Duration of phases of left ventricular systole using indirect methods
II: Acute myocardial infarction

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Fifty-one patients with acute myocardial infarction had serial measurements of left ventricular systolic time intervals by indirect methods. Patients were divided into Group 1 without left ventricular failure and Group 2 with left ventricular failure. Total electromechanical systole (Q–A_2 interval) and left ventricular ejection time were shortened. The pre-ejection period and isovolumetric contraction time were not significantly changed. The alterations in systolic time intervals were most conspicuous in Group 2 patients with left ventricular failure. The maximal changes occurred 2 to 3 days after acute myocardial infarction with a progressive return towards normal over a period of 3 weeks.

Cardiac output studies in 9 patients showed an excellent positive correlation between left ventricular ejection time and stroke volume. The lowest values were in patients with left ventricular failure.

The isovolumetric contraction time was shorter in anterior than in posterior infarction, possibly due to myocardial dyskinesis producing a delay in the onset of the apex cardiogram in anterior infarcts. Indirect measurement of the isovolumetric contraction time and pre-ejection period did not provide any clinically useful information. Increased circulating catecholamines may be responsible for the absence of change in isovolumetric contraction time and pre-ejection period after infarction, as compared to patients with chronic heart failure.

The left ventricular ejection time was the most valuable measurement and served as an index of left ventricular stroke volume and therefore indirectly as a guide to left ventricular function. Study of serial changes in left ventricular ejection time appeared to be more useful prognostically than single isolated measurements.

The use of systolic time intervals as an indirect non-traumatic method of measuring cardiovascular function in normal subjects has been described in a previous paper (Fabian, Epstein, and Coulshed, 1972).

Tennant and Wiggers (1935) demonstrated changes in ventricular function in experimental myocardial infarction in dogs. Jezek (1963) described alterations in systolic time intervals, using indirect methods in a small number of patients with acute myocardial infarction, and further studies have been reported by Wayne (1968), Halpern *et al.* (1969), Toutouzas *et al.* (1969), Samson (1970), and Diamant and Killip (1970).

This paper describes the serial changes in systolic time intervals in patients with acute myocardial infarction admitted to an acute coronary care unit, and attempts to relate the findings to changes in cardiac function.

Patients and methods

Studies were performed on 51 patients with 53 episodes of acute myocardial infarction. All patients were initially admitted to a Coronary Care Unit and then transferred to the cardiac or general medical wards. There were 36 men and 15 women, and ages ranged from 36 to 76 years, with a mean of 56 years.

The diagnosis of myocardial infarction was based on generally accepted clinical criteria of a typical history and physical signs and confirmed by the electrocardiogram and increase in serum transaminase levels. All patients were in sinus rhythm and the duration of the QRS interval did not exceed 100 msec at the time of the study.

Twenty-eight infarcts were predominantly anterior and 25 were predominantly posterior. Nine patients had previously had a myocardial infarction.

The patients were divided clinically into 2 groups. Group 1 – those without left ventricular failure, and Group 2 – those with left ventricular failure. The diagnosis of left ventricular failure was based principally on radiological changes. The chest *x*-ray films were assessed, using a modification of the criteria of Tattersfield *et al.* (1969). Only intra-alveolar pulmonary oedema, septal lines, and pleural fluid were taken as definite evidence of left ventricular failure. Additional clinical criteria were breathlessness, extensive lung crepitations, and the presence of a third heart sound gallop rhythm.

Fifteen patients had signs of left ventricular failure and one of these had associated cardiogenic shock. Ten of the patients with left ventricular failure were treated with frusemide and 4 of these patients also had digoxin before the study. Nine patients died in hospital and 42 patients were eventually discharged from hospital (5 of them after successful resuscitation from cardiac arrest).

The initial study was carried out within 24 hours of the onset of myocardial infarction and repeated on the 2nd, 3rd, 7th, and approximately 21st day. To exclude possible diurnal variations in systolic time intervals, all recordings were made on the same patient at the same time of day. To avoid postural effects, the patient's position was kept the same for successive recordings.

The duration of the phases of left ventricular systole were measured from simultaneous recordings of the electrocardiogram, the phonocardiogram, the right carotid pulse, and the apex cardiogram on a Cambridge Multichannel Recorder at a paper speed of 100 mm/sec. The methods used have been previously described (Fabian *et al.*, 1972).

The following intervals were measured or calculated: (1) Q–A$_2$ interval or total electromechanical systole; (2) left ventricular ejection time (LVET); (3) pre-ejection period (PEP); (4) isovolumetric contraction time (IVCT). The results were statistically evaluated and the findings in patients with myocardial infarction were compared with normal values.

The Student 't' test was performed on all correlation coefficients and significance was established at the 95 per cent confidence level.

Haemodynamic studies In 9 patients with acute myocardial infarction (8 men and 1 woman) and in 6 male control subjects with normal hearts, cardiac output and stroke volume were measured with near simultaneous recordings of external pulse tracings. Four patients with myocardial infarction were in left ventricular failure and one of these patients was in severe cardiogenic shock. Four patients with myocardial infarction were studied on two different days, whereas the other 5 patients and the control subjects were investigated on one occasion only. Cardiac output was measured either by the dye dilution method using indocyanine-green (6 patients with infarction and 5 controls), or by the isotope dilution technique using RISA 131 (3 patients with infarction and 1 control). Both methods are routinely employed in this unit and show a close linear correlation (R = 0·89) (Clarke, 1968).

Results

Table 1 shows the number of patients on whom satisfactory records were available for measurement on days 1, 2, 3, 7, and 21, after infarction. They have been divided into those without left ventricular failure (Group 1) and those with left ventricular failure (Group 2).

1) **Total electromechanical systole – Q–A$_2$ interval** A total of 49 patients had satisfactory records. The Q–A$_2$ interval was reduced after myocardial infarction (Fig. 1 and Table 2). The shortening was maximal on Day 2, and then gradually returned towards normal over the subsequent 21 days. The changes were more conspicuous in Group 2 patients than in those in Group 1. However, on days 1, 2, and 7 the statistical significance could not be assessed because the numbers were too small.

2) **Left ventricular ejection time (LVET)** Fifty-one patients had satisfactory records. The left ventricular ejection time was shortened after myocardial infarction (Fig. 2 and Table 2). The shortening was maximal at 2 to 3 days and then gradually returned to normal over a period of 21 days. The changes were more conspicuous in Group 2 patients though the numbers were only of statistical significance on days 2 and 3 (P < 0·001).

3) **Pre-ejection period (PEP)** Forty-nine patients had satisfactory records. There was

TABLE 1 *Number of measurements made on each day in patients with and without left ventricular failure*

	Q–A$_2$ (49)*		Left ventricular ejection time (51)		Pre-ejection period (49)		Isovolumetric contraction time (43)	
	Left ventricular failure							
	without	*with*	*without*	*with*	*without*	*with*	*without*	*with*
Day 1	22	4	26	4	22	4	22	2
Day 2	31	3	32	7	31	3	26	3
Day 3	24	8	25	9	24	8	19	7
Day 7	11	2	12	2	11	2	9	1
Day 21	30	—	31	2	30	—	25	2

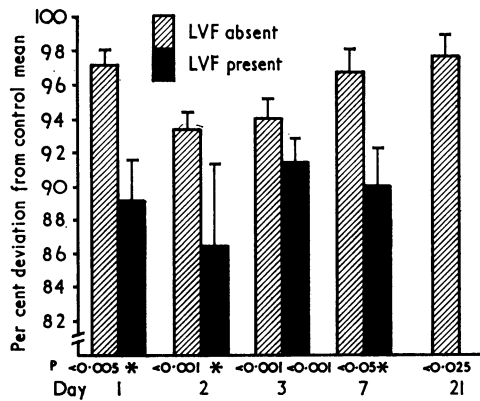* Total number of patients studied is given in parentheses.

FIG. I   *Mean total electromechanical systole (Q–A₂) in acute myocardial infarction – Group 1, left ventricular failure absent: Group 2, left ventricular failure present. Serial studies on Days 1, 2, 3, 7, and 21. The data are expressed as percentage deviation from the control regression line. Bars represent percentage deviation from the mean of controls corrected for heart rate ± standard error of the mean. In this and all subsequent Figures, P values are shown at the bottom: * = too small a group for statistical evaluation: n = not significant.*

no statistically significant increase after myocardial infarction apart from those patients in Group 2 studied on day 3 (Fig. 3 and Table 2). In general Group 2 patients had a longer pre-ejection period. In contrast, Group 1 patients on days 1 and 2 had a significant degree of shortening of the pre-ejection period.

All measurements of systolic time intervals have been combined to show the average values for $Q-A_2$ interval, left ventricular ejection time, and pre-ejection period in the 51 patients studied (Fig. 4).

4) Isovolumetric contraction time (IVCT) Forty-three patients had satisfactory records. The actual values expressed in milliseconds are shown in Fig. 5. No correction has been made for heart rate since the contraction time showed no significant relation to heart rate in our study of normal subjects (Fabian *et al.*, 1972).

On days 1 and 2 the isovolumic contraction time was significantly shortened in Group 1 patients compared to normal controls. On the other days of the study (3, 7, and 21) the time was within normal limits. Group 2 patients generally had a longer contraction time than Group 1 patients, though the numbers were too small to be statistically significant.

The average isovolumetric contraction time was slightly shorter in patients with anterior infarction (54 ± 9 msec) compared to those with posterior infarction (62 ± 10 msec).

TABLE 2   *Statistical data on patients studied with acute myocardial infarction*

| Day			1	2	3	7	21	Total
Q–A₂	Without left ventricular failure	x̄	97·05	93·39	94·00	96·77	97·69	95·60
		SE	0·86	0·87	1·10	1·24	0·96	0·47
		No.	22	31	24	11	30	118
		P	0·005	0·001	0·001	0·05	0·025	0·001
	With left ventricular failure	x̄	89·12	86·43	91·31	90·00	—	89·78
		SE	2·40	4·90	1·45	2·20	—	1·20
		No.	4	3	8	2	—	17
		P	*	*	0·001	*	—	0·001
LV ejection time	Without left ventricular failure	x̄	98·72	93·17	91·70	94·55	97·25	95·15
		SE	1·30	0·96	1·24	1·18	1·14	0·58
		No.	26	32	25	12	31	126
		P	n	0·001	0·001	0·01	0·025	0·001
	With left ventricular failure	x̄	83·77	79·10	82·17	84·95	80·20	81·61
		SE	3·51	2·07	2·36	2·45	3·30	1·25
		No.	4	7	9	2	2	24
		P	*	0·001	0·001	*	*	0·001
Pre-ejection period	Without left ventricular failure	x̄	91·76	93·10	98·7	103·03	95·42	95·51
		SE	3·05	2·44	3·42	3·20	2·24	1·30
		No.	22	31	24	11	30	118
		P	0·025	0·01	n	n	0·05	0·001
	With left ventricular failure	x̄	109·42	101·70	112·29	107·15	—	109·14
		SE	10·92	14·09	4·13	13·25	—	3·92
		No.	4	3	8	2	—	17
		P	*	*	0·025	*	—	0·05
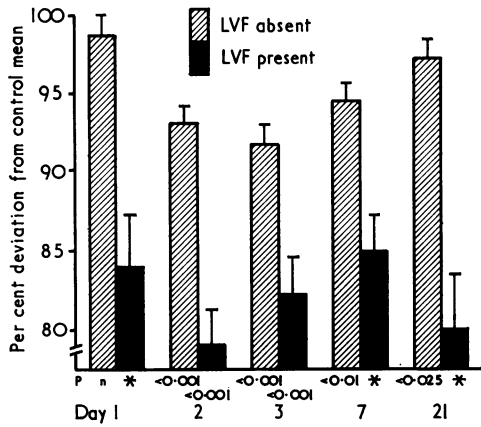
FIG. 2   *Mean left ventricular ejection time in acute myocardial infarction. Bars represent percentage deviation from mean of controls corrected for heart rate ± standard error of the mean.*

**Cardiac output studies**   Nine patients with acute myocardial infarction and 6 control subjects were studied. Four patients with myocardial infarction had the study repeated. A total of 19 measurements of cardiac output has been compared with a near simultaneous indirect record of systolic time intervals (Fig. 6).

There was a statistically significant positive linear relation between stroke volume and both the $Q-A_2$ interval ($R = 0.59 : P < 0.001$) and the left ventricular ejection time ($R = 0.80 : P < 0.001$). The lowest stroke volumes

FIG. 3   *Mean pre-ejection period (PEP) in acute myocardial infarction. Bars represent percentage deviation from mean of controls, corrected for heart rate, ± standard error of the mean.*
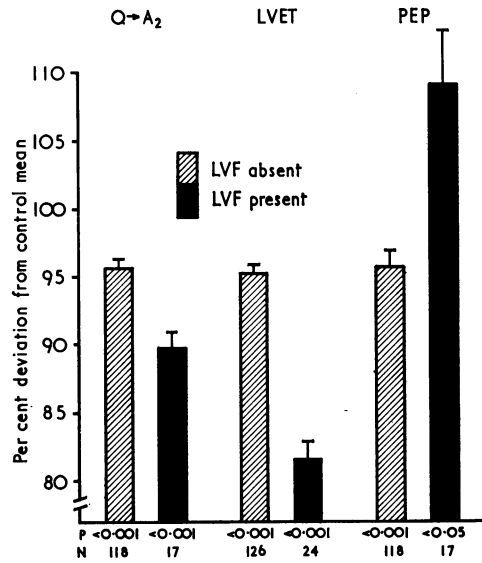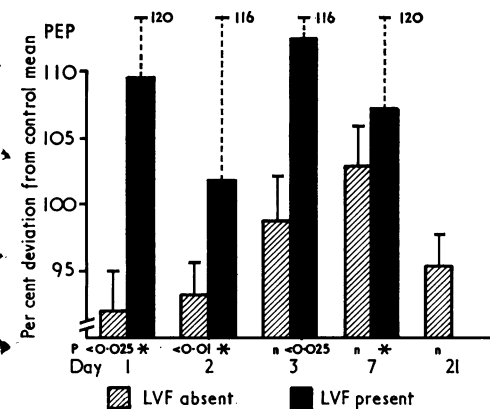
FIG. 4   *Data from Days 1, 2, 3, 7, and 21 combined in acute myocardial infarction, to illustrate the overall changes in $Q-A_2$, left ventricular ejection time and pre-ejection period in patients with and without left ventricular failure. N = number of observations.*

and systolic time intervals were found in those patients with left ventricular failure. In these patients the stroke volume was always less than 48 ml. The smallest measurements were recorded in a patient with cardiogenic shock.

There was no statistical relation between stroke volume and the pre-ejection period or isovolumetric contraction time.

Discussion

For these measurements to be of any value, it is essential to have a recording which shows a clear onset of the QRS complex of the electrocardiogram and of the aortic second sound (A_2). The beginning and end of the carotid pulse wave and the onset of the apex cardiogram should also be sharply defined. Any tracings which did not meet these criteria have been rejected.

This study has shown that there is shortening of both the $Q-A_2$ interval and the left ventricular ejection time after acute myocardial infarction. In the majority of patients the changes are maximal by the 2nd or 3rd day, with a gradual return to normal over the subsequent 21 days. These findings are in agreement with those of Toutouzas *et al.* (1969), Samson (1970), and Diamant and Killip (1970). The degree of shortening was more
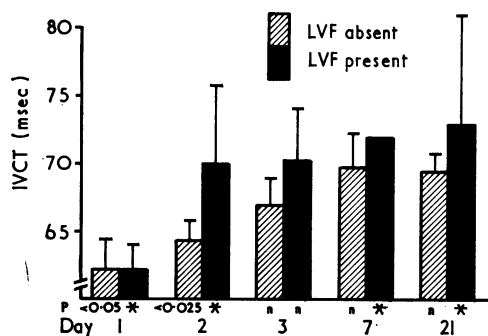
FIG. 5   *Mean isovolumetric contraction time (IVCT) in acute myocardial infarction. Bars represent mean values expressed in msec ± standard error of the mean.*

conspicuous in those patients with left ventricular failure. The pre-ejection period generally showed no significant change though it was longer in patients with left ventricular failure (Group 2) than in those without (Group 1). A statistically significant increase in the pre-ejection period was only found in Group 2 patients on Day 3. These findings therefore differ from those of Diamant and Killip (1970) who found a prolonged pre-ejection period after acute myocardial infarction particularly in those patients with transmural infarction. Samson (1970) found either a normal or a prolonged pre-ejection period with little difference between those with and those without left ventricular failure. Halpern et al. (1969) however failed to show any significant change in acute transmural myocardial infarction.

The mechanism of the changes in the systolic time intervals is of considerable interest and importance. None of the patients had gross evidence of conduction defects since there was no prolongation of ventricular depolarization. Therefore alteration in conduction is unlikely to be responsible for the changes observed.

The $Q-A_2$ interval comprises both the pre-ejection period and left ventricular ejection time. Since the pre-ejection time showed little change, other than a tendency to be longer in patients with left ventricular failure, the shortening of the $Q-A_2$ interval in myocardial infarction is principally due to a decrease in left ventricular ejection time.

The principal determinants of left ventricular ejection time are heart rate and stroke volume. Heart rate has been shown to influence left ventricular ejection time indepen-

dently of its effects on stroke volume, both experimentally (Braunwald, Sarnoff, and Stainsby, 1958; Wallace et al., 1963) and clinically (Harley, Starmer, and Greenfield, 1969). Such studies show that it is inversely related to heart rate and directly related to stroke volume. In this study the effects of heart rate on ejection time have been excluded by comparing measured values to normal control values at the same heart rate.

The left ventricular ejection time has been shown to correlate directly with stroke volume in normal subjects and in patients with heart disease by Weissler, Peeler, and Roehll (1961) and by Harley et al. (1969). Our own studies of stroke volume and left ventricular ejection time in normal subjects and after acute myocardial infarction confirm these observations (Fig. 6). Haemodynamic studies after myocardial infarction have shown a reduced stroke volume which is more severely depressed in

FIG. 6   Above. *Relation between $Q-A_2$ interval and stroke volume (SV) ($r = 0.592$; $P < 0.001$). Below. Relation between LVET and stroke volume (SV). ($r = 0.8032$; $P < 0.001$). The meaning of the symbols is shown on the upper graph. The normal regression lines on the lower graph are taken from the paper by Weissler et al. (1961).*
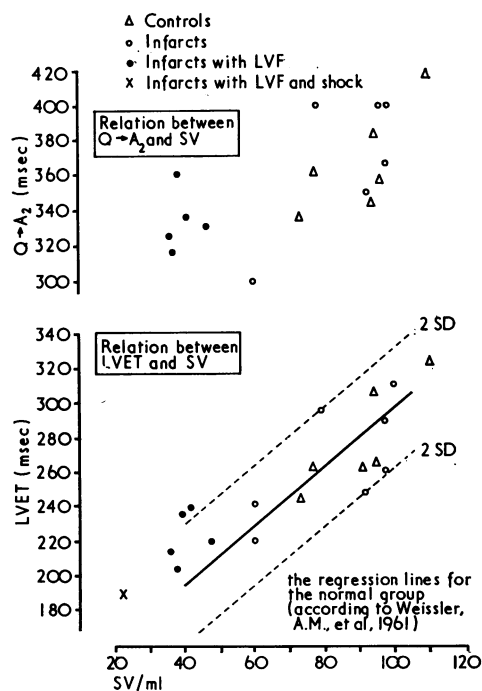
the more seriously ill patients (Freis *et al.*, 1952; Smith, Wikler, and Fox, 1954; Lee, 1957; Murphy *et al.*, 1963; Thomas, Malmcrona, and Shillingford, 1965; Mackenzie *et al.*, 1964; Gunnar *et al.*, 1966; Ramo *et al.*, 1970). The patients in our series with left ventricular failure who had cardiac output studies had a lower stroke volume. The lowest stroke volume was in a patient with left ventricular failure and cardiogenic shock (Fig. 6). The left ventricular ejection time was correspondingly reduced. Similarly, Samson (1970) and Diamant and Killip (1970) showed a greater fall in ejection time in patients with more severe myocardial damage.

Nager, Thomas, and Shillingford (1967) performed serial studies in stroke volume after myocardial infarction, and found a maximal fall at 3 to 4 days, with a gradual return to normal over the subsequent 2 to 3 weeks depending on the severity of the infarction. These findings closely resemble the serial changes in ejection time after myocardial infarction.

Stroke volume is influenced by ventricular preload, afterload, and myocardial contractility. Patients with left ventricular failure usually have a raised left ventricular enddiastolic pressure and some increase in ventricular diastolic volume. Thus increased ventricular preload may well be a factor in shortening left ventricular ejection time in such patients. Afterload is principally related to mean aortic pressure which is likely to be normal or reduced in myocardial infarction particularly in patients with left ventricular failure. Experimentally, Wallace *et al.* (1963) have shown that left ventricular ejection time is reduced by raising mean aortic pressure. It is therefore probable that a reduced mean aortic pressure in the clinical situation would prolong rather than shorten the ejection time. Myocardial contractility will also be impaired due to ventricular asynergy with paradoxical pulsation over the area of infarction and hence a generally decreased overall rate of myocardial fibre shortening (Herman and Gorlin, 1969).

The left ventricular ejection time appears to be a good index of left ventricular stroke volume. Despite the general relation between stroke volume or ejection time and the clinical state of the patient, wide variations may occur in individual patients. Isolated measurements of left ventricular ejection time are, therefore, of relatively limited value. However, the shortest measurements were in Group 2 patients with left ventricular failure, with an average ejection time of 210 msec SD ± 18 msec. An ejection time less than 240 msec was frequently associated with evidence of pulmonary oedema on the chest x-ray film, whereas no patient with left ventricular ejection time above 245 milliseconds had heart failure. Serial measurements in the same patient may be of great prognostic value and show evidence of changes in cardiac function. For example, clinical improvement as shown by resolution of radiological pulmonary oedema was always associated with lengthening of the ejection time.

The isovolumetric contraction time in this study was measured from simultaneous records of the apex cardiogram and the carotid pulse wave (Fabian *et al.*, 1972). The time was slightly increased in patients with left ventricular failure though the numbers were too small to be of statistical significance (Fig. 5).

When patients were divided into those with anterior infarction and those with posterior infarction the isovolumetric contraction time was shorter on average with anterior infarction (Fig. 7). The shortened isovolumetric contraction time in anterior infarction was statistically significant on Day 1, but not on any other day. The reasons for this finding are uncertain since the clinical severity of infarction was similar in both anterior and posterior infarction. It could be related to the time of onset of the systolic upstroke of the apex cardiogram. The infarcted myocardium is dyskinetic and this is the area of myocardium from which the apex cardiogram is recorded in anterior infarction. Any delay in

FIG. 7 *Mean isovolumetric contraction time in acute myocardial infarction divided into those with predominantly anterior infarction and those with predominantly posterior infarction. Bars represent mean values of isovolumetric contraction time in msec ± standard error of the mean.*
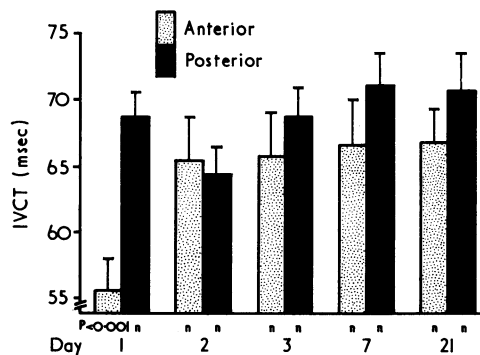
praecordial movement over the infarcted muscle will shorten the time interval between the onset of the apex cardiogram and that of the carotid pulse and hence give a smaller measurement of isovolumetric contraction time.

Our findings differ from those of Inoue *et al.* (1970) who found a prolonged isovolumetric contraction time in patients studied within 72 hours of myocardial infarction using the same technique.

The slight prolongation of isovolumetric contraction time in patients with left ventricular failure may be related to impaired contractility of the left ventricle with a reduced rate of rise in systolic pressure. The results of the present study show that the changes are too small to provide any consistently useful information concerning left ventricular function.

The pre-ejection period also failed to show any consistent change after myocardial infarction though this measurement does not depend on the timing of the apex cardiogram. The pre-ejection period combines the period of electromechanical delay and the isovolumetric contraction time. With normal conduction electromechanical delay is unlikely to be prolonged and changes in pre-ejection period are principally due to changes in isovolumetric contraction time. Thus, the absence of a significant change in pre-ejection period after infarction is in agreement with the absence of change in isovolumetric contraction time.

Bed rest (Diamant and Killip, 1970), posture (Stafford, Harris, and Weissler, 1970), digitalis (Bhardwaj, Schoenfeld, and Samet, 1970), and diuretics all influence systolic time intervals. Both groups of patients in this study had a similar degree of bed rest and a similar environment. Posture was kept constant for the recordings throughout the study. Drugs could not be withheld on ethical grounds from critically ill patients with left ventricular failure though the majority of these patients had the initial study before treatment was begun. Ten of the 15 patients with left ventricular failure had frusemide and 4 also had digoxin. The effect of these drugs could not therefore be ruled out. Other workers, who have studied systolic ejection times in uncomplicated myocardial infarction where drug therapy could be withheld, have still shown reduction in the $Q–A_2$ interval and the left ventricular ejection time (Dowling, Sloman, and Urquhart, 1971; Jain and Lindahl, 1971). Those patients with left ventricular failure studied by Samson (1970) did not have digitalis but no information about drug therapy is given for the patients studied by Diamant and Killip (1970) and Inoue *et al.* (1970).

Inotropic agents have been shown to shorten systolic ejection times experimentally in dogs (Braunwald *et al.*, 1958). It has been suggested that the inotropic influence of the increased circulating catecholamines after myocardial infarction may be a major factor in reducing systolic ejection times (Valori, Thomas, and Shillingford, 1967; Toutouzas *et al.*, 1969). However, Samson (1970) found no correlation between the mean daily urinary catecholamine excretion and the degree of shortening of the left ventricular ejection time and $Q–A_2$ interval.

In chronic heart failure left ventricular ejection time is shortened, pre-ejection period and isovolumetric contraction time are prolonged, and the $Q–A_2$ interval remains within normal limits (Weissler, Harris, and Schoenfeld, 1968). Acute myocardial infarction shows certain differences since both the ejection time and $Q–A_2$ interval are shortened while pre-ejection period and isovolumetric contraction time remain unchanged.

In both acute myocardial infarction and chronic heart failure the shortened left ventricular ejection time correlates well with diminished stroke volume (Weissler *et al.*, 1968; Garrard, Weissler, and Dodge, 1970). It is therefore fairly certain that the main cause of the shortened ejection time after infarction is reduced stroke volume.

The lack of change in pre-ejection period and isovolumetric contraction time in acute myocardial infarction as compared to chronic heart failure may be due, principally, to the inotropic action of increased catecholamines after infarction.

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