Systolic Time Intervals in Mitral Incompetence

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Systolic Time Intervals in Mitral Incompetence*

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The systolic time intervals were measured in 17 patients with pure mitral incompetence (MI) in sinus rhythm. These were compared with hemodynamic and angiographic measurements of the severity of mitral regurgitation and the degree of left ventricular dysfunction. Pre-ejection phase (PEP), on an average, was normal in patients with MI, and the patients had normal left ventricular function. Left ventricular ejection time (LVET) was shortened: LVET was related to the forward stroke index ($r = +0.81$), and the abbreviation of LVET reflected the severity of mitral incompetence. Total electromechanical systole ($Q\text{-}S_2$) was shortened; this was due to the shortened LVET ($r = +0.95$). The ratio PEP/LVET reflected the left ventricular ejection fraction, but the ratio was increased in patients with severe mitral incompetence due to the shortening of LVET. In a second comparative group of patients with congestive cardiomyopathy (COCM) and MI there was a significant prolongation of PEP and a further reduction in forward stroke index and LVET. In these patients, $Q\text{-}S_2$ was normal and the PEP/LVET ratio was greatly increased.

The systolic time intervals are useful noninvasive measurements of left ventricular function.[1-6] Pre-ejection period (PEP) is an index of left ventricular celerity: it is related to LVdp/dt, but it is also influenced by preload, afterload and heart rate.[6,7] Left ventricular ejection time (LVET) is related to stroke index and the velocity of muscle fiber shortening: it also depends on heart rate and afterload. LVET is of predictive value in estimating forward stroke volume.[9,10] The ratio PEP/LVET is directly related to left ventricular ejection fraction.[11]

We have examined the systolic time intervals in 17 patients with mitral incompetence to find whether these measurements are useful to predict the severity of mitral incompetence and volume of regurgitant flow and the state of myocardial function.

The Patients

We selected for study 17 patients with pure mitral incompetence. Patients with important additional mitral stenosis or aortic valve disease were excluded. The study was confined to patients in sinus rhythm. Two patients had a congenital defect with prolapse of the posterior leaflet of the mitral valve, another patient had ruptured chordae tendineae. The other 14 patients had rheumatic mitral incompetence. All the patients with acquired heart disease were receiving digitalis therapy: we presume that they were fully digitalized.

The clinical and hemodynamic profile of the patients is given in Table 1. The group was comprised of young patients with severe mitral incompetence who were studied with a view to valve replacement; the valve was replaced in 12.

We compared these measurements with measurements made in another group of seven patients who had congestive cardiomyopathy with important mitral incompetence; these patients were reported in detail in a study of the systolic time intervals in congestive cardiomyopathy (COCM).[12]

Methods

Patients were assessed according to standard clinical criteria. Right and left heart catheterization was performed, using the midchest level as the zero reference for pressures. LVdp/dt was measured through a fluid-filled catheter

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Table 1—*Clinical and Hemodynamic Measurements*

Patient No.	Age, Yrs	Sex	Race	Disability[17] Grading	Etiology	SI	CI	LVEDP	Peak LVdp/dt	LVEF	PCWP	PCWP 'v' Wave	MPAP	Angio SI	Angio RVI	Angio RF	LV Ejection Rate
1	12	M	W	1	prolapsing posterior leaflet	48	4.6	10	1419	68	9	—	14	66.7	18.7	28	192
2	10	F	B	1	prolapsing posterior leaflet	33	4.2	12	2597	74	8	11	14	86.9	53.9	62	199
3	51	F	C	2b	rheumatic	56	4.9	12	2420	—	7	9	20	—	—	—	181
4	12	F	B	2b	rheumatic	55	4.7	12	—	73	20	32	35	103.5	48.5	47	196
5	17	F	W	2b	rheumatic	71	6.2	14	1210	—	17	24	25	—	—	—	282
6	5	F	B	2b	rheumatic	38	3.7	8	1359	46	13	20	21	45.1	7.1	16	190
7	16	F	B	2b	rheumatic	34	3.9	12	1570	58	28	51	34	84.3	50.3	60	155
8	4	F	B	2b	rheumatic	50	5.0	10	1147	—	13	19	22	—	—	—	244
9	10	F	B	2b	rheumatic	47	5.2	2	1570	—	33	—	42	—	—	—	224
10	57	M	W	3	ruptured chordae	48	3.3	16	1057	77	12	13	18	170.9	122.9	72	160
11	6	M	B	3	rheumatic	56	4.2	14	1268	70	9	30	43	108.5	52.5	48	224
12	10	M	B	3	rheumatic	26	3.1	7	1510	70	22	70	84	113.5	87.5	77	163
13	11	F	B	3	rheumatic	61	4.1	16	785	—	23	30	37	—	—	—	218
14	4	F	B	3	rheumatic	39	3.9	11	1100	57	23	45	35	65.5	26.3	40	187
15	13	F	As	3	rheumatic	25	3.2	18	1691	58	33	58	57	96.5	71.5	74	167
16	12	F	B	4	rheumatic	15	1.8	24	1380	62	45	85	70	127.5	112.5	88	94
17	27	F	B	4	rheumatic	12	1.5	23	—	72	—	80	63	88.2	75.8	86	74
					Mean	42	4.0	13	1472	65	20	38	37	88.1	60.8	58	185
					±S.D.	16	1.2	5	482	9	11	25	21	36.6	35.8	23	50
					Normal value	35±5	3.5±0.5	10±4		67±10	10±4		15±5	35±5	0	0	159±39[29]

Angio SI = total angiographic stroke index (ml/beat/M²); As = Asiatic; B = Bantu; CI = cardiac index (L/min/M²); C = colored; HR = heart rate (beats/min); LVdp/dt = 1st derivative of left ventricular pressure (mm Hg/sec); LVEDP = left ventricular end-diastolic pressure (mm Hg); LVEF = left ventricular ejection fraction (%); LV ejection rate = forward left ventricular ejection rate (ml/sec/M²); MPAP = mean pulmonary artery pressure (mm Hg); PCWP = pulmonary capillary wedge pressure (mm Hg); RF = regurgitant fraction (%); RVI = regurgitant volume (index) (ml/beat/M²); SI = stroke index (ml/beat/M²); W = white

manometer system (Statham P23 Db transducers) with care being taken to debubble the tubing and manometer so that the frequency response was flat to 20 Hz. Cardiac output was measured by the direct Fick method and normalized for body surface area. Left ventriculography was performed in the right anterior oblique view using 50 ml of meglumine diatrizoate (76 percent Urografin) at 600 pounds per square inch (psi) and ventricular volumes were calculated according to the uniplane technique of Greene et al[13] after allowing for magnification. Measurements were made only in technically perfect angiograms, which were not influenced by ventricular premature beats. Ejection fraction was then calculated in which

$$\text{ejection fraction (EF)} = \frac{\text{end-diastolic volume (EDV)—end-systolic volume (ESV)}}{\text{end-diastolic volume}} \times 100.$$

The regurgitant volume (index) was calculated by subtracting the forward stroke index measured by the direct Fick principle from the angiographic stroke index. Regurgitant fraction was calculated in which

$$\text{regurgitant fraction (RF)} = \frac{\text{regurgitant volume (index)}}{\text{total angiographic stroke index}} \times 100.$$

The time intervals of the cardiac cycle were measured at cardiac catheterization. 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 them with the hemodynamic measurements made at the same time. An electrocardiogram was compared with the simultaneous pressure recording in the left ventricle and the ascending aorta, using a paper speed of 100 mm/sec. 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. Preejection phase (PEP), LV ejection time (LVET) and Q-S_2 were measured (Fig 1), correcting the measurement of PEP for the delay in the fluid mechanical system. The result by this method of measurement is identical to the measurements obtained from external tracings. The forward left ventricular ejection rate was calculated in which

$$\text{LV ejection rate (ml/sec/M}^2) = \frac{\text{stroke index (ml/beat/M}^2)}{\text{LVET (msec)}} \times 10^3$$

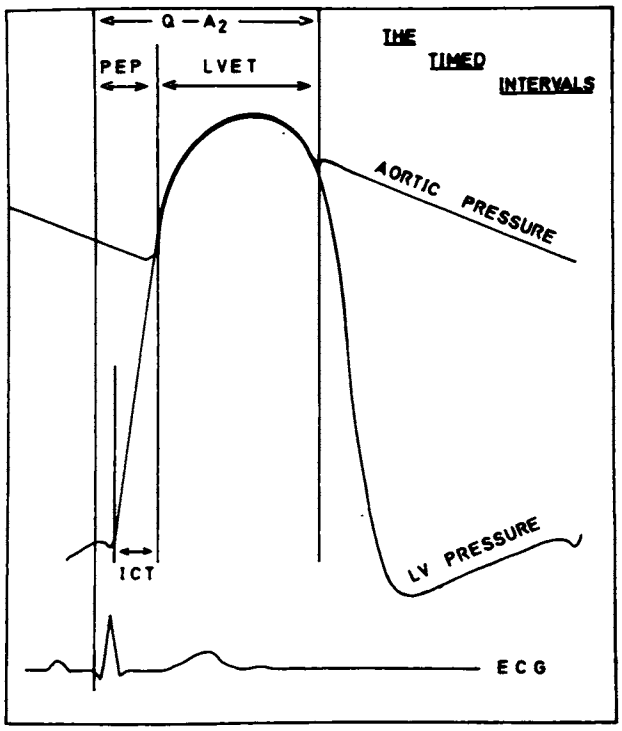

FIGURE 1. Method of measuring systolic time intervals. Aortic and left ventricular pressure pulses and electrocardiogram are shown. Timing of pressure pulses was corrected to allow for catheter manometer pulse transmission time delay. Preejection phase (PEP) is interval from onset of electrical systole (earliest q or R wave on ECG) to time of 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 (Q-S_2) is sum of PEP and LVET.

Table 2—*Time Interval Measurements*

Patient, No.	PEP	LVET	Q-S_2	PEP/LVET	HR	Δ PEP	Δ PEP_{dig}	Δ LVET	Δ $LVET_{dig}$	Δ Q-S_2	Δ Q-S_{2dig}
1	110	250	360	.44	88	+14.2	+14.2	−13.4	−13.4	−1.2	−1.2
2	50	166	216	.30	150	−23.0	−23.0	−12.0	−12.0	−33.0	−33.0
3	70	310	380	.23	86	−28.6	−13.6	+29.6	+44.6	+3.0	+33.0
4	100	280	380	.36	88	+2.2	+17.2	+2.8	+17.8	+7.0	+37.0
5	65	250	315	.26	85	−34.0	−19.0	−32.0	−17.0	−64.0	−34.0
6	100	200	300	.50	102	+7.8	+22.8	−54.8	−39.8	−45.0	−16.0
7	100	220	320	.45	113	+12.2	+27.2	−17.2	−2.2	−3.0	+27.0
8	60	205	265	.29	110	−29.0	−14.0	−37.0	−22.0	−64.0	−34.0
9	110	210	320	.52	105	+19.0	+34.0	−40.0	−25.0	−19.0	+11.0
10	85	300	385	.28	68	−18.8	−3.8	+2.6	+17.6	−18.2	+11.8
11	70	250	330	.28	60	−37.0	−22.0	−61.0	−46.0	−90.0	−60.0
12	80	160	240	.50	120	−3.0	+12.0	−49.0	−34.0	−54.0	−24.0
13	110	280	390	.39	80	+11.0	+26.0	+3.0	+18.0	−12.0	+42.0
14	65	210	275	.31	125	−18.0	−3.0	−8.0	+7.0	−24.0	+6.0
15	90	150	240	.60	133	+10.2	+25.2	−55.2	−40.2	−43.0	−13.0
16	80	160	240	.50	125	−3.0	+12.0	−58.0	−43.0	−59.0	−29.0
17	93	168	261	.56	140	+16.0	+31.0	−26.0	−11.0	−8.0	+22.0
Mean	85	222	307	.40	105	−6.0	+7.2	−25.0	−11.8	−29.6	−3.2
± S.D.	19	52	58	.12	26	19.5	19.9	26.4	26.0	29.9	30.0
Normal value				.35 ± 0.4		0 ± 12.0	0 ± 12.0	0 ± 10.0	0 ± 10.0	0 ± 14.0	0 ± 14.0

PEP = pre-ejection phase (Msec); LVET = left ventricular ejection time (Msec); Q-S_2 = total electromechanical systole (Msec); Δ Value = deviation of heart rate-corrected time interval measurement from normal regression (Msec)[2]; Δ $Value_{dig}$ = correction made for digitalis (Msec)[16]

PEP, LVET and Q-S_2 are heart-rate dependent. We calculated ΔPEP, ΔLVET and ΔQ-S_2 from the regression equations of Weissler, Harris and Schoenfeld, in which ΔPEP, ΔLVET and ΔQ-S_2 are the deviations from the normal value for a given heart rate, although the normal regression data were limited to the range of heart rate from 50-110 beats per minute. We extended the relationship to higher heart rates in six patients with mitral incompetence. ΔPEP, ΔLVET and ΔQ-S_2 were again calculated in the patients on digitalis therapy, using the revised regression of Weissler et al[14-16] and Schoenfeld[16] for digitalized normal subjects: these indices were called ΔPEP_{dig}, $\Delta LVET_{dig}$ and $\Delta Q\text{-}S_{2dig}$. The mean values of ΔPEP_{dig}, $\Delta LVET_{dig}$ and $\Delta Q\text{-}S_{2\ dig}$ were calculated: the mean values include two patients not receiving digitalis. In these two patients, the Δ values were derived from the regression for undigitalized normal subjects.

The measurements PEP, LVET, ΔPEP, ΔPEP_{dig}, ΔLVET, $\Delta LVET_{dig}$, PEP/LVET, Q-S_2, ΔQ-S_2 and $\Delta Q\text{-}S_{2\ dig}$ were then compared with the underlying hemodynamic and angiographic measurements. Their relationships were analyzed by standard statistical methods, using a Wang 700 programmable calculator.

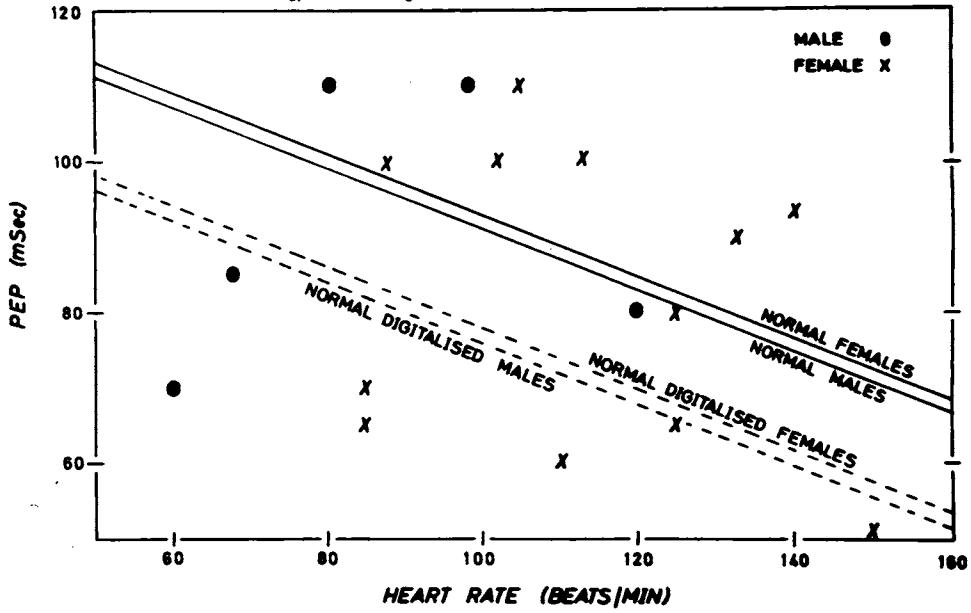

FIGURE 2. Relationship between pre-ejection phase (PEP) and heart rate (HR) in patients with mitral incompetence. Regression lines of Weissler,[2] Harris and Schoenfeld[16] for undigitalized normal subjects are shown as two solid lines; relationship for normal digitalized subjects is shown as dotted lines. PEP was normal, shortened or prolonged in mitral incompetence.

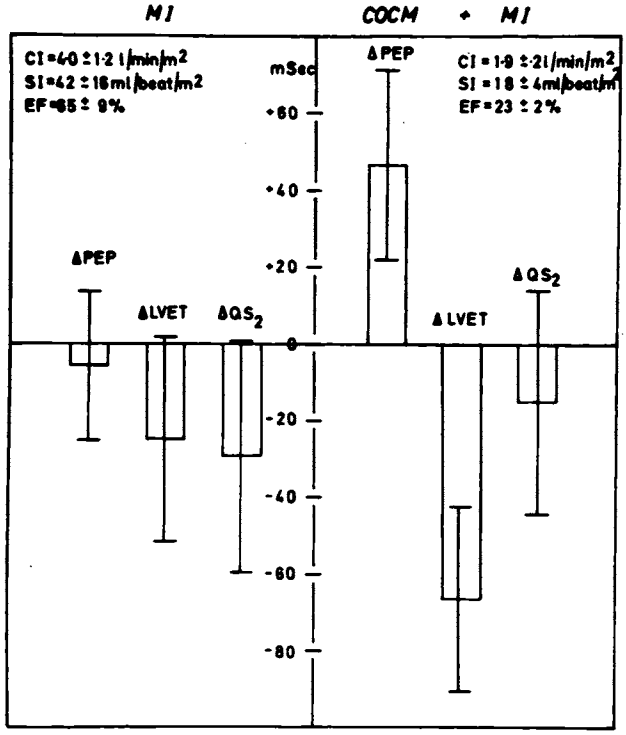

FIGURE 3(a). Systolic time intervals in 17 patients with mitral incompetence (MI) and in 7 patients with congestive cardiomyopathy (COCM) and additional MI. Mean deviations from normal undigitalized subjects of PEP, LVET and Q-S_2 are shown. (CI) = cardiac index, (SI) = stroke index, (EF) = left ventricular ejection fraction. (I) = standard deviation.

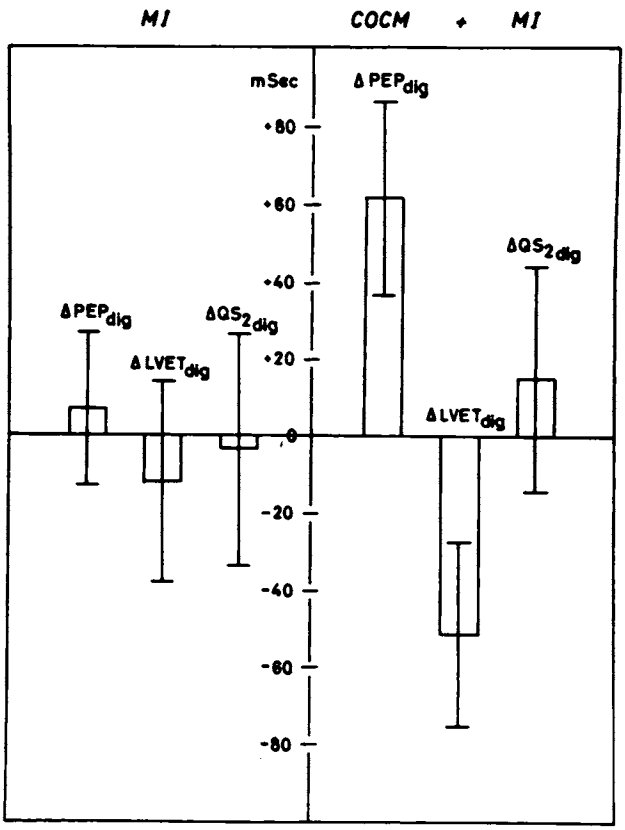

FIGURE 3(b). Systolic time intervals corrected for digitalis therapy. In digitalized patients Δ values were derived from regression of Weissler and Schoenfeld[16] for normal digitalized subjects. Two patients with mitral incompetence who were not receiving digitalis therapy were compared with normal undigitalized subjects.

RESULTS

The hemodynamic, quantitative angiographic and systolic time interval measurements are given in Tables 1, 2. The patients are classified according to their clinical disability at the time of investigation.[17] All of the patients with rheumatic mitral incompetence had been in congestive cardiac failure prior to management with intensive medical therapy. The disability (shortness of breath) correlated with the degree of mitral incompetence (regurgitant volume and regurgitant fraction) and left atrial and pulmonary arterial pressure, but it was not related to left ventricular ejection fraction, which was normal or only slightly decreased. Despite the severity of the clinical symptoms (half of the patients were in Class 3 or 4), the ejection fraction was within the range of normal. The detailed statistical analyses of the relationship between the time interval and hemodynamic measurements are summarized in Table 3.

Figure 2 shows the relationship between PEP and heart rate (HR). There was no consistent deviation of PEP from normal: PEP was prolonged in a few and shortened in some of the patients (mean $\Delta PEP_{MI} = -6.0 \pm 19.5$ msec, mean $\Delta PEP_{MI\text{-}dig} = +7.2 \pm 19.9$ msec), so that the average values were normal. An obvious cause for the aberration in individual patients could not be found. PEP was much shorter in this group of patients than in the comparable group of patients with mitral regurgitation due to conges-

Table 3—*Statistical Analyses—Correlation Coefficients

	SI	CI	Peak LVdp/dt	LVEF	RF	PCWP 'v' Wave	HR	LVET
PEP	—	—	−.34	—	−.26	—	−.22	—
Δ PEP	−.44	−.38	−.12	−.34	—	—	—	—
Δ PEP_{dig}	−.42	−.40	−.24	−.41	—	—	—	—
LVET	+.81	+.52	—	+.33	−.42	−.68	−.86	—
Δ LVET	+.40	+.28	—	+.44	—	—	—	—
Δ $LVET_{dig}$	+.41	+.25	—	+.39	—	−.43	—	—
PEP/LVET	−.70	—	—	−.42	—	—	—	—
Q-S_2	—	—	—	—	—	—	−.85	+.95

*Same abbreviations as Table 1, 2

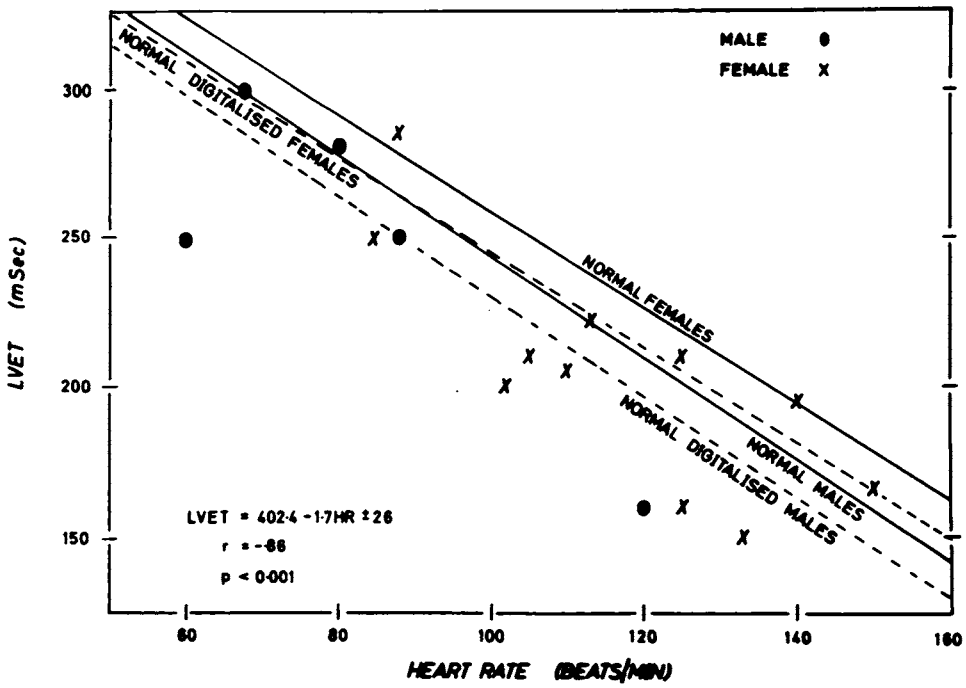

FIGURE 4. Relationship between left ventricular ejection time (LVET) and heart rate. Regression lines of Weissler,[2] Harris and Schoenfeld[16] for normal subjects are shown as solid lines and for digitalized subjects as dotted lines. LVET was abbreviated.

tive cardiomyopathy (COCM) (mean ΔPEP_{COCM} = +46.7±24.9 msec, mean $\Delta PEP_{COCM\text{-}dig}$ = +61.7± 24.9 msec, $p<0.001$) (Table 4, Fig 3). PEP and ΔPEP were not useful in the prediction of LVdp/dt or the volume of mitral regurgitant flow, ΔPEP and ΔPEP_{dig} bore some relation to SI, CI and LVET, but this was not significant (Table 3).

LVET was shortened in patients with mitral incompetence and the relationship to HR is shown in Figure 4 (mean $\Delta LVET_{MI}$ = −25.0±26.4 msec, mean $\Delta LVET_{MI\text{-}dig}$ = −11.8±26.0 msec). The duration of LVET was related to the forward stroke index (Fig 5). Patients with a short LVET had a rapid heart rate, low forward stroke index, cardiac index and LV forward ejection rate, a large volume of mitral regurgitant flow, a high regurgitant fraction and a tall 'v' wave in the left atrium (Fig 6). These results showed that LVET was determined by the rate and amount of blood which was ejected into the aorta and if this fell, LVET was shortened. It was also determined by digitalis therapy. LVET was not related to angiographic LV ejection fraction. Patients with COCM and MI had an even shorter LVET ($\Delta LVET_{COCM}$ = −66.6±23.9 msec, $\Delta LVET_{COCM\text{-}dig}$ = −51.6±23.9 msec, $p<0.01$) (Table 4, Fig 3).

The ratio PEP/LVET was not always related to LV ejection fraction, although the patients' findings

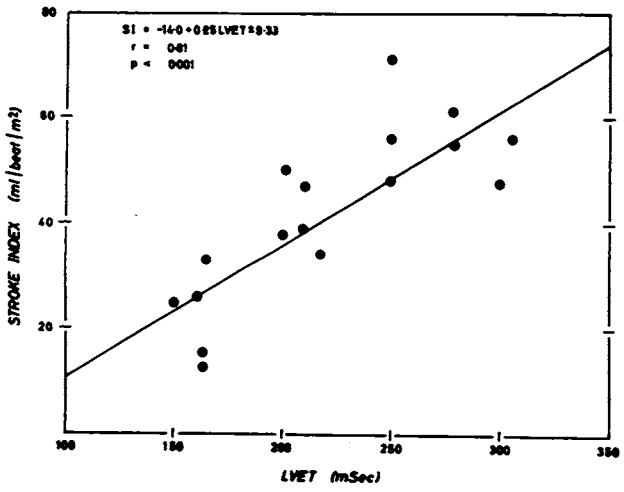

FIGURE 5. Linear relationship between LVET and forward left ventricular stroke index.

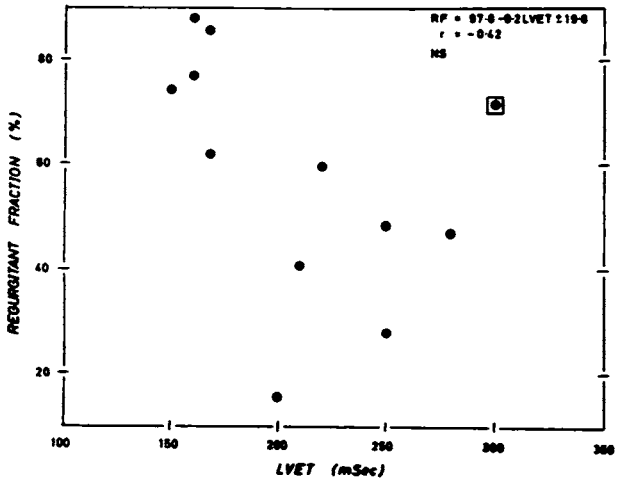

FIGURE 6. Relationship between LVET and regurgitant fraction (RF). There was negative relationship between these measurements, but this was not significant. One patient with ruptured chordae (within square) disturbed relationship.

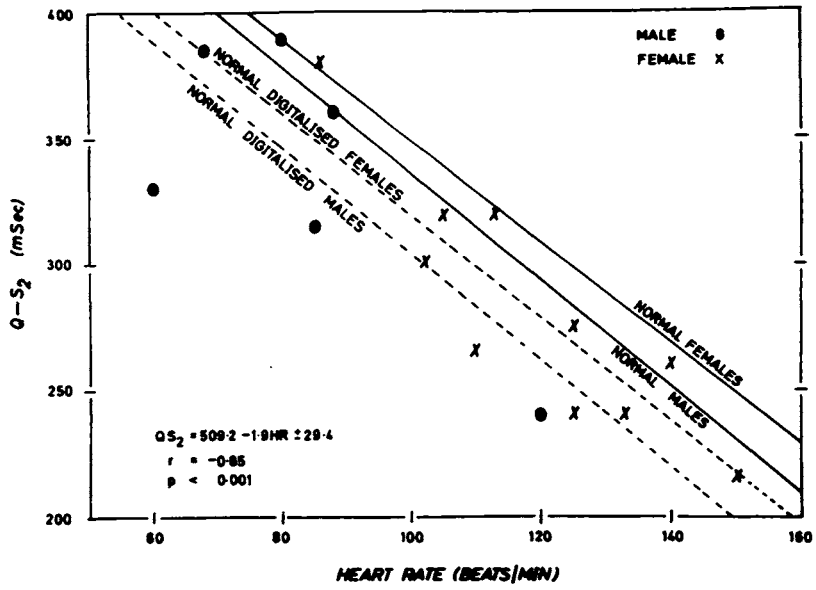

FIGURE 7. Relationship between Q-S_2 and heart rate. Regression lines of Weissler,[2] Harris and Schoenfeld[16] for normal subjects are shown as solid lines; for digitalized subjects as dotted lines. Q-S_2 is normal in digitalized patients with mitral incompetence.

clustered around the relationship established by Garrard, et al[11]: in four patients the ratio was increased for the calculated ejection fraction. Because of the normal ejection fraction in nearly all the patients and the small range of values, the degree of correlation was meaningless. The increased PEP/LVET ratio in four patients was a consequence of severe mitral incompetence, with an abbreviated LVET. The ratio was much higher in patients with a myopathic ventricle (Table 4).

Q-S_2 was shortened in some patients (Fig 7): this was a consequence of the abbreviation of LVET due to mitral incompetence and the effect of digitalis. The mean ΔQ-$S_{2\ MI}$ was -29.6 ± 29.9 msec (mean ΔQ-$S_{2\ MI\text{-}dig}$ = -3.2 ± 30.0 msec) compared with the mean ΔQ-$S_{2\ COCM}$ of -15.3 ± 29.2 msec (mean ΔQ-$S_{2\ COCM\text{-}dig}$ = $+14.7\pm29.2$ msec). The difference was not significant since PEP_{COCM} was prolonged (Table 4, Fig 3).

DISCUSSION

There are three important problems in mitral incompetence: (1) the assessment of the volume of regurgitation; (2) the compensatory mechanisms which occur in response to valvular incompetence; and (3) the quantitation of ventricular dysfunction.

Volume of Mitral Incompetence

The regurgitant volume depends on the area of the regurgitant orifice, the heart rate, systolic ejection period and the relationship between systemic and left atrial impedance: the left atrial impedance is a function of the severity of the lesion, the compliance of the left atrium and the position of the left atrial volume on its compliance curve.[18,19] Patients with severe mitral incompetence have a large left atrial 'v' wave and regurgitant fraction.

We measured the volume of mitral regurgitation by comparing the stroke volume of the LV measured by angiocardiography and the forward stroke volume measured by the direct Fick principle. These measurements were made sequentially, and the patients' steady state was disturbed by the delivery of a large volume of contrast medium into the left ventricle. It is possible that we overestimated the volume of mitral regurgitation or that interpatient comparisons are not valid. Nonetheless, the derived volume correlated with the clinical status of the patient, the height of the 'v' wave in the left atrium and the reduction in forward stroke index. The tachycardia associated with severe incompetence was noteworthy.

Nixon and Wagner[21] made the same measure-

Table 4—*Comparison Between Time Interval Measurements in Mitral Incompetence (MI) and Congestive Cardiomyopathy (COCM) and MI*

Diagnosis	Patients, No.	Mean Δ PEP, Msec	Mean Δ PEP_{dig}, Msec	Mean Δ LVET, Msec	Mean Δ $LVET_{dig}$, Msec	Mean Δ Q-S_2, Msec	Mean Δ Q-$S_{2\ dig}$, Msec	Mean PEP/LVET	Mean EF, %
Mitral incompetence	17	-6.0 ± 19.5	$+7.2\pm19.9$	-25.0 ± 26.4	-11.8 ± 26.0	-29.6 ± 29.9	-3.2 ± 30.0	.40±.12	65±9
Congestive cardiomyopathy + MI	7	$+46.7\pm24.9$	$+61.7\pm24.9$	-66.6 ± 23.9	-51.6 ± 23.9	-15.3 ± 29.2	$+14.7\pm29.2$	.77±.17	23±2
t		5.56		3.59		1.07		6.15	10.06
p		<0.001		<0.01		NS		<0.001	<0.001

Δ $value_{dig}$ = Correction made for digitalization in 15 of 17 patients with MI and in all 7 patients with COCM and MI

ments of LVET in patients with mitral incompetence who were in atrial fibrillation. They used the normal values of Katz and Feil[20] for the systolic time intervals and concluded that the LVET was normal or prolonged in some patients. If their measurements are compared with the normal values derived by Weissler et al,[2] LVET was shortened in all their patients.

The abbreviation of LVET was a good guide to the severity of mitral incompetence and is useful in the clinical assessment of the patient. LVET and the width of splitting of the second sound are easily measured at the bedside. These observations confirm previous clinical and experimental findings and justify the quantitative use of these measurements.[22-25]

Compensatory Mechanisms

In mitral incompetence there is a decrease in forward LV stroke volume, the total LV stroke output increases and there is dilatation and compensatory hypertrophy of the ventricle. Ejection fraction is normal. In experimental acute mitral incompetence, the forward stroke volume is ejected more rapidly, the maximal acceleration of flow increases, peak flow is greater and is achieved earlier during the ejection period.[26,27]

Ventricular Dysfunction

The changes in length, tension and velocity of shortening of the muscle fibers of the left ventricle may be due to acute rheumatic carditis, the mechanical effect of great ventricular dilatation (Laplace relationship) or longstanding disease with myocardial fibrosis. In these circumstances, the forward and regurgitant flow decrease, the LVEDP rises, LVdp/dt falls and the ejection fraction is low. However, measurement of the transition from normality to abnormality is vague and it is not known which parameter becomes abnormal in the earliest phase of ventricular dysfunction. Moreover, the influence of digitalis on these measurements may be important in patients with marginal dysfunction.

LVdp/dt falls in the presence of poor contractility, but its meaning in mitral incompetence is uncertain because true isovolumic systole does not occur. Although the volume of regurgitation in early systole may be insignificant, the measurement of LVdp/dt does not reflect the true velocity of muscle fiber shortening.

Ejection fraction falls and reflects an abnormality of the length-tension relationship in patients with severe left ventricular dysfunction who do not have valvular incompetence.[28] The same relationship probably exists in patients with mitral incompetence. In our patients, ejection fraction was normal or slightly decreased: this suggests that ventricular function or changes in length under these loading conditions was normal. We elected to study a group of young patients with severe mitral incompetence in sinus rhythm: it is likely that they had a severe mechanical abnormality and good myocardial function.

Time Interval Measurements

PEP, LVET and PEP/LVET are a function of the velocity of fiber shortening. Since ventricular function, as measured by LVdp/dt and the ejection fraction, was normal or normalized under the influence of digitalis, PEP and the ratio PEP/LVET were normal in most patients. These measurements contrast with similar measurements made in the other group of patients with congestive cardiomyopathy in whom additional mitral incompetence was due to ventricular dilatation and papillary muscle inadequacy. In these patients the duration of PEP was prolonged and LVET further shortened. LVET reflects forward stroke index: both mitral incompetence and myocardial dysfunction reduce stroke index and LVET.

Four important observations have emerged from this study. PEP, on an average, is normal in mitral incompetence. LVET is shortened and is a good guide to the volume of regurgitant flow. It is necessary to interpret the ratio PEP/LVET with caution: it is a good guide to ejection fraction but when LVET is reduced in the presence of severe mitral incompetence the ratio may be high despite normal ventricular function. In mitral incompetence and myocardial failure, PEP is prolonged and there is additional shortening of LVET, with a further increase in the ratio PEP/LVET.

References

1 Wallace AG, Mitchell JH, Skinner NS, et al: Duration of the phases of left ventricular systole. Circ Res 12:611, 1963

2 Weissler AM, Harris WS, Schoenfeld CD: Systolic time intervals in heart failure in man. Circulation 37:149, 1968

3 Weissler AM, Harris WS, Schoenfeld CD: Bedside technics for the evaluation of ventricular function in man. Am J Cardiol 23:577, 1969

4 Kumar S, Spodick DH: Study of the mechanical events of the left ventricle by atraumatic techniques: Comparison of methods of measurement and their significance. Am Heart J 80:401, 1970

5 Weissler AM, Garrard CL Jr: Systolic time intervals in cardiac disease (1). Mod Concepts Cardiovasc Dis 40:1, 1971

6 Weissler AM, Garrard CL Jr: Systolic time intervals in

cardiac disease (II). Mod Concepts Cardiovasc Dis 40:5, 1971
7 Metzger CC, Chough CB, Kroetz FW, et al: True isovolumic contraction time. Its correlation with two external indexes of ventricular performance. Am J Cardiol 25:434, 1970
8 Talley RC, Meyer JF, McNay JL: Evaluation of the preejection period as an estimate of myocardial contractility in dogs. Am J Cardiol 27:384, 1971
9 Braunwald E, Sarnoff SJ, Stainsby WN: Determinants of duration and mean rate of ventricular ejection. Circ Res 6:319, 1958
10 Weissler AM, Peeler RG, Roehll WH: Relationships between left ventricular ejection time, stroke volume, and heart rate in normal individuals and patients with cardiovascular disease. Am Heart J 62:367, 1961
11 Garrard CL Jr, Weissler AM, Dodge HT: Relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. Circulation 42:455, 1970
12 Lewis BS, Armstrong TG, Everson RC, et al: Presdictive value of the systolic time intervals in primary myocardial disease. Chest, in press
13 Greene DG, Carlisle R, Grant C, et al: Estimation of left ventricular volume by one-plane cineangiography. Circulation 35:61, 1967
14 Weissler AM, Gamel WG, Grode HE, et al: The effect of digitalis on ventricular ejection in normal human subjects. Circulation 29:721, 1964
15 Weissler AM, Kamen AR, Bornstein RS, et al: The effect of deslanoside on the duration of the phases of ventricular systole in man. Am J Cardiol 15:153, 1965
16 Weissler AM, Schoenfeld CD: Effect of digitalis on systolic time intervals in heart failure. Am J Med Sci 259:4, 1970
17 NY Heart Assoc: Disease of the Heart and Blood Vessels (ed 6) New York, Little Brown & Co, 1964, p 110
18 Rodbard S, Williams F: The dynamics of mitral insufficiency. Am Heart J 48:521, 1954
19 Urschel CW, Covell JW, Sonnenblick EH: Myocardial mechanics in aortic and mitral valvular regurgitation: The concept of instantaneous impedance as a determinant of the performance of the intact heart. J Clin Invest 47:867, 1968
20 Katz LN, Feil HS: Clinical observations on the dynamics of ventricular systole. I. Auricular fibrillation. Arch Intern Med 32:672, 1923
21 Nixon PGF, Wagner GR: The duration of left ventricular systole in mitral incompetence. Br Heart J 24:464, 1962
22 Brigden W, Leatham A: Mitral incompetence. Br Heart J 15:55, 1953
23 Perloff JK, Harvey WP: Auscultatory and phonocardiographic manifestations of pure mitral regurgitation. Progr Cardiovasc Dis 5:172, 1962-1963
24 Moskowitz RL, Wechsler BM: Left ventricular ejection time in aortic and mitral valve disease. Am J Cardiol 15:809, 1965
25 Talano JV, Nagel MR, de Leon AC Jr: Left ventricular performance in acute severe and chronic mitral regurgitation. Circulation (Suppl 2) 44:232, 1971
26 Braunwald E. Welch GH, Sarnoff SJ: Hemodynamic effects of quantitatively varied experimental mitral regurgitation. Circ Res 5:539, 1957
27 Elkins RC, Morrow AG, Vasko JS, et al: The effects of mitral regurgitation on the pattern of instantaneous aortic blood flow. Circulation 36:45, 1967
28 Chatterjee K, Sacoor M, Sutton GC, et al: Assessment of left ventricular function by single plane cineangiographic volume analysis. Br Heart J 33:565, 1971
29 Levine HJ, Neill WA, Wagman RJ, et al: The effect of exercise on mean left ventricular ejection rate in man. J Clin Invest 4:1050, 1962

To The Attention of Authors

Goethe (1749-1832) was by no means without business acumen. When he received a serious offer for an authorized Collected Edition of his works, he made exacting demands: two thousand *thalers* in gold, paid in advance. The publisher was a young man in Leipzig who had just founded a firm. His name was Georg Joachim Göschen, and he was to become the first great publisher of German classics. He was the only one who printed not only much but beautifully, and in grand style. Goethe was his first author of note, but the partnership was of short duration; Goethe soon grew dissatisfied and Göschen saw him go without much regret. For this first authorized edition of Germany's first poet, in eight small volumes, proved a striking failure. In addition to the ordinary edition, Göschen hopefully announced one on Dutch paper for connoisseurs and princely patrons. As a particularly subtle stroke, he reprinted his own edition in a cheap one of four volumes so as to be able to pounce upon the expected pirates. But no pirate showed his head, and this was the surest sign of the public's indifference. The cheap edition remained unsold, the ordinary one sold only slowly, and the printing of the de luxe edition never got beyond the first few volumes.

Friedenthal, R: Goethe—His Life and Times, Cleveland, World Publishing Co., 1965