	12·0	1250	1300	65	27·2	43·00	10	—
10	59	140	80	100	10·0	1710	1700	70	24·2			307
11	90	115	70	82	9·0	1660	1410	70	29·6			217
12	72	160	88	105	6·0	2000	1710	70	28·5	47·25	0	—
13	56	120	70	85	13·0	1200	1300	56	25·0	27·14	25	326
14	80	100	60	70	11·0	930	930	63	19·0	10·25	60	120
15	70	120	70	90	5·0	1160	1260	80	18·0	22·80	25	139
16	55	180	75	112	10·0	2220	1334	180	26·4			225
17	78	150	80	100	8·0	2560	1760	58	34·1			—
18	69	100	60	80	5·0	2190	1750	50	49·8	63·00	0	292
19	103	175	104	130	10·0	2260	1550	40	39·5	63·54	0	93
20	75	140	80	90	2·0	2200	2300	59	32·4	21·50	30	—
21	90	120	70	95	13·0	1750	1700	53	44·5	27·95	30	—
22	84	136	90	110	20·0	2900	2320	80	48·0			—
23	79	148	74	100	22·0	1960	1668	45	43·8	34·48	10	216
24	80	168	114	130	5·0	1660	1800	70	23·3	28·24	10	167
25	72	135	80	110	6·0	1950	1750	65	26·6	46·63	10	126
26	70	130	90	100	8·0	1600	1600	60	26·0			119
27	68	114	75	87	12·0	1557	1112	60	28·3	44·80	0	280
28	76	130	74	90	10·0	1496	1496	53	30·2			337
29	89	190	94	128	5·0	2210	2200	68	26·3	40·51	0	—
30	67	130	70	100	5·0	2070	1810	53	33·7			209
31	67	160	80	110	8·0	1960	2300	80	23·3	49·79	16	174
32	73	160	80	110	20·0	1700	1800	63	26·2			139
33	89	125	75	96	11·0	1600	1600	58	32·0	50·42	0	165
34	75	120	75	92	28·0	1600	1550	55	38·0	31·28	0	—
35	68	160	76	100	8·0	1984	1526	55	28·4	22·55	30	224
36	55	150	65	90	5·0	2230	1360	75	37·0			—
Mean	75·5			97·1	11·8	1697	1513	64·8	29·8			
SD	15·1			15·1	6·9	484	417	13·4	7·8			

Ao = aortic pressure. LVEDP = left ventricular end-diastolic pressure.
dp/dt max, t-dp/dt max, (dp/dt max)/IP = velocity related contractility indices of isovolumic contraction time (Krayenbühl, 1969).
dp/dt relax = maximum velocity of relaxation. EF = ejection fraction.
Asyn. = area of asynergic contraction in per cent of total ventricular circumference. MSER = mean systolic rate of ejection.

in dp/dt max were, however, observed in individual cases, and there were significant correlations with cardiac performance as expressed by ejection fraction and extent of asynergic contraction, the relation with EF being direct ($r = 0{\cdot}67$, $P < 0{\cdot}01$) and with percentage asynergy inverse ($r = 0{\cdot}53$, $P < 0{\cdot}01$). The variables MSER and (dp/dt max)/IP responded similarly. Of note was a decrease in dp/dt relax as compared to dp/dt max in 23 patients, well over half the patient group. The degree of significance obtained by comparison of dp/dt relax with EF and asynergy was not improved over that gained from the comparison of dp/dt max with these variables.

Ejection fraction (EF) and asynergy

An excellent inverse relation ($r = 0{\cdot}78$, $P < 0{\cdot}01$) was obtained between calculated ejection fraction and per cent estimate of asynergic contraction.

Systolic time intervals

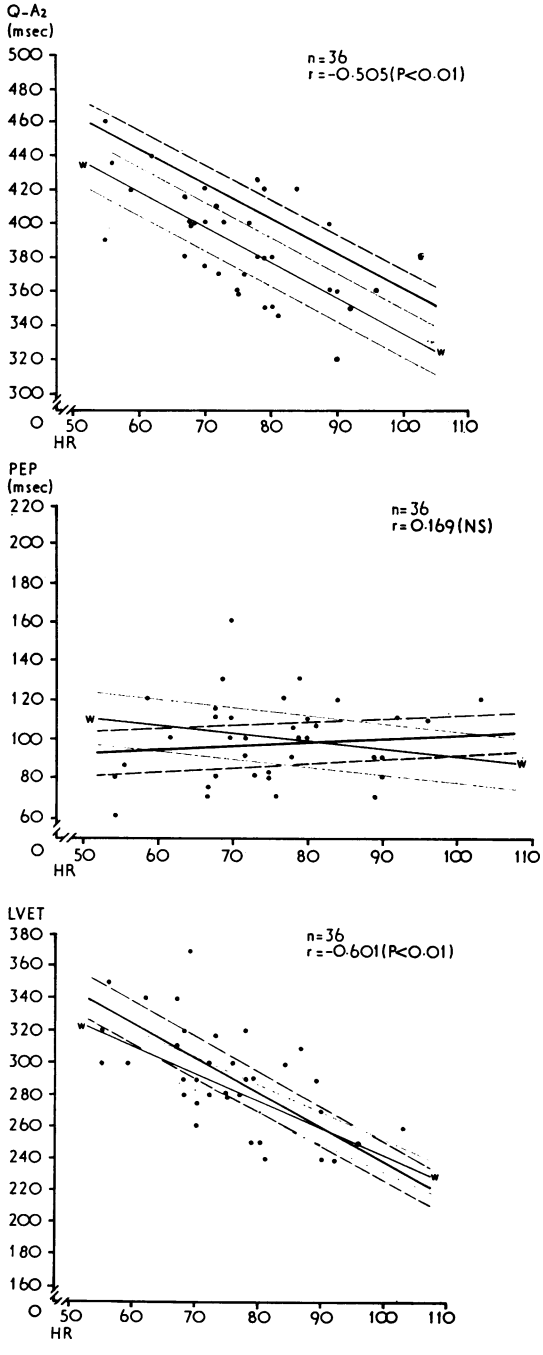
The absolute systolic time intervals, with an expression of deviation from the normal regression curve of Weissler *et al.* (1968), and the quotient LVET/PEP, are presented in Table 2. Fig. 2 illustrates the scatter of values for PEP, LVET, and QA2 about the normal regression slopes for male patients.

While pronounced deviations were present in individual cases, the values for PEP, LVET, and

TABLE 2 *Systolic time intervals*

Case No.	*HR*	*QA2* (*msec*)	*ΔQA2* (*msec²*)	*LVET* (*msec*)	*ΔLVET* (*msec*)	*PEP* (*msec*)	*ΔPEP* (*msec*)	*ICT* (*msec*)	*LVET/PEP* (*units*)
1	78	425	+43	320	+40	105	+5	85	3·0
2	70	420	+21	260	−34	160	+57	70	1·6
3	79	420	+40	290	+11	130	+30	20	2·2
4	96	360	+24	250	0	110	+17	90	2·3
5	77	400	+16	280	−2	120	+20	70	2·3
6	92	350	−3	240	−17	110	+16	50	2·2
7	81	345	−45	240	−35	105	+6	90	2·3
8	62	440	+24	340	+32	100	−6	80	3·4
9	68	400	−3	290	−7	110	+6	70	2·6
10	59	420	−2	300	−13	120	+13	80	2·5
11	90	320	−37	240	−20	80	−15	80	3·0
12	72	410	+15	300	+9	90	−12	70	3·3
13	56	435	+7	350	+32	85	−24	65	4·1
14	80	350	−28	250	−27	100	+1	80	2·5
15	70	400	+1	290	−4	110	+7	90	2·6
16	55	400	−31	320	0	80	−29	60	4·0
17	78	380	−2	290	+10	90	−10	65	3·2
18	69	500	+99	370	+74	130	+27	110	2·9
19	103	380	+50	260	+22	120	+30	75	2·2
20	75	360	−29	280	−6	80	−21	80	3·5
21	90	360	+3	270	+10	90	−5	60	3·8
22	84	420	+50	300	+30	120	+23	105	2·5
23	79	350	−30	250	−29	100	0	80	2·5
24	80	380	+2	270	−7	110	+11	100	2·4
25	72	370	−25	280	−11	100	−2	70	2·8
26	70	375	−24	275	−19	100	−3	80	2·7
27	68	400	−3	320	+23	80	−24	60	4·0
28	76	370	−16	300	+16	70	−31	50	4·3
29	89	360	+1	290	+28	70	−25	50	4·1
30	67	380	−15	310	+11	70	−34	55	4·4
31	67	415	+10	340	+59	75	−29	60	4·5
32	73	400	+7	318	+29	80	−22	60	3·9
33	89	400	+41	310	+48	90	−5	70	3·4
34	75	360	−29	280	−6	80	−21	60	3·5
35	68	400	−3	280	−17	115	+11	70	2·4
36	55	390	−59	300	−20	60	−49	60	5·0

QA2 = total duration of systole; LVET = left ventricular ejection time; PEP = pre-ejection period; ICT = isovolumic contraction time; ΔQA2, ΔPEP, ΔLVET = deviation from normal regression curves (Weissler *et al.*, 1968, see text).



QA2 were distributed in such a manner that no group deviation from the normal could be identified. Indeed, as shown in Fig. 2, the overall distribution of systolic time intervals with regard to heart rate might appear to have been derived from normal controls rather than from a patient group with the extent of myocardial damage known to be present. In contrast to the observations of Blumberger as early as 1942, and of Weissler *et al.* more recently (1968), and Weissler, Harris, and Schoenfeld (1969), that the pre-ejection period (PEP) is prolonged and left ventricular ejection time (LVET) shortened in heart failure, the PEP and LVET in our patients showed random distribution about the normal regression slopes, even in cases where pathologically raised end-diastolic pressure or clinical evidence might be indicative of a pre-failure state. Similarly, even where extensive three-vessel disease was angiographically demonstrable, the PEP and LVET were scattered over a wide range of values, in contrast to the PEP prolongation and LVET shortening remarked in coronary artery disease by other observers (McConahay *et al.*, 1972).

To assess the relation of pre-ejection and ejection times and total length of systole to parameters of contractility and function, both the absolute values and the deviations in these intervals relative to heart rate (ΔPEP, ΔLVET, and ΔQA2) were plotted individually against the first derivative of the pressure pulse (dp/dt max), ejection fraction, and asynergy. As might have been expected from the random distribution of absolute values about the normal regression curve, no significant correlations between either these values or change in the systolic intervals relative to dp/dt max, ejection fraction, or asynergy were observed (Table 3, Fig. 3).

Similarly unproductive were comparisons of the quotient LVET/PEP to these indices (Fig. 4). This quotient, expressed either as LVET/PEP or the inverse PEP/LVET, has been seen in previous studies (McConahay *et al.*, 1972; Blumberger, 1942) to show characteristic variations in both cardiac insufficiency and in coronary artery disease.

Consideration of the interval ICT did not add to information already gained from the PEP relative to ejection fraction or contractility. ICT tended to vary

FIG. 2 Above, *total electromechanical systole (QA2) and heart rate;* middle, *pre-ejection period (PEP) and heart rate;* below, *left ventricular ejection time (LVET) and heart rate. Each graph shows the appropriate normal regression line with one standard deviation as given by Weissler* et al. *(1968) labelled by 'W', and from our own figures.*

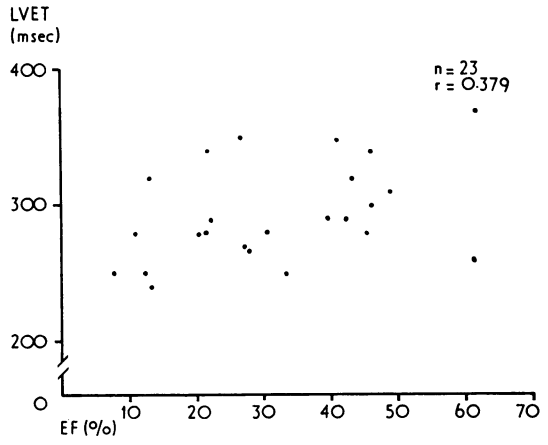


FIG. 3 *Left ventricular ejection time (LVET) and ejection fraction (EF).*

TABLE 3 *Correlation coefficients for systolic time intervals with parameters of left ventricular function*

	dp/dt max (*n* = 36)	*EF* (*n* = 23)	*Asynergy* (*n* = 23)
PEP	r = 0·221	0·060	0·149
LVET	r = 0·224	0·379	0·007
QA2	r = 0·101	0·340	0·266

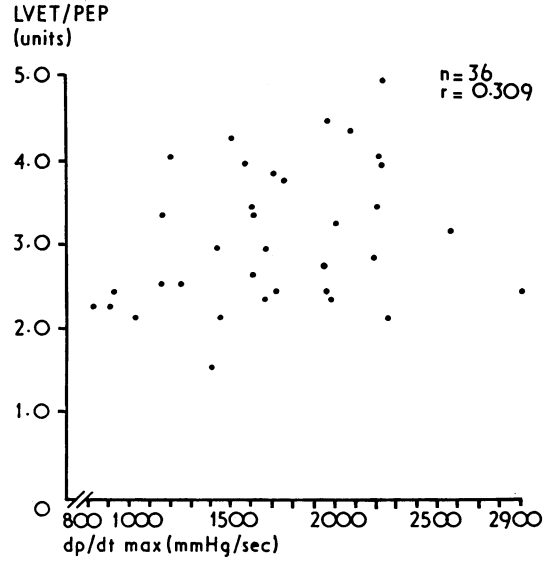


FIG. 4 *LVET/PEP correlated with dp/dt max.*

directly with the corresponding PEP. Though a relative diminution in the contribution of the ICT to the PEP appeared to occur in the presence of high values for dp/dt max, the quotient LVET/ICT offered no advantages over LVET/PEP in predicting behaviour of the pressure pulse slope or level of ejection capacity. This is in agreement with previous observations (McConahay *et al.*, 1972), and the ICT will not be further considered. The intervals t–dp/dt relax and Q–dp/dt relax were not informative either as indices of contractility or when compared to the total duration of systole or to ejection time, and will likewise not be further discussed.

The inclusion of one case of left bundle-branch block in the study did not alter significantly the overall results relative to systolic time intervals or contractility. In this patient PEP was prolonged and LVET shortened in comparison to normal values. In no patients were the coronary arteries free of disease, extensive stenoses occurring in two or more vessels for the majority of the group. In cases of previous infarction no relation between infarct localization and contractility or time interval variables could be established. Electrocardiographic and angiographic localization of lesions was in good agreement.

Discussion

This study was designed to compare contractility variables with performance and further to test the validity of applying systolic time intervals to the assessment of ventricular function in coronary artery disease. The maximal rate of change of ventricular pressure during isovolumic contraction (dp/dt max), when taken with related variables (EF, MSER), has been interpreted as an adequate index of the state of myocardial contractility (Mason, 1969; Siegel and Sonnenblick, 1963; Mason *et al.*, 1965; Krayenbühl, 1969). Patients with ischaemic heart disease may show abnormalities in contractility and ejection even in the absence of overt myocardial insufficiency or, indeed, of symptoms of angina pectoris (Malmborg, 1965; Raftery, Banks, and Oram, 1969; Chatterjee *et al.*, 1971). Alterations of these variables could be expected to influence the pre-ejection period and the ejection phase of systole. Furthermore, changes in ventricular compliance or diastolic relaxation are common in acute (Diamond and Forrester, 1972) and chronic (Mathes and Just, 1973) ischaemic heart disease. Changes of this kind tend to alter the latter part of systole as well as the velocity of contraction and ejection.

With respect to contractility and ventricular function we were able to show significant interrelation between increased dp/dt max and good ejection fraction, and between depressed dp/dt max and increasing

degree of asynergic contraction. This is in agreement with previous studies which have shown uniform decrease of dp/dt, as more and more left ventricular surface area displays pathological motion, even when clinical evidence of congestive failure is minimal or absent (Klein, Herman, and Gorlin, 1967).

A particularly strong relation was obtained between ejection fraction and degree of asynergy. One patient (Case 14) showed extreme impairment of ejection fraction, 60 per cent ventricular asynergy, extensive triple vessel disease, and pronounced depression of contractility indices, yet was able to carry out a vigorous physical training programme for a prolonged period without obvious disability. That the congestive failure that eventually ensued was delayed for such a remarkable length of time was difficult to explain in view of the extent of disease present, and lends support to the observation that a severe degree of ventricular dysfunction as determined angiographically and confirmed by abnormal parameters of myocardial performance (dp/dt, EF, MSER) may be present without pronounced clinical evidence of functional embarrassment. When myocardial insufficiency does occur in coronary artery disease it may reflect the presence of a mixture of functional cardiac muscle with nonfunctional scar tissue; that is, diffuse involvement and asynergy, rather than gross fibrous scarring, may be the ultimate aetiological factor in failure (Gorlin, Klein, and Sullivan, 1967), leading even before the onset of decompensation to more severe ventricular dysfunction than a more compact, discrete lesion (Hort *et al.*, 1968).

Turning to the application of systolic time intervals for the analysis of function, we were unable to show characteristic abnormalities even in the presence of severe derangement of ventricular performance as registered by changes in contractility and ejection. In an attempt to apply systolic time intervals to the detection of functional impairment, it is important to realize that so many factors influence each interval that a direct and precise relation to any single haemodynamic event cannot be expected (McConahay *et al.*, 1972). It has been suggested that the prolongation of the pre-ejection period observed in heart failure might be due to a diminished rate of left ventricular pressure rise during isovolumic contraction (Weissler *et al.*, 1968, 1969). Our data did not demonstrate a significant relation between change in the pre-ejection period and diminished maximal rate of pressure rise (dp/dt). A positive correlation of these variables implies decreased dp/dt in the presence of a steady state with respect to aortic diastolic pressure. In this connexion the augmentation of the pre-ejection period prolongation by diastolic hypertension should be mentioned (Weissler *et al.*, 1968; Blumberger, 1942). What might occur should dp/dt and aortic diastolic pressure fall simultaneously? Even drastically reduced levels of rate of development of dp/dt max would not be reflected in changes in the pre-ejection period. It has been shown in experimental myocardial infarction that a drop in arterial pressure occurs and is maintained over prolonged periods, in part assisting the functional capacity of non-ischaemic areas by decreasing afterload (Hort, Just, and da Canalis, 1964). A similar mechanism may be operative in coronary artery disease, particularly where earlier infarction has occurred, shifting the chronological sequence of events before aortic valve opening to the left on the ventricular pressure curve. As a result, even where dp/dt is compromised, the pre-ejection period need not be prolonged.

Similarly one must consider the effect of sympathetic tonus on systolic time intervals. The reflex mechanisms affecting sympathetic activity are extremely complex. Increased sympathetic excitation increases heart rate and strengthens the force of myocardial contractility. Increased heart rate alone has been shown to increase contractility (Sonnenblick, Morrow, and Williams, 1966). Associated is an increased rate of ventricular relaxation. These factors would be expected to result in both pre-ejection period and left ventricular ejection time shortening, and yet even in the failing heart, with demonstrably increased sympathetic activity, the pre-ejection and ejection periods have been found to change in opposite directions. So many factors are operative at the same time that the role played by sympathetic activity alone, without consideration of such factors as pre- and after-load, medical treatment, vagal tone, and venous pressure, may exert a varying influence on systolic time intervals in different patients at different points on the compensation scale. Under these conditions systolic time intervals would not be expected to reflect adequately a state of cardiac compensation or level of decompensation which is not already clinically obvious. It is pertinent to mention at this point that the role played in our study by the stress of the catheterization procedure was not great, as judged by the small scatter of resting heart rates. Sympathetic activity cannot, however, be overlooked in an evaluation of systolic time intervals.

Stroke volume has been demonstrated to correlate with changes in systolic time intervals, especially LVET (Weissler *et al.*, 1968), and should likewise be discussed as a possible determinant of time relations. It is reasonable to assume that a low stroke volume with constant heart rate and peripheral resistance could occur in conjunction with pro-

longed PEP and shortened LVET, even if no effect on total duration of systole were observed. Though mean systolic ejection rate was seen to be reduced in our patient group, decreased stroke work was not reflected in characteristic changes in either pre-ejection period or left ventricular ejection time. The pressure-volume relation in the ischaemic heart is not static but dynamic, not only over time but at any one point in time, with variations over the entire period of diastole. Myocardial fibres which are chronically embarrassed by ischaemic disease may constantly rearrange to achieve the best, albeit a tenuous, balance between pressure, volume, and work. Under these conditions it is not surprising that the measurement of systolic time intervals, except conceivably in the overtly insufficient heart, fails to reflect true intracardiac relations. Indeed, other studies, from in part the same observers, have shown divergent results with regard to changes in systolic time intervals in relation to stroke volume (Garrard *et al.*, 1970; Weissler *et al.*, 1968).

Changes occurring not only during diastole but also during the relaxation phase of systole may offer an additional explanation for poor correlation of systolic time intervals with other parameters of cardiac performance. It has been shown that ventricular ejection is completed well before the end of systole. Even if the first two-thirds of systole were inscribed at a rapid rate, the relaxation phase, with onset before the end of systole, may be retarded, resulting in no net change in left ventricular ejection time or, even with concurrent changes in pre-ejection time, in the total duration of systole. We have shown a definite decrease in the rate of change of left ventricular pressure (dp/dt) from the phase of isovolumic contraction to that of isovolumic relaxation in well over half of our patient group, and yet ejection time and total electromechanical systole did not significantly deviate from normal.

A consideration of the therapeutic regimen is also important. Digitalis, for example, improves cardiac contraction and increases stroke volume and cardiac output. Blumberger (1942) showed that the most definitive effect of digitalis was on the pre-ejection period, and went so far as to recommend the evaluation of changes in the pre-ejection period before and after digitalization as an index of successful therapy. Other observers have reported contradictory findings with regard to the effects of digitalis administration on the total duration of systole (Weissler *et al.*, 1969, 1965). It must be recalled that digitalis is frequently given in combination with diuretic agents, and changes in blood volume with varying degrees of diuresis would also play a part in the time required for systolic contraction and relaxation.

Finally, not only normal pre-ejection periods but no significant changes in other time intervals have been observed in acute myocardial infarction (Samson, 1970; Halpern *et al.*, 1969), even when paradoxical systolic pulsations present over the praecordium would imply an extreme reduction in contractility, and the greater use of the contractile element, requiring more time for the development of pressure within the left ventricle.

We have attempted to show that the determinants of systolic time intervals are complex and varied, and that in consequence application of systolic time intervals to the momentary haemodynamic status can be made only with caution. The time required for the accomplishment of intracardiac events, each dependent on many variables, is naturally predisposed to variance. Abnormal time relations may adequately reflect that stage in the disease process at which compensatory mechanisms have been exhausted, but not the indices of function as long as the cardiovascular reserve is sufficient to prevent manifest failure. Changes over a period of time may be useful in the ongoing evaluation of the individual patient, but alterations in the time intervals at an individual examination provide only rough approximations of patient status. From our observations it is doubtful whether consideration of systolic time intervals, either internally or at the bedside, offer a reliable index of cardiac function in the damaged but compensated ischaemic heart.

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