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Predictive Value of the Systolic Time Intervals in Primary Myocardial Disease*

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The systolic time intervals were studied in 33 patients with primary myocardial disease and correlated with the underlying hemodynamic disturbance. Seven patients had associated functional mitral incompetence. Pre-ejection phase (PEP) correlated with mean left ventricular dp/dt (LVdp/dt), and left ventricular ejection time (LVET) correlated with stroke index (SI), cardiac index (CI), left ventricular end-diastolic pressure (LVEDP) and ejection fraction (EF). Patients with additional functional mitral incompetence had a shorter LVET and Q-A_2 than patients without mitral incompetence. The measurements were of value in predicting hemodynamic aberrations, and the predictive value could be enhanced by using two or more parameters simultaneously.

Simple noninvasive ("bedside") techniques are attractive methods of assessing left ventricular function. The duration of the time intervals in systole has been measured in normal subjects at rest and during various physiologic interventions and in patients with cardiac disease. The time interval measurements have been shown to correlate with the underlying hemodynamic disturbance.[1-13]

Left ventricular electromechanical systole can be divided into two phases: the pre-ejection phase (PEP) from the onset of the Q wave of the electrocardiogram to aortic valve opening and the left ventricular ejection time (LVET) from the time of aortic valve opening until its closure. PEP has three components: (1) it represents the period of the electromechanical delay; (2) the time interval from myocardial activation to mitral valve closure; and (3) the isovolumic contraction time. A change in the duration of PEP may be a consequence of altered electromechanical delay or a consequence of a decrease in the rate of rise of left ventricular pressure. It depends on preload, afterload and heart rate, but it is ultimately a function of left ventricular contractility.[14] Left ventricular ejection time is a function of stroke volume and left ventricular ejection rate: therefore it is related to cardiac index, heart rate and velocity of fiber shortening. It is also determined by the afterload and is indirectly related to ejection fraction.

Patients with primary myocardial disease have severe left ventricular dysfunction. The disease is common in the South African Bantu population and presents as congestive cardiomyopathy. Its etiology is unknown.[15-21] Clinically, the patients develop heart failure of insidious onset, which may become more severe during pregnancy, alcoholic incursions or the ingestion of herbal remedies. The heart failure usually improves with rest in bed. The heart may be normal in size or enlarged, and a third or fourth heart sound is present in severe disease.

The basis of the hemodynamic abnormality is impaired contractile function of the muscle, with gross dilatation of the ventricle: there is a low cardiac output, a wide arteriovenous oxygen difference and impaired left ventricular function with an elevated end-diastolic pressure, a small stroke volume, an increase in end-diastolic volume and a reduction in ejection fraction. The essential abnormality is pump failure; there is no evidence of pericardial, endocardial or coronary artery disease. When the electrocardiogram was suggestive of disease, coronary

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Table 1—*Clinical Data of Thirty-three Bantu Patients with Cardiomyopathy*

Group 1 CMO

	Age, Yrs	Sex	Disability	ECG	HV	MPAP	LVEDP	MAP	Mean LVdp/dt	CI	SI	LVEF
1	27	M	1	PVC's	460	10	2	118	1633	3.5	64	37
2	47	M	1	PAT	515	11	6	87	700	3.0	43	35
3	19	F	2a	LVH	—	—	20	87	733	5.3	63	23
4	65	M	2a	LVH	560	22	30	110	833	4.1	51	35
5	30	F	2a	LVH	505	15	1	105	933	2.9	29	12
6	14	M	2a	LVH; PVC's	—	23	15	75	643	5.1	42	—
7	50	M	2b	LVH; PVC's	830	22	20	86	867	2.5	15	30
8	60	M	2b	LAHB	715	37	27	117	683	1.8	20	23
9	44	M	2b	LAHB	935	37	28	117	1171	2.9	26	13
10	65	M	3	LAHB	640	50	6	115	978	2.1	23	38
11	72	M	3	LVH; PVC's	1410	20	8	70	940	2.8	31	37
12	52	M	3	LVH	1000	27	22	87	600	3.3	37	34
13	67	M	3	1st° AV block; LAHB; PVC's	710	10	10	90	1625	3.3	47	27
14	60	M	3	LBBB	610	25	15	102	1200	2.9	29	28
15	20	F	3	LVH	—	40	25	80	409	2.4	24	22
16	48	M	3	LAHB	890	25	25	100	500	2.0	25	19
17	55	M	3	LVH; PAC's	955	50	35	105	550	1.5	13	17
18	38	M	3	RBBB + LAHB; PVC's	1260	40	25	108	750	2.2	27	—
19	27	M	3	LVH	900	38	20	78	625	1.9	17	16
20	50	M	3	LVH	840	57	40	137	1063	1.4	13	14
21	50	M	4	LVH; LAHB	1000	25	25	97	455	2.2	31	35
22	20	M	4	LVH	740	44	27	96	700	2.1	19	—
23	14	F	4	LVH; LPHB	850	32	20	100	1040	—	—	25
24	34	M	4	LVH; LAHB	—	43	30	80	590	3.5	32	21
25	42	M	4	LVH; LAHB	910	—	35	107	813	1.3	13	20
26	51	M	4	LVH; PVC's	1200	52	35	126	542	1.7	15	18
				Mean	838	31	21	99	830	2.7	30	25
				± S.D.	248	14	11	17	318	1.0	15	9

Group 2 CMO + MI

	Age, Yrs	Sex	Disability	ECG	HV	MPAP	LVEDP	MAP	Mean LVdp/dt	CI	SI	LVEF
27	56	M	3	LVH	835	34	22	90	558	2.2	24	23
28	38	F	3	LVH; PVC's	970	35	30	110	700	2.0	20	21
29	30	M	4	LVH	900	40	25	117	938	1.7	17	24
30	29	F	4	LVH	875	36	16	92	800	1.7	14	—
31	18	F	4	LVH	900	40	39	96	—	2.2	22	26
32	24	F	4	LVH; LPHB	1120	37	25	98	—	1.8	15	—
33	25	M	4	RBBB + LAHB	835	46	27	80	456	1.9	17	20
				Mean	919	38	26	98	690	1.9	18	23
				± S.D.	100	4	7	12	191	.2	4	2
				Normal Value	450 ± 45	15 ± 5	9 ± 4	90 ± 15		3.5 ± 0.7	46 ± 8	67 ± 8
Statistical comparison between Groups 1 and 2.												
				t	0.84	1.27	1.17	0.24	0.94	1.90	2.04	0.61
				p	ns	ns	ns	ns	ns	ns	0.05	ns

Disability = New York Heart Association grading; MI = mitral incompetence; HV = heart volume (ml/M²); MPAP = mean pulmonary artery pressure (mm Hg); LVEDP = left ventricular end-diastolic pressure (mm Hg); MAP = mean arterial pressure (mm Hg); LVdp/dt = 1st derivative of LV pressure (mm Hg/sec); CI = cardiac index (1/min/M²); SI = stroke index (ml/beat/M²); LVEF = LV ejection fraction (%); LVH = left ventricular hypertrophy; LAHB = left anterior hemiblock; LPHB = left posterior hemiblock; LBBB = left bundle branch block; RBBB = right bundle branch block; PVC = premature ventricular contraction; PAC = premature atrial contraction; PAT = paroxysmal atrial tachycardia.

angiography was undertaken to exclude coronary artery disease.

In some patients the clinical picture is dominated by atrioventricular valvular insufficiency in which great ventricular dilatation makes the papillary muscles inadequate to maintain competence of the mitral or tricuspid valves. Severe pulmonary hypertension may be a result of left ventricular failure or repeated pulmonary emboli which originate from the endocardium of the right atrium or from the deep veins in the legs: this causes right ventricular failure. In some patients endocardial thrombosis occurs, and detachment of thrombus leads to further systemic or pulmonary emboli.

Measurement of the systolic time intervals has been made only in small groups of patients with severe myocardial disease, and detailed information in this group is lacking.[4,5,7]

We have examined the systolic time intervals in patients with cardiomyopathy (CMO) and correlated the changes with the altered hemodynamic picture to determine whether the relationship is also valid in extreme left ventricular dysfunction, to assess the effect of additional functional mitral incompetence and to see whether the measurements are of predictive value.

Materials and Methods

Thirty-three consecutive adult patients with Bantu cardiomyopathy were studied. The diagnosis was made on clinical, electrocardiographic, radiologic and hemodynamic criteria,[21-25] and these are given in Table 1. Seven patients had mitral incompetence, and the patients were divided into two groups: Group 1, patients who had primary myocardial disease; and Group 2, patients who had primary myocardial disease with additional functional mitral incompetence. Three patients had bundle branch block: right bundle branch block was present in two, and left bundle branch block was present in one. The patients all received digitalis therapy and were in a stable state at the time of study. Serial studies made in four patients showed that the time intervals did not alter during the stay in hospital.

Heart volume was measured from standard posteroanterior and lateral chest radiographs, using a 6-foot tube-film distance and calculated from the ellipsoid formula of Jonsell,[22] making allowances for magnification. Right and left heart catheterization was performed using the mid-chest level as the zero reference for pressures, and cardiac output was measured by the direct Fick method. Left ventricular cineangiography was undertaken in the right anterior oblique (RAO) view, and ventricular volumes were calculated according to the uniplane method of Greene et al[26] after allowing for magnification. Ejection fraction was then calculated in which

$$\text{Ejection fraction (EF)} = \frac{\text{End-diastolic volume (EDV)} - \text{End-systolic volume (ESV)}}{\text{End-diastolic volume (EDV)}} \times 100$$

The time intervals of the cardiac cycle were measured at cardiac catheterization using a paper speed of 50 and 100 mm/sec. These intervals are easily measured at the bedside, but we elected to use, in this study, the measurements made at catheterization in order to correlate the intervals with hemodynamic measurements made at the same time. We showed, in several subjects, that the "internal" and "external" measurements of PEP and LVET are identical. The "external" measurements were made on a twin-channel photographic recording Sanborn Twin-Beam recorder with two general purpose amplifiers, where one channel made superimposed electrocardiographic and phonocardiographic records and a separate carotid pulse tracing was made with the second amplifier. The time constant was 50 seconds. The "internal" measurements were made by comparing an electrocardiogram with the simultaneous pressure recording in the left ventricle, then in the ascending aorta. The delay time of the catheter manometer system was measured by tapping a phonocardiogram microphone with the tip of a fluid filled catheter and the appropriate correction made in the measurements. Pre-ejection phase (PEP), left ventricular ejection time (LVET) and isovolumic contraction time (ICT) were measured as shown in Figure 1. Isovolumic contraction time was measured from the onset of left ventricular pressure rise to the instant of aortic valve opening.

PEP, LVET, PEP/LVET, ICT and heart rate (HR) were then compared to the hemodynamic measurements cardiac index (CI), stroke index (SI), LVdp/dt, LV end-diastolic pressure (LVEDP) and ejection fraction (EF) and the relationships analyzed by standard statistical methods using an IBM 1130 computer.

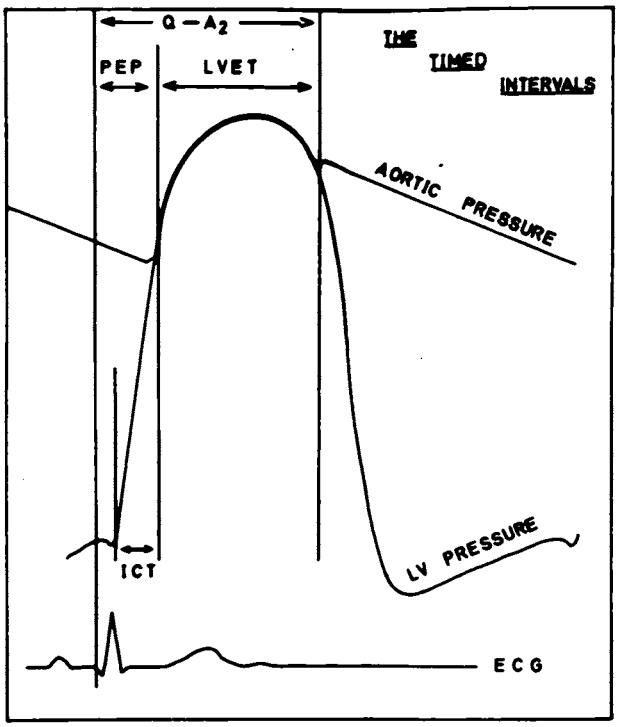

Figure 1. Method of measuring systolic time intervals. Aortic and left ventricular pressure pulses and electrocardiogram are shown. Timing of pressure pulses has been corrected to allow for catheter manometer pulse transmission time delay. PEP (pre-ejection period) is the interval from the onset of electrical systole (earliest q or R wave on ECG lead) to time of aortic valve opening. Isovolumic contraction time is interval from onset of LV pressure rise until aortic valve opening. Left ventricular ejection time (LVET) is duration of LV ejection, from onset of aortic pressure rise to nadir of incisura of aortic pressure pulse tracing. Q-A_2 is sum of PEP and LVET.

Table 2—*Systolic Time Interval Measurement in Each Patient*

Group 1 CMO

	MSec									
	PEP	ΔPEP	ΔPEP_{dig}	LVET	ΔLVET	$\Delta LVET_{dig}$	ICT	$Q\text{-}A_2$	HR/Min	PEP/LVET
1	110	17.0	32.0	220	−38.0	−23.0	60	330	100	.50
2	110	3.8	18.8	270	−14.0	+ 1.0	80	380	67	.40
3	125	87.0	102.0	243	−58.0	−43.0	75	368	73	.51
4	130	32.3	47.3	280	+ 3.0	+18.0	60	410	88	.46
5	150	55.8	70.8	220	−42.0	−27.0	90	370	97	.68
6	140	51.4	66.4	260	+20.0	+35.0	70	400	111	.53
7	90	−12.2	2.8	290	− 4.0	+11.0	60	380	77	.31
8	180	84.6	99.6	200	−67.0	−52.0	120	380	94	.90
9	140	51.4	66.4	170	−70.0	−55.0	70	310	111	.82
10	140	41.4	56.4	220	−60.0	−45.0	90	360	86	.63
11	110	13.4	28.4	250	−22.0	− 7.0	50	360	91	.44
12	150	47.8	62.8	230	−64.0	−49.0	80	380	77	.65
13	90	−18.6	− 3.6	260	−60.0	−45.0	40	350	61	.34
14	120	27.0	42.0	260	+ 2.0	+17.0	50	380	100	.46
15	180	21.2	36.2	210	−48.0	−33.0	110	390	100	.85
16	190	83.0	98.0	240	−74.0	−59.0	110	430	65	.79
17	160	69.8	84.8	170	−76.0	−61.0	100	330	107	.94
18	160	55.4	70.4	220	−84.0	−69.0	100	380	71	.72
19	150	67.0	82.0	190	−28.0	−13.0	80	340	125	.78
20	130	39.8	54.8	160	−86.0	−71.0	80	290	107	.81
21	160	57.0	72.0	230	−68.0	−53.0	110	390	75	.69
22	150	67.0	82.0	180	−38.0	−23.0	80	330	125	.83
23	130	37.0	52.0	240	−18.0	− 3.0	50	370	100	.54
24	110	23.0	38.0	180	−54.0	−39.0	80	290	115	.61
25	130	39.8	54.8	150	−96.0	−81.0	80	280	107	.86
26	160	71.4	86.4	170	−70.0	−55.0	120	330	111	.94
Mean	138	+42.8	+57.8	220	−46.7	−31.7	81	358	94	.65
± S.D.	26	28.2	28.2	39	30.9	30.9	22	38	19	.19

Group 2 CMO + MI

	MSec									
	PEP	ΔPEP	ΔPEP_{dig}	LVET	ΔLVET	$\Delta LVET_{dig}$	ICT	$Q\text{-}A_2$	Heart Rate (Beats/ Min)	PEP/LVET
27	170	72.2	87.2	180	−97.0	−82.0	120	350	88	.94
28	150	55.8	70.8	160	−102.0	−87.0	100	310	97	.93
29	150	56.6	71.6	210	−43.0	−28.0	80	360	94	.71
30	140	55.0	70.0	160	−66.0	−51.0	80	300	120	.87
31	90	− 1.4	13.6	200	−51.0	−36.0	60	290	104	.45
32	110	28.6	43.6	150	−61.0	−46.0	60	260	129	.73
33	150	59.8	74.8	200	−46.0	−31.0	90	350	107	.75
Mean	137	+46.7	+61.7	180	−66.6	−51.6	84	317	106	.77
± S.D.	28	24.9	24.9	24	23.9	23.9	21	37	15	.17
Normal value		0 ± 12.0			0 ± 10.0					.35 ± .04
Statistical comparison between Groups 1 and 2										
t	0.10	0.33	0.33	2.53	1.57	1.57	0.39	2.53	1.54	1.45
p	ns	ns	ns	<0.05	ns	ns	ns	<0.05	ns	ns

ICT = isovolumic contraction time; LVET = left ventricular ejection time; PEP = pre-ejection period; $Q\text{-}A_2$ = total electromechanical systole; Δvalue = deviation in time interval measurement when corrected for heart rate; $\Delta value_{dig}$ = Δvalue corrected for state of digitalis therapy.

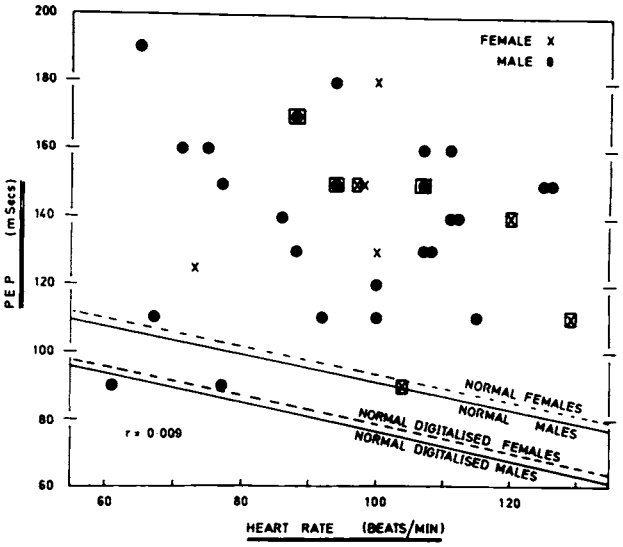

FIGURE 2. Pre-ejection period measurements in CMO. PEP is heart rate dependent and relationship to heart rate is shown. Normal regression lines of Weissler et al[4,30] are shown for normal subjects and for normal digitalized subjects. PEP is prolonged in patients with CMO. Patients with additional mitral incompetence are shown within squares.

Multiple regression analyses were then performed to find whether measurement of more than one time interval improved the prediction of the severity of the underlying hemodynamic disturbance.

RESULTS

The hemodynamic profile in each patient correlated with his clinical status: in general, patients who were most disabled showed the largest heart on x-ray film, the highest LVEDP and the lowest mean LVdp/dt, CI, SI and ejection fraction (Table 1). In some patients, vigorous therapy with prolonged bedrest and the intensive use of diuretics had decreased the LVEDP to normal. The systolic time interval measurements in each patient are shown in Table 2.

In normal subjects PEP depends on heart rate. The values of PEP and their relationship to heart rate in patients with CMO are shown in Figure 2. PEP was prolonged in our patients and was normal in only four patients whose overt cardiac failure had been controlled by vigorous therapy. Additional functional mitral incompetence had no effect on PEP. The prolongation of PEP was probably due to a decrease in the velocity of fiber shortening and myocardial contractility, and a significant negative correlation with mean LVdp/dt is shown in Figure 3. Three patients in this group had bundle-branch-block: left bundle branch block has been shown to prolong left ventricular activation time, but the patients were included in this consecutive series.[27] There was a similar direct relationship between ICT and mean LVdp/dt ($r = -0.70$; $p<0.001$). ICT is

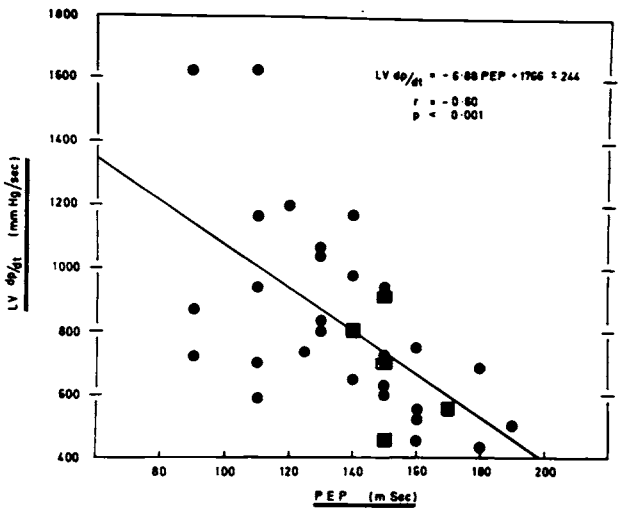

FIGURE 3. Linear relationship between PEP and LVdp/dt.

determined by LVdp/dt, LVEDP and aortic diastolic pressure.

LVET is also rate dependent, and the relationship between LVET and heart rate in the patients is shown in Figure 4. LVET was shortened in CMO, but it was of normal duration in six patients with mild or moderate disease. Additional functional mitral incompetence may have further reduced LVET. The reduction in LVET was a consequence of a decrease in stroke volume and cardiac output: its relationship to forward stroke index is shown in Figure 5. There was a similar linear relationship between LVET and LVEDP ($r = -0.67$; $p<0.001$) This showed that patients with severe disease and reduced LV compliance also had a shortened LVET and a low stroke volume, a result of decreased contractility: additional mitral incompetence further reduced the forward stroke volume and decreased the LVET.

It is possible to normalize PEP and LVET for changes in heart rate by using the regression equations derived by Weissler et al[4] for normal subjects. $\triangle$PEP is the deviation of PEP from normal when corrected for heart rate, while $\triangle$LVET is the deviation of LVET from normal when corrected for heart rate. Digitalis therapy shortens the time interval measurements,[28,29] and $\triangle$PEP and $\triangle$LVET were again calculated in the patients using the revised regression of Weissler and Schoenfeld[30] for digitalized normal subjects: these indices were called $\triangle PEP_{dig}$ and $\triangle LVET_{dig}$. The derived values were also related to the underlying hemodynamic disturbance (Table 3).

The ratio PEP/LVET is nearly rate independent, but it has the advantage of magnifying the directional changes in the two measurements in relation to ventricular dysfunction.[7] The significant relationship of this ratio to stroke index, ejection fraction

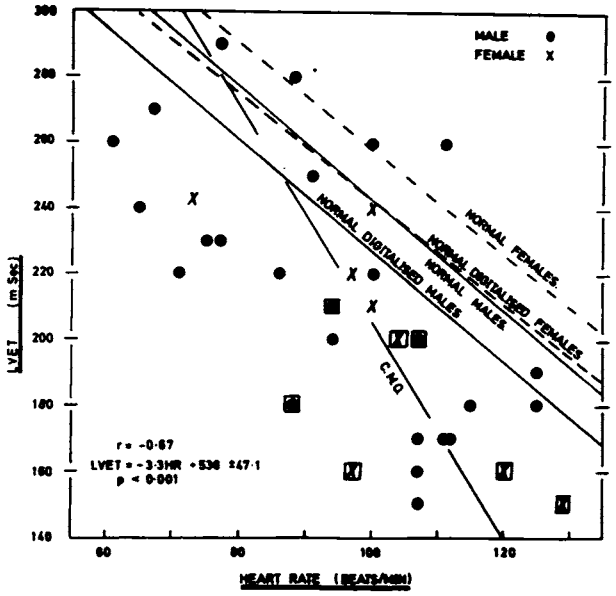

FIGURE 4. Left ventricular ejection time in CMO. LVET is heart rate dependent and its relationship to heart is shown by normal regression lines of Weissler et al[4,30] making allowance for sex difference and for state of digitalis therapy. Graph shows that patients with CMO have short LVET. Patients with additional mitral incompetence are shown within squares. These patients always had short LVET.

and cardiac index is shown in Table 3 and Figures 6 and 7. It was slightly higher in patients with mitral incompetence, a consequence of a shorter LVET (Table 2).

Total electromechanical systole (Q-A_2) was normal or nearly normal in all patients. The small scatter around the normal range in relation to heart rate is shown in Figure 8. This has been shown before, but its mechanism and meaning await elucidation. Q-A_2 was shorter in patients with additional mitral incompetence (Table 2).

The statistical analysis of the results is summarized in Table 3. PEP and △PEP reflect LVdp/dt

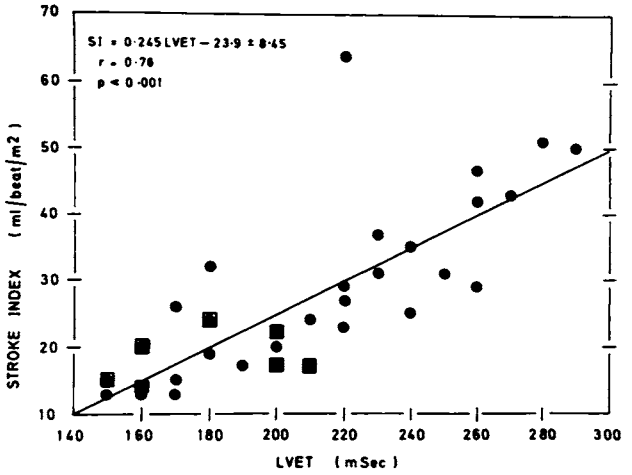

FIGURE 5. Simple linear relationship between LVET and stroke index (SI). Patients with additional mitral incompetence cluster in lower lefthand corner of graph.

Table 3—*Correlation of Systolic Time Intervals and Hemodynamics*

	SI	CI	EF	LVdp/dt	LVEDP	HR
PEP	−0.46	−0.32	−0.38	−0.60	0.17	0.009
LVET	0.76	0.63	0.64	0.15	−0.68	−0.67
ICT	−0.47	−0.45	−0.34	−0.70	0.28	—
PEP/LVET	−0.76	−0.62	−0.62	−0.45	0.54	—
△PEP	−0.57	−0.36	−0.47	0.58	0.27	—
△LVET	0.54	0.64	0.40	0.17	0.52	—
Q-A_2	—	—	—	—	—	−0.65

but also correlate with stroke index, cardiac index and ejection fraction, which reflect poor left ventricular contractility. LVET and △LVET correlate with stroke index, cardiac index and ejection fraction, but are also related to LVEDP. The use of the ratio PEP/LVET does not significantly improve the correlation coefficients.

Multiple regression analyses were used to predict the hemodynamic aberrations from measurement of the time intervals. The results are shown in Table 4.

DISCUSSION

Bantu cardiomyopathy causes severe left ventricular dysfunction. Patients have generalized ventricular hypokinesis without evidence of regional myocardial dysfunction (asynergy). We have had an unusual opportunity to study consecutively a large group of patients with this disorder: only a limited number of patients with this degree of left ventricular dysfunction as their primary problem have been studied before.

The essential defect in primary myocardial disease is impaired left ventricular contractility with a reduction in the velocity of fiber shortening, although there may be important additional changes in the modulus of elasticity of the series and parallel elastic elements. The reduced velocity of shortening in-

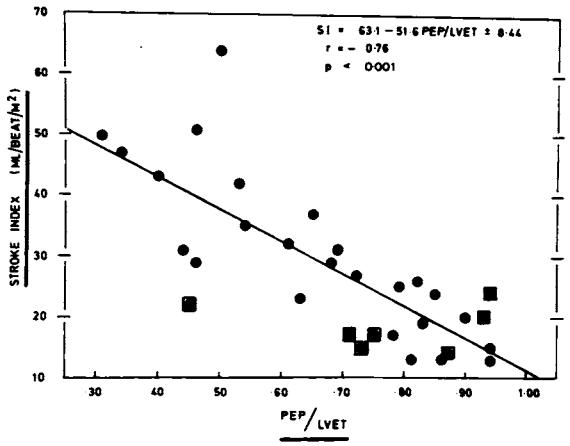

FIGURE 6. Simple linear relationship between PEP/LVET ratio and forward stroke index (SI). Patients with additional mitral incompetence are shown within squares and always had low SI.

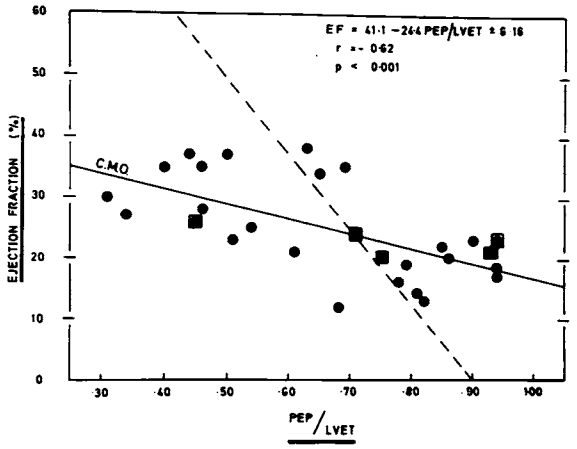

FIGURE 7. Simple linear relationship between PEP/LVET ratio and ejection fraction (EF). Regression line for patients with CMO is compared with heterogenous group of patients studied by Garrard et al.[7]

creases the duration of the time interval from the onset of left ventricular activation to mitral valve closure and also increases the isovolumic contraction time: the former is related to LVEDP and the latter to aortic diastolic pressure. Our results are in keeping with this hypothesis so that in patients with CMO, PEP and ICT are prolonged, and the degree of prolongation is greatest in patients with the most severe disease. Both parameters are closely related to LVdp/dt.

We have assumed that the electromechanical interval is constant in normal subjects and in patients with severe heart disease. Patients with cardiomyopathy usually have mild disturbances of intraventricular conduction: three had frank bundle branch block and 12 had hemiblock: moreover, the QRS duration in nearly all patients was prolonged to 70-100 msec. This could account in part for the prolongation of PEP.

ICT was readily measured in this study. It is more

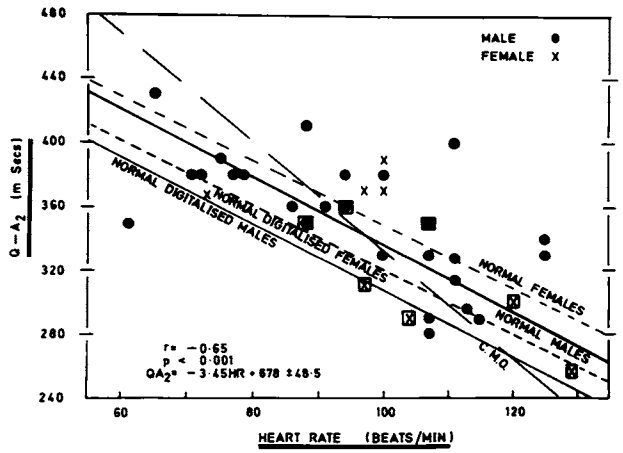

FIGURE 8. Relationship between Q-A_2 and heart rate in CMO. Values for normal digitalized and undigitalized subjects are taken from Weissler et al.[4,30]

Table 4—*Results of Measurement of Time Intervals for Determinations of Hemodynamic Aberrations*

		Multiple Regression Analyses
SI	=	7.53 − 0.136 (PEP − 1.5 LVET + 0.35 HR)
CI	=	−2.77 − 0.009 (0.3 PEP − 2 LVET − 2 HR)
LVEDP	=	84.09 − 0.01 (2.0 PEP + 23.4 LVET + 8.7 HR)
LVdp/dt	=	2078.5 − (7.17 PEP + 0.66 LVET + 1.39 HR)
EF	=	23.20 − 0.01 (5.5 PEP − 8.6 LVET + 9.9 HR)

Correlation Coefficients

	SI	CI	LVEDP	LVdp/dt	EF
PEP/LVET/HR	0.81	0.71	0.68	0.60	0.67

difficult to measure at the bedside. The time interval starts at the moment of mitral valve closure. The onset of the first heart sound is often difficult to define, ICT is of short duration and small errors in the measurement of the onset of the first heart sound may introduce a large error into the measurement. Others[6,8] have suggested that the onset of movement of the apex in systole should be taken as the start of this interval.

LVET is also determined by the rate of muscle fiber shortening and stroke volume: mean arterial pressure is normal in patients with Bantu CMO. Each factor operates in an opposite direction, the reduction in rate of fiber shortening will tend to prolong LVET, while the decrease in stroke volume will reduce it. LVET correlates closely with SI, CI and EF. Additional mitral incompetence further reduces LVET.

The correlations, as expected, are improved by multiple regression analyses, in keeping with the fact that several factors determine each time interval. In the same way, the use of two or more simple measurements improves the predictive value of noninvasive techniques. We believe that it is possible to predict the hemodynamic disturbance from the time intervals (Table 4).

We have observed that left ventricular ejection fraction appears to be an exquisitely sensitive index of myocardial dysfunction in power failure. Garrard et al[7] found a remarkable correlation between the PEP/LVET ratio and ejection fraction in a large group of normal subjects and a heterogenous group of patients with cardiac disease. Their regression line is superimposed on our data in Figure 7. Our regression equation is different and is weighted in favor of patients with severe myocardial dysfunction. It is possible that if Garrard et al[7] had studied a homogenous group or had included more patients with severe left ventricular dysfunction, they may have demonstrated a curvilinear relationship. It is also interesting that ejection fraction is more sensitive than the time intervals, particularly in patients with mild disease in whom there is only minor alteration in the PEP/LVET ratio, but a marked de-

crease in ejection fraction. Functional mitral incompetence modifies these findings, since the forward stroke volume falls. This reduces LVET and Q-A_2 and prolongs PEP/LVET, but PEP is unaltered. Measurement of LVET or PEP/LVET alone would overestimate the severity of the myocardial disease. Furthermore, patients with mitral incompetence seem to have more severe disease, but there is no significant difference in ejection fraction or LVEDP between the two groups (Table 1).

Our results are important in clinical practice, as it is important to assess the severity of the disease in patients with CMO and to follow their course and response to therapy by simple yet sensitive techniques. The time intervals and hemodynamic measurements correlate well with each other in primary myocardial disease as they do in normal subjects: alterations in SI, EF and LVdp/dt are reflected by the "external" indices in CMO as they are in other disorders. Cardiac catheterization provides valuable information but cannot be repeated at frequent intervals. The systolic time intervals are readily measured at the bedside: when several simple measurements are made and multiple regression analysis is used they are a useful and informative clinical tool.

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