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Systolic Time Intervals in Heart Failure in Man

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SUMMARY

The duration of the systolic time intervals in nondigitalized patients with heart failure was determined from simultaneous fast speed recordings of the electrocardiogram, phonocardiogram, and carotid arterial pulsation. These were compared with the systolic time intervals corrected for heart rate and sex in 211 normal subjects. The failing left ventricle is characterized by a prolongation in the systolic pre-ejection period and a diminution in the left ventricular ejection time while total electromechanical systole remains relatively unaltered. Both components of the pre-ejection period, the Q-1 interval and the isovolumic contraction time, were prolonged. These alterations in the phases of systole occur in the absence of a measurable change in ventricular depolarization time. The prolongation in the pre-ejection period is well correlated with the reduced stroke volume and cardiac output in heart failure and is independently augmented by high levels of arterial pressure. The abbreviation in left ventricular ejection time is also correlated significantly with the stroke volume and cardiac output. It is postulated that a defect in the mechanical performance of the heart is responsible for the abnormal systolic time intervals in human heart failure.

Additional Indexing Words:

Left ventricular failure — Electrocardiogram — Phonocardiogram
Systolic ejection period — Isovolumic contraction time — Stroke volume
Cardiac index — Peripheral resistance

THE POTENTIAL USEFULNESS of the systolic time intervals as measures of ventricular performance in man was first recognized almost a century ago. Garrod[1] in 1874 described the inverse relationship between heart rate and the ejection phase of left ventricular systole. Employing sphygmographic recordings of the arterial pulse, Bowen[2] described the effect of exercise on the systolic ejection period and Lombard and Cope[3] demonstrated the influence of posture and sex on this phase of systole. The contemporary use of simultaneous photographic recordings of the electrocardiogram, the heart

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sounds, and the central arterial pulse to measure the systolic phases of the cardiac cycle was introduced by Katz and Feil.[4]

Studies in recent decades on alterations in cardiac performance in human heart failure have focused largely on measures of flow, pressure, and cardiac chamber volume while changes in the systolic intervals have received relatively little attention. Blumberger[5] and Jezek[6] reported that patients with left ventricular failure exhibited prolongation of the pre-ejection phase and abbreviation of the ejection period of systole. In an attempt to determine whether these abnormalities in the systolic time intervals might offer a quantitative estimate of cardiac performance in heart failure, the present investigation of the relationship between hemodynamic alterations and the duration of the phases of ventricular systole was initiated.

Method

The duration of the phases of left ventricular systole was measured from simultaneous recordings of the electrocardiogram, the phonocardiogram, and the carotid arterial pulse tracing employing a multichannel photographic system (Electronics for Medicine DR-8). A chest pneumogram was recorded as well. The recordings were obtained at a paper speed of 100 mm/sec (fig. 1). The electrocardiographic lead most clearly demonstrating the onset of ventricular depolarization (usually lead II or a precordial lead) was employed. A microphone (Peiker) was placed over the upper part of the precordium in a position optimal for recording the initial high frequency vibrations of the first and second heart sounds. Two microphones were sometimes necessary to define the initial vibrations of both sounds. Observations on inspiratory splitting of the second heart sound and the relationship of the carotid incisura to the vibrations of the second sound were used to confirm the aortic component of the second sound. The carotid arterial pulsation was recorded with a funnel-shaped pick-up attached by polyethylene tubing (length, 8 cm; internal diameter, 4 mm) to a Statham P23Db strain gauge. The system was air-filled and was amplified to maximum gain. The funnel was placed firmly over the carotid artery with the gauge vented to air. The vent was then closed manually to record the pulse.

The following phases of the cardiac cycle were measured directly: (1) The total electromechanical systolic interval (QS_2) was measured from the onset of the QRS complex to the first high frequency vibrations of the aortic component of the second heart sound; (2) the left ventricular ejection time (LVET) was measured from the beginning upstroke to the trough of the incisura of the carotid arterial pulse tracing; and (3) the interval between the first and second heart sounds (S_1S_2) was measured from the onset of the first heart sound to the beginning of the aortic component of the second heart sound. Only recordings clearly demonstrating the beginning of the upstroke and the trough of the incisura were employed for measurement of the left ventricular ejection time. The S_1S_2 interval was measured only if the initial vibrations of the first and second heart sounds were clearly defined.

The following intervals were calculated from the above measurements: (1) the pre-ejection

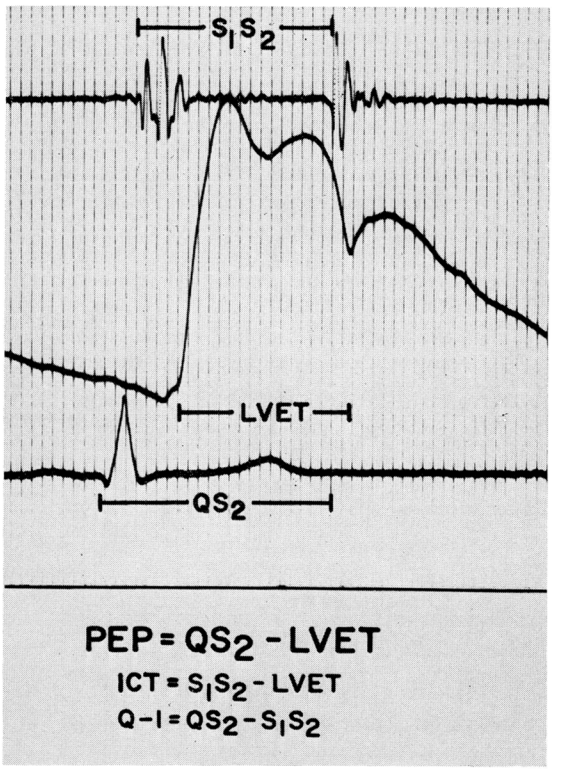

Figure 1

Simultaneous recording of the heart sounds, the carotid arterial pulse tracing, and the electrocardiogram in a normal subject (paper speed, 100 mm/sec; time markers, 0.02 sec). QS_2 = total electromechanical systole; S_1S_2 = heart sounds interval; LVET = left ventricular ejection time; PEP = pre-ejection period; Q-I = interval from onset of QRS to first heart sound; ICT = isovolumic contraction time.

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period (PEP), derived by subtracting the left ventricular ejection time from the QS_2 interval, (2) the interval from beginning depolarization to the first heart sound (Q-1), derived by subtracting S_1S_2 from QS_2, and (3) the isovolumic contraction time (ICT), derived by subtracting LVET from S_1S_2. The QRS duration was measured directly. All intervals were calculated from the mean of measurements made on 20 to 30 consecutive beats, each read to the nearest 5 msec. Care was taken to begin and end a series of consecutive readings with the same phase of the respiratory cycle. Heart rate (HR) was calculated from the relationship 60/average R-R interval. Three sets of determinations were averaged for each final reading.

These studies were performed on a normal group of 121 men and 90 women (age range, 19 to 65 years) and on a group of 27 patients with clinically conspicuous heart failure. The patients with heart failure had obvious cardiomegaly on chest roentgenogram and conspicuous dyspnea and edema. All patients were in functional class III or IV of the New York Heart Association classification. The heart failure was due to arteriosclerotic heart disease (ASHD) in 10 patients, hypertensive cardiovascular disease (HCVD) in 12 patients, and primary myocardial disease (PMD) in five patients. Because of the diurnal variation in the systolic intervals,[7] all observations were made between 8:00 and 10:00 a.m. The subjects were supine and fasting. All medication was stopped 48 hours before the hemodynamic observations. The patients with hypertension had received no antihypertensive therapy. Only five patients had received digitalis therapy previously, and none had received digitalis for 4 weeks prior to the study. All patients had a QRS interval of 0.10 sec or less and were in sinus rhythm at the time of the study.

Hemodynamic observations were made and correlated with the systolic time intervals in 19 of the patients. Cardiac output was determined by the indicator-dilution technique employing central injection of indocyanine-green dye and continuous sampling from the brachial artery. The indicator injection was accomplished in 15 patients through a polyethylene catheter (PE50), the tip of which was inserted through a no. 17 thin-walled needle into an antecubital vein and advanced to the right ventricle while pressure was monitored. The catheter tip was then withdrawn until a right atrial pressure configuration was seen and injections were made at this site. In four patients the right ventricle could not be entered and the injections were made at a site where the venous pressure showed accentuated respiratory variation (central venous site). Brachial arterial pressure, mean right atrial pressure (RAm), and mean central venous pressure (CVPm) were recorded with a Statham P23Db strain gauge positioned on a horizontal plane 5 cm below the sternal angle. Mean arterial pressure (MAP) was determined electronically. Total peripheral resistance (TPR) in dynes-sec cm^{-5} was calculated from the equation, $TPR = (MAP-RAm \text{ [or CVPm]}) \times 1{,}332/CO$, where CO is cardiac output in ml/sec and 1,332 is the conversion factor of pressure to dynes/cm.[2] All recordings of hemodynamic data and systolic time intervals were obtained serially and in triplicate.

Regression equations relating heart rate and the systolic time intervals in normal individuals were calculated with a programmed computer (IBM 7094). The deviations from the normal in the QS_2, LVET, PEP, and Q-1 intervals among the patients were calculated as the difference between the observed interval and those predicted from the normal regression line for heart rate and sex. These deviations could be calculated from the regression equations, as the difference between the observed and predicted regression values for the heart rate, or from the plotted regression lines. The ICT intervals in patients with heart failure were compared to the normal mean value for males and females since this interval followed no significant regression with respect to heart rate. Statistical analyses were performed according to Snedecor.[8]

Results

Systolic Time Intervals in Normal Individuals

The relationships in normal individuals between heart rate and the duration of the phases of left ventricular systole are summarized in table 1. The duration of electromechanical systole (QS_2), the left ventricular ejection time (LVET), and the pre-ejection period (PEP) were related inversely and linearly to heart rate. The diminution in QS_2 with increasing heart rate reflected a summation of a major negative slope of the LVET and a lesser negative slope of the PEP with respect to heart rate. The slopes of the regression equations relating heart rate and the QS_2, LVET, and PEP did not vary with sex. However, the QS_2 relative to heart rate was longer by an average of 11 msec ($P < 0.01$) in females than males. This prolongation in QS_2 was accounted for by the greater duration of the LVET relative to heart rate among the females. The inverse relationship of PEP to heart rate reflected largely a diminution of

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Table 1

*Systolic Time Intervals in Normal Individuals: Regression Data**

Systolic interval	Sex	Regression equation	SD
QS_2	M	$QS_2 = -0.0021\ HR + 0.546$	0.014
	F	$QS_2 = -0.0020\ HR + 0.549$	0.014
PEP	M	$PEP = -0.0004\ HR + 0.131$	0.013
	F	$PEP = -0.0004\ HR + 0.133$	0.011
LVET	M	$LVET = -0.0017\ HR + 0.413$	0.010
	F	$LVET = -0.0016\ HR + 0.418$	0.010
S_1S_2	M	$S_1S_2 = -0.0018\ HR + 0.456$	0.015
	F	$S_1S_2 = -0.0016\ HR + 0.461$	0.012
Q-1	M	$Q\text{-}1 = -0.0004\ HR + 0.090$	0.011
	F	$Q\text{-}1 = -0.0003\ HR + 0.089$	0.009
ICT	M	$ICT = 0.038$	0.010
	F	$ICT = 0.039$	0.009

*Data derived from observations on 121 male and 90 female subjects. Recordings of systolic intervals were made between 8 and 10 a.m. with subjects supine and fasting. All intervals expressed in seconds. Regression coefficients for QS_2, PEP, LVET, S_1S_2, and Q-1 are significant to $P < 0.005$.

Abbreviations: SD = sample standard deviation from regression in seconds; QS_2 = total electromechanical systole; PEP = pre-ejection period; LVET = left ventricular ejection time; S_1S_2 = interval between first and second heart sounds; Q-1 = interval between onset of ventricular depolarization and first heart sound; ICT = calculated isovolumic contraction time; HR = heart rate.

the Q-1, while the ICT remained relatively constant, with increasing heart rate. The duration of the PEP, Q-1, or ICT did not vary significantly with sex. The mean QRS duration in the normal female group, 0.078 sec (SD ± 0.010), was slightly less than that of the males, 0.085 sec (SD ± 0.011).

Systolic Time Intervals in Heart Failure

The systolic intervals in the patients with heart failure are presented in table 2. Hemodynamic observations are summarized in table 3. The systolic time intervals in heart failure are compared to the normal regression lines in figures 2 to 4. For the purpose of graphic presentation of the data, the regression slopes of the male group of −0.0021 for QS_2, −0.0017 for LVET, and −0.0004 for the PEP are shown. The vertical axes are

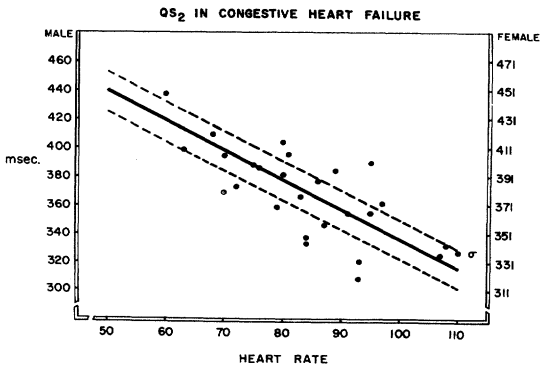

Figure 2

The duration of electromechanical systole (QS_2) in 27 patients with congestive heart failure (•) compared to the normal regression line (± 1 SD) for heart rate.

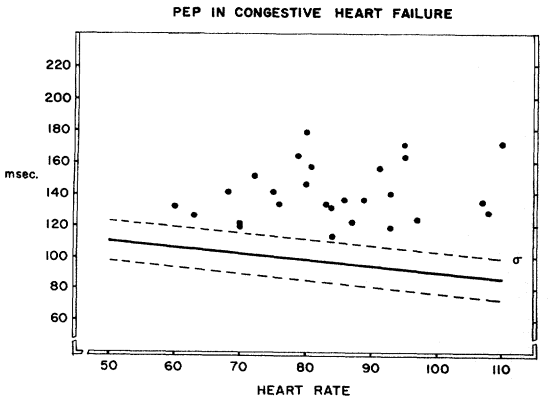

Figure 3

The duration of the pre-ejection period (PEP) in 27 patients with congestive heart failure (•) compared to the normal regression line (± 1 SD) for heart rate.

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Table 2

Systolic Time Intervals in Twenty-seven Patients with Congestive Heart Failure

Patient	Age	Sex	Dx	HR (beats/min)	QRS (msec)	QS_2 (msec)	PEP (msec)	Q-1 (msec)	ICT (msec)	S_1S_2 (msec)	LVET (msec)
R.B.	64	M	ASHD	75	95	388	142	—	—	—	246
S.H.	44	M	ASHD	110	60	327	171	—	—	—	156
E.H.	59	F	ASHD	89	90	395	136	65	71	330	259
F.B.	62	M	ASHD	76	80	386	133	75	58	311	253
R.K.	75	M	ASHD	70	80	395	121	83	38	312	274
A.H.	70	F	ASHD	70	78	380	119	72	47	308	261
J.P.	69	M	ASHD	83	95	366	133	91	42	275	233
T.P.	49	M	ASHD	97	70	362	124	76	48	286	238
W.W.	61	M	ASHD	84	80	333	113	82	31	251	220
H.M.	82	M	ASHD	84	80	337	131	—	—	—	206
P.W.	56	M	HCVD	95	100	390	171	75	96	315	219
A.A.	60	M	HCVD	68	100	409	141	92	49	317	268
E.C.	50	M	HCVD	107	70	326	135	81	54	245	191
O.H.	64	M	HCVD	80	95	404	178	101	77	303	226
J.H.	62	M	HCVD	91	80	355	156	82	74	273	199
A.H.	50	F	HCVD	63	70	410	126	87	39	323	284
C.T.	48	F	HCVD	79	85	370	164	88	76	282	206
M.S.	50	M	HCVD	95	100	355	162	100	62	255	193
E.J.	61	F	HCVD	93	80	332	119	—	—	—	213
M.P.	47	F	HCVD	93	85	320	140	74	66	246	180
R.B.	63	M	HCVD	87	95	346	122	86	36	260	224
O.B.	35	M	PMD	72	75	373	151	86	65	287	222
E.K.	64	M	PMD	86	90	377	136	59	77	318	241
C.B.	52	F	PMD	60	70	448	132	70	62	378	316
H.B.	42	M	PMD	81	75	396	157	68	89	328	239
A.B.	62	F	PMD	108	72	343	128	89	39	254	215
N.S.	36	M	PMD	80	85	381	146	110	36	271	235
						Average Data—All Patients					
Average				84	83	371	140	82	58	293	230
SEM				2.5	2.1	6.0	3.4	2.5	3.8	7.1	6.6
Mean deviation from normal						−2	+42	+23	+20	−20	−43
SED						4.2	3.8	3.0	3.8	5.4	4.0

Abbreviations: Dx = diagnosis; HR = heart rate; ASHD = arteriosclerotic heart disease; HCVD = hypertensive cardiovascular disease; PMD = primary myocardial disease; SEM = standard error of the mean; SED = standard error of the mean deviation from normal. For systolic time intervals see table 1.

corrected for the mean difference of 11 msec between the normal male and female values for QS_2 and LVET.

The patients with heart failure had long pre-ejection periods, short left ventricular ejection times, and normal QS_2 intervals. The prolongation in the PEP was due to a lengthening of both the Q-1 and ICT (table 2). The mean QRS interval among the 27 patients with heart failure was 0.079 sec (SD ± 0.008) in females and 0.084 sec (SD ± 0.012) in males, values which are not significantly different from normal.

The relationships of the deviations in the PEP and the LVET to the levels of cardiac index and stroke index among the patients with heart failure are illustrated in figures 5 and 6 and table 4. The deviations from the normal in the PEP and LVET were calculated from the appropriate male and female regression equations. The prolongation in PEP was well correlated with the cardiac index ($r = -0.71$; $P < 0.01$) and the stroke index ($r = -0.77$; $P < 0.01$). The diminution in LVET relative to heart rate was similarly, but less closely, correlated with cardiac index ($r = 0.59$; $P < 0.01$) and stroke index ($r = 0.50$; $P < 0.05$).

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Table 3

Hemodynamic Data in Nineteen Patients with Congestive Heart Failure

Patient	Dx	BSA (m^2)	HR (beats/min)	CI (L/min/m^2)	SI (ml/m^2)	AP S/D (mean) (mm Hg)	RAm* (mm Hg)	TPR (dynes-sec cm^{-5})
R.B.	ASHD	2.23	75	2.59	35	130/65(87)	1.0	1193
S.H.	ASHD	1.65	106	1.29	12	126/91(105)	7.0	3694
E.H.	ASHD	1.82	93	1.55	17	124/70(89)	5.0	2367
F.B.	ASHD	2.28	75	2.11	28	128/69(93)	3.5	1497
R.K.	ASHD	1.88	70	2.43	35	137/71(96)	−0.5	1686
A.H.	ASHD	1.89	69	2.03	31	141/58(95)	−2.0	2016
J.P.	ASHD	1.91	85	1.96	23	132/76(93)	3.5	1907
T.P.	ASHD	2.05	99	1.94	20	129/69(89)	4.5	1714
P.W.	HCVD	1.80	93	1.71	18	181/113(140)	0	3645
A.A.	HCVD	2.66	72	2.25	31	213/100(142)	3.0	1855
E.C.	HCVD	2.20	105	2.02	19	175/111(125)	11.0	2057
O.H.	HCVD	2.07	84	0.91	11	153/95(112)	12.0	4229
J.H.	HCVD	1.87	88	1.42	14	200/141(163)	16.0	4427
A.H.	HCVD	1.72	63	2.47	40	134/72(98)	1.0	1820
O.B.	PMD	1.70	70	1.44	22	105/69(86)	1.5	2741
E.K.	PMD	1.62	86	2.14	25	135/70(91)	−1.5	2130
C.B.	PMD	2.06	55	2.43	44	135/72(100)	2.0	1566
H.B.	PMD	1.70	91	2.29	26	113/76(94)	5.0	1870
A.B.	PMD	1.45	108	2.39	22	110/62(79)	4.0	1725

*RAm refers to right atrial mean pressure in 15 patients and mean central venous pressure in four patients (F.B., R.K., O.H., and J.H.).

Abbreviations: Dx = diagnosis; BSA = body surface area; HR = heart rate; CI = cardiac index; SI = stroke index; AP = arterial pressure; RAm = mean right atrial pressure; TPR = total peripheral resistance; ASHD = arteriosclerotic heart disease; HCVD = hypertensive cardiovascular disease; PMD = primary myocardial disease.

To assess the contributions of peripheral resistance and arterial pressure to the deviations in PEP and LVET relative to heart rate, these deviations were correlated with the mean and diastolic arterial pressure, the calculated peripheral resistance, the ratios of mean and diastolic arterial pressure to stroke index (MAP/SI and DP/SI), and the products of cardiac and stroke index and mean arterial pressure. The data are summarized in table 4. Maximum correlations were found between the deviation in the PEP and the total peripheral resistance, MAP/SI and DP/SI. This suggests that the deviation in PEP is related not only inversely to measures of flow but directly to arterial pressure as well. In contrast, the inclusion of pressure did not improve the correlation of the deviation in LVET with measures of flow.

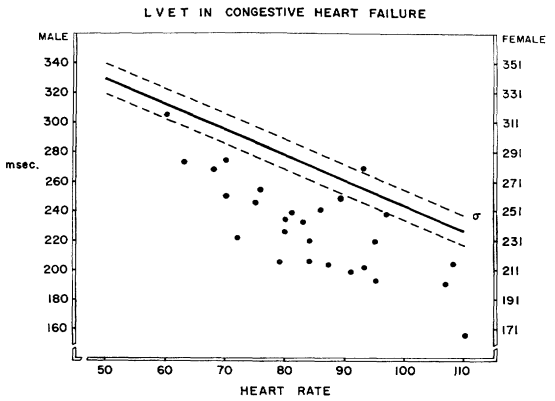

Figure 4

The duration of left ventricular ejection (LVET) in 27 patients with heart failure (•) compared to the normal regression line (± 1 SD) for heart rate.

Among the patients with heart failure, the deviation in PEP relative to heart rate (ΔPEP) was related to stroke index by the linear equation: $\Delta PEP = -1.7\ SI + 85.9$ ($P < 0.01$; for regression coefficient, sample SD from regression ± 0.014 sec). To analyze further the effect of arterial pressure on the deviation in the PEP, the distribution of points about this regression line was plotted against the mean and diastolic arterial pressure (fig. 7). Below either a mean arterial pressure of 110 mm Hg or a diastolic arterial pressure of 90, the ΔPEP was randomly distributed relative to stroke index. At higher pressure levels, however, the values for the ΔPEP tended to cluster above the regression line. Thus, in patients with heart failure, the prolongation in PEP

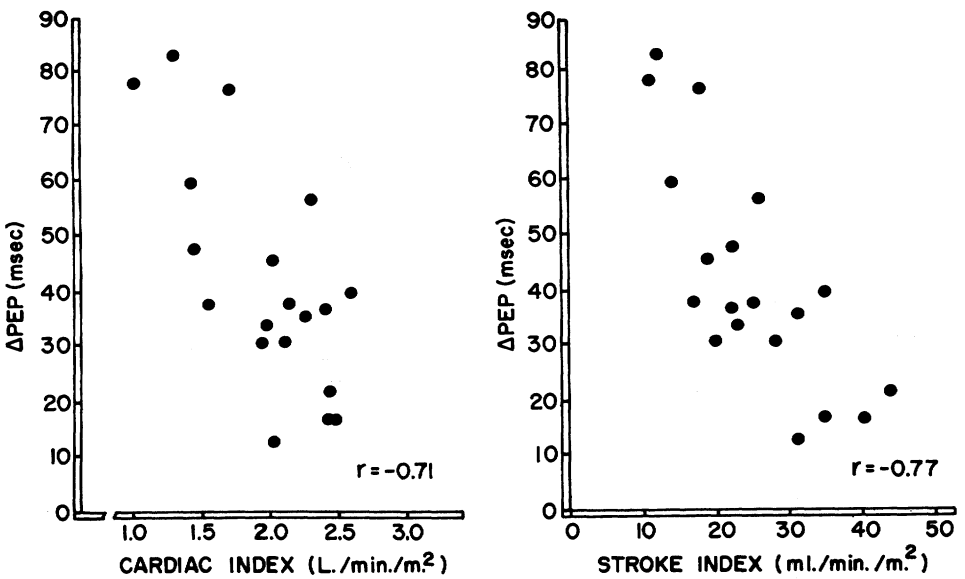

Figure 5

The relationship of the deviation in PEP from the normal regression equation for heart rate to the stroke index and cardiac index in 19 patients with heart failure (•).

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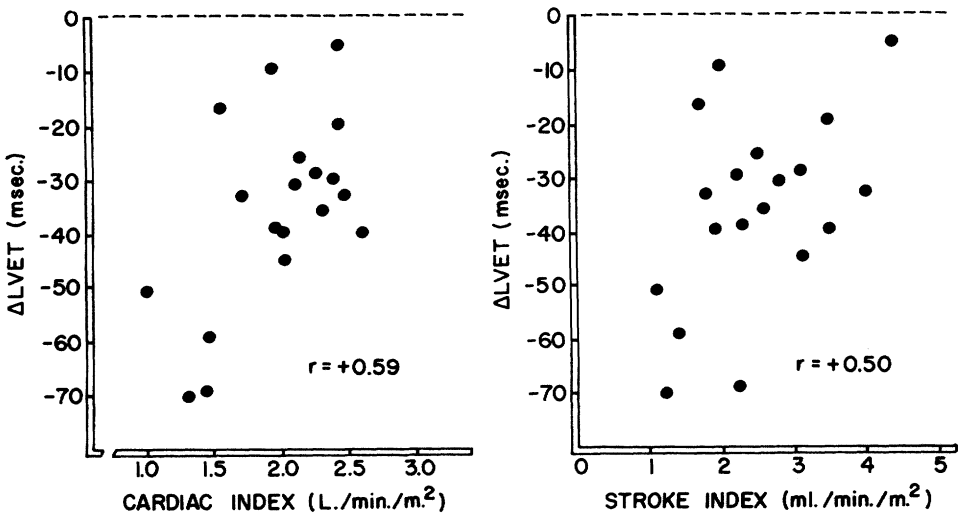

Figure 6

The relationship of the deviation in LVET from the normal regression equation for heart rate to the stroke index and cardiac index in 19 patients with heart failure (•).

Table 4

*Correlation of ΔPEP and ΔLVET with Hemodynamic Measures in Heart Failure**

	ΔPEP	ΔLVET
CI	−0.71†	0.59†
TPR	0.80†	−0.61†
SI	−0.77†	0.50‡
MAP/SI	0.80†	0.52‡
DP/SI	0.81†	0.54‡
CI × MAP	−0.33	−0.37
SI × MAP	−0.58†	0.42
MAP	0.43	−0.24
DP	0.60†	−0.35

*Refers to deviations of PEP and LVET from the normal regression equation for the heart rate.

†$P < 0.01$.

‡$P < 0.05$.

Abbreviations: PEP = pre-ejection period; LVET = left ventricular ejection time; CI = cardiac index; TPR = calculated peripheral resistance; SI = stroke index; MAP = mean arterial pressure; DP = diastolic arterial pressure.

relative to heart rate not only correlated well with the diminished stroke volume but also appeared to be independently augmented by a high level of mean and diastolic arterial pressures. The additive influence of high pressure on the prolongation in PEP accounted for the slightly better correlation when measures of arterial pressure were expressed proportional to the stroke index. A similar influence of arterial pressure on the deviation in LVET could not be demonstrated. Except for the effects of hypertension on the PEP, the deviation in the systolic intervals was unrelated to the etiology of the heart disease.

Discussion

The systolic time intervals in man can be conveniently determined from simultaneous recordings of the electrocardiogram, the phonocardiogram, and the carotid arterial pulsation. The validity of the measurements depends upon a clear definition of the onset of the QRS, the onset of the first and second heart sounds, and the beginning and end of ejection. Each patient in this study showed a sharp onset and normal duration of the QRS complex and a well-demarcated initial deflection of the aortic component of the second heart sound. The interval between the heart sounds was determined only when the initial vibrations of each heart sound were clearly inscribed. The ejection period was measured only when the beginning of the carotid upstroke and the notch of the incisura were clearly delineated. These landmarks for the beginning and end of the ejection period can

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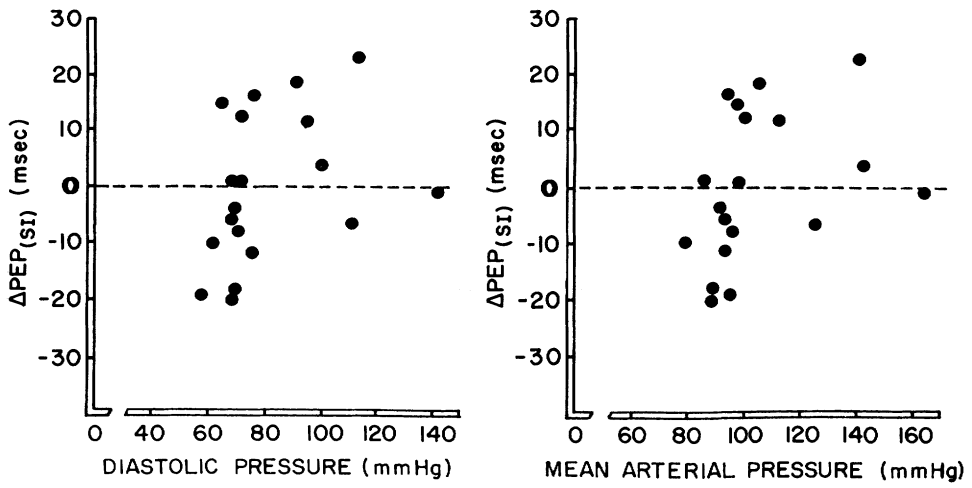

Figure 7

The relationship of diastolic and mean arterial pressures to the variation in the pre-ejection period ($\Delta PEP_{(SI)}$) about the regression equation relating the deviation in the pre-ejection period for heart rate to the stroke index ($\Delta PEP = -1.7\ SI + 85.9$).

be identified with precision when careful attention is given to the placement of the pulse pickup, to minimizing venous pulsation on the tracing, to amplification of the transducer signal, and to examination of minute details of the initial upstroke and the incisura of the arterial pulse as displayed on the oscilloscopic image. The limit of accuracy in estimating a systolic interval in a single complex is 5 msec. The deviation from normal in the pre-ejection and ejection periods in the patients with heart failure fell well beyond this limit.

Normal subjects in the basal state exhibit a narrow range of these time intervals relative to heart rate. The inverse relationship between the duration of electromechanical systole and heart rate among normal individuals is due primarily to the shortening of left ventricular ejection. The pre-ejection period diminishes only slightly with increasing cardiac rate. The isovolumic contraction time remains constant over a wide range of heart rates. At any heart rate, total electromechanical systole and left ventricular ejection are significantly longer in females than in males. The pre-ejection period, Q-1 interval, and the isovolumic contraction time are of the same magnitude in both sexes.

The normal systolic intervals corrected for heart rate and sex provide a basis for comparison with the findings in disease. Left ventricular failure is characterized by a prolongation in the pre-ejection period and an abbreviation in the left ventricular ejection time while total electromechanical systole remains relatively unaltered. These abnormalities occur in the absence of a measurable alteration in the ventricular depolarization time. In left ventricular failure the prolongation of the pre-ejection period is well correlated with the cardiac and stroke indices and is independently augmented by high levels of mean and diastolic arterial pressure. A significant, but lesser, correlation occurs between the diminution in left ventricular ejection time and the cardiac and stroke indices. An independent influence of arterial pressure on this relation was not demonstrated.

The results of these correlations are consistent with the findings of previous experimental studies. Braunwald and associates[9] and Wallace and associates[10] determined the independent effects of changes in stroke volume and peripheral resistance on the duration of the phases of systole in the isolated dog heart. With heart rate and peripheral resistance kept

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constant, an increase in stroke volume shortened the isovolumic period and prolonged the left ventricular ejection time but had little or no effect on the duration of total systole. Conversely, a lowering in stroke volume prolonged the isovolumic period and shortened the left ventricular ejection time. With heart rate and stroke volume held constant, an elevation in mean aortic pressure abbreviated the left ventricular ejection time and prolonged the isovolumic period but had no effect, or only a slight shortening effect, on the duration of total systole. The studies of Braunwald and associates[9] suggested that extreme levels of arterial pressure (above 200 mm Hg systolic) may actually prolong left ventricular ejection. These experimental studies are in general agreement with previous reports on the hemodynamic determinants of the duration of the systolic intervals in frog, turtle, and dog hearts.[11–15] In the present investigation of patients with chronic heart failure, the findings of a low stroke volume and elevated peripheral resistance were accompanied, as in the experimental studies, by prolongation of the pre-ejection period and isovolumic contraction time, abbreviation of the left ventricular ejection time, and a virtually unaltered duration of total electromechanical systole.

The prolonged pre-ejection period in heart failure could be caused by a prolongation of ventricular depolarization, an elevation of diastolic arterial pressure, an increased electromechanical delay, or a diminished rate of left ventricular pressure rise during the isovolumic contraction period. The first two possibilities can be excluded since our patients with heart failure had a normal duration of ventricular depolarization while those with arteriosclerotic or primary myocardial disease had normal diastolic arterial pressures. This suggests that the prolonged pre-ejection period in heart failure is due either to a delay in the onset of mechanical systole relative to the initiation of ventricular depolarization (electromechanical delay), a phenomenon not known to occur in heart failure, or to a diminished rate of isovolumic pressure rise. As the present study shows, both subdivisions of the pre-ejection period, the Q-1 interval and the isovolumic contraction time, are prolonged in patients with heart failure. The prolonged Q-1 interval could reflect an increased electromechanical delay or a reduced rate of left ventricular pressure rise prior to the first heart sound. Since electromechanical delay, as defined here, ends before isovolumic contraction begins, an increase in this delay cannot be considered a cause for the prolongation of the isovolumic contraction time in heart failure. Previous studies have demonstrated that the maximum rate of isovolumic systolic pressure rise is reduced in patients with left[16] or right heart failure.[17] Thus, a principal cause for the prolonged pre-ejection period in heart failure would appear to be a diminished rate of isovolumic left ventricular pressure rise. The possibility of an additional contribution by an increase in electromechanical delay has not been excluded.

In patients with heart failure the prolongation of the pre-ejection period and the shortening of the ejection time correlate remarkably well with the reduced stroke volume and cardiac output. This close relationship between the temporal and flow abnormalities raises the possibility that both may be caused by the same underlying defect (s) in the mechanical performance of the heart. Spann and associates[18] recently determined the isometric length-tension and the force-velocity curves for papillary muscles taken from the failing right ventricle of the cat. The studies of Spann and associates demonstrate that the intrinsic contractile state of the myocardium from failing hearts as reflected in the maximal isotonic velocity and isometric tension and in the active length tension curves is decreased in heart failure. This myocardial contractile abnormality, as well as possible defects in the number, organization, and synchrony of the myofibers, may be primary causes of the altered systolic time intervals and stroke volume in patients with heart failure. According to this view, the pre-ejection period is prolonged because, at any level of

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end-diastolic volume, a deficient rate of myocardial force development secondary to any, or all, of these factors increases the time required for the intraventricular pressure to reach arterial diastolic levels. Since the duration of total electromechanical systole is essentially unaltered in patients with heart failure, this lengthening of the isovolumic period of ventricular contraction might encroach on, and possibly shorten, the subsequent systolic ejection period. A reduced velocity of myocardial fiber shortening during the ejection period would diminish the stroke volume, especially if the time available for ejection were limited. Substantiation of these hypotheses requires direct studies of the myocardial contractile state in human heart failure.

In contrast to the present observations of a normal QS_2 interval in heart failure, Krayenbühl and associates[19] found an abbreviation of this interval in 17 of 57 patients with heart failure. The reasons for this difference from our data are not entirely clear. Recent studies in this laboratory have demonstrated that the administration of cedilanid-D decreases the duration of electromechanical systole in heart failure. Perhaps digitalis therapy explains the abbreviated electromechanical systole found in some of the patients studied by these investigators.

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