

Attempt to quantitate relation between cardiac function and infarct size in acute myocardial infarction¹

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In 82 patients with acute myocardial infarction, observed haemodynamic changes were compared with the average maximal serum enzyme rise and the infarct size, as calculated from serial determinations of creatine phosphokinase concentration. For this purpose, patients were divided into 3 groups according to their pulmonary artery end-diastolic pressure at the time of admission. There were 19 patients in group I with pulmonary artery end-diastolic pressure < 12 mmHg; they had an average infarction size of 17 g and no impairment of cardiac function. In the 35 patients in group II with pulmonary artery end-diastolic pressure 12 to 20 mmHg, the pressure was raised to a mean value of 15.4 ± 0.4 mmHg with a slight decrease of cardiac index (2.5 ± 0.1 l./min per m^2) and left ventricular stroke work index (51.4 ± 4.7 g m/m^2). Loss of myocardium in group II was 42 g and mortality was 21 per cent. There were 28 patients in group III with pulmonary artery end-diastolic pressure > 20 mmHg, who had an average infarct size of 99 g. Cardiac index (1.9 ± 0.2 l./min/ m^2), and stroke work index (27.5 ± 5.7 g m/m^2) declined significantly ($P < 0.001$). Mean end-diastolic pressure rose to 28.3 ± 1.1 mmHg. Mortality in group III (60%) was mainly due to cardiogenic shock.

It is concluded that the decrease of cardiac function in the acute phase of myocardial infarction must usually be ascribed to the amount of recent myocardial necrosis. Stiffening of the infarct area and normal or increased contractility of the non-infarcted myocardium are regarded as compensatory mechanisms. The combined investigation of haemodynamic and serial enzyme changes is considered to be an appropriate method for the separation of old from recent myocardial necrosis and for providing information predictive of the immediate and the long-term prognosis.

At present heart failure is the most serious complication of acute myocardial infarction in coronary care units (Bleifeld *et al.*, 1972; Rutherford, McCann, and O'Donovan, 1971). There are probably several mechanisms by which acute myocardial infarction causes left heart failure. One is obviously the loss of left ventricular myocardium by previous or acute infarcts (Page *et al.*, 1971; Harnarayan *et al.*, 1970). The amount of acute myocardial necrosis can be estimated by measuring the serum enzyme rise after coronary occlusion. In order to quantitate the relation between the extent of myocardial infarction and the impairment in left ventricular function, serum enzyme changes were correlated with left ventricular haemodynamics.

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Methods

Patients

Included in the study were 82 patients with acute transmural myocardial infarction. The diagnosis of acute myocardial infarction was based on the following. 1) The relevant history; 2) the typical electrocardiographic criteria (evolution of Q waves, alterations in the ST segments and T waves); and 3) serial rises in creatine phosphokinase (CPK), aspartate aminotransferase (GOT), lactic dehydrogenase (LDH), and α -hydroxybutyrate dehydrogenase (α -HBDH) in serum.

The patients were considered to be in cardiogenic shock, if 1) reduced blood flow was evident from cold, clammy, cyanotic skin, mental obtundation, and from a urine output less than 20 ml/hour; and 2) systolic blood pressure was below 90 mmHg or, in previous hypertensive subjects, 30 mmHg less than their normal values, during a period of at least 30 minutes.

Patients with atrial fibrillation, ectopic tachycardias,

ventricular fibrillation, and total AV block were excluded from the study.

The patients were split into 3 groups according to left ventricular filling pressure at the time of admission. Though this was measured directly in 41 patients, pulmonary artery end-diastolic pressure which is obtained more easily and without risk (Bleifeld *et al.*, 1973) was used for the classification. This was possible, because in agreement with Kaltman *et al.* (1966), Hunt *et al.* (1970) and Scheinmann *et al.* (1973), 43 simultaneous measurements of left ventricular end-diastolic pressure and pulmonary artery end-diastolic pressure in 22 patients gave an excellent correlation ($r=0.93$) between the two pressures. Group I consisted of 19 patients with an end-diastolic pulmonary artery pressure below 12 mmHg. In group II ($n=35$) end-diastolic pulmonary artery pressure ranged between 12 and 20 mmHg. End-diastolic pulmonary artery pressure exceeded 20 mmHg in group III ($n=28$).

Haemodynamic data

All patients were examined in the coronary care unit, on an average, 6 hours after the beginning of pain, while lying in bed. Under local anaesthesia and without fluoroscopy, catheters were inserted via the medial antecubital vein or the femoral vein and via the femoral artery using the Seldinger technique. Pressures in the right heart and the pulmonary artery were obtained in all patients by means of double- or triple-lumen Swan-Ganz balloon-catheter¹ (Swan *et al.*, 1970; Bleifeld, 1973). In 41 patients 7 F Oedman catheters² with the lumen at the end and a preshaped bent tip were manipulated via the femoral artery into the central aorta and from there during continuous pressure and electrocardiographic monitoring into the left ventricle. All pressures were recorded with Statham P23dB³ strain gauges mounted at the level of the mid-thorax for the zero position.

Cardiac output determinations were performed by the dye dilution technique using injections of indocyanine green into the pulmonary artery and sampling from the central aorta using a Waters X 350 cuvette densitometer.⁴

Pressures and dye dilution curves were recorded on an 8-channel-printer.⁵ With the exclusion of a haematoma at the site of arterial puncture in one patient with an unknown bleeding disorder, no serious complications were seen.

Serum enzyme determinations

Serum samples for CPK, GOT, LDH, and α -HBDH determinations were obtained at the time of admission, the next morning, and daily in the further course. In some patients, samples were taken every 3 hours for serial determinations of creatine phosphokinase. Enzyme activities were determined kinetically at 25°C. CPK

¹ Edwards Laboratories, Santa Ana, California, U.S.A.

² KIFA, Stockholm, Sweden.

³ Statham Instruments, Inc., California, U.S.A.

⁴ Waters Instruments, Inc., Los Angeles, California, 90064, U.S.A.

⁵ Oscillomink, Siemens, Erlangen, West Germany.

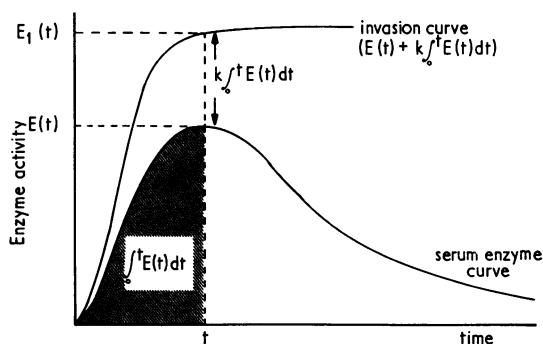


FIG. 1 The invasion curve represents the enzyme concentration that would appear in the distribution space if the enzyme were not eliminated. The invasion curve can be reconstructed from the serum enzyme curve by adding the product of the rate constant of elimination k with the integral $\int_0^t E(t) dt$ to the actual enzyme concentration $E(t)$.

activity was measured with Boehringer CPK-activated test sets.¹ GOT-, LDH-, and α -HBDH-activities in the serum were assayed in a suboptimal substrate concentration with Boehringer test sets.¹ The upper normal values are as follows: CPK 40 mU/ml, GOT 12 mU/ml, LDH 200 mU/ml, and α -HBDH 140 mU/ml.

Calculations

Haemodynamic values

For the determination of cardiac output from the dye dilution curves the formula of Williams, O'Donovan, and Wood (1966) was used. Left ventricular stroke work index (LVSWI) was determined from the following relation.

$$LVSWI = \frac{(MSP - LVDEP) \cdot SVI \cdot 1.36}{100} \text{ g m/m}^2$$

with MSP = mean systolic pressure; LVDEP = left ventricular end-diastolic pressure; SVI = stroke volume index.

Diastolic stiffness is defined as the pressure change dP for a given change in volume dV . In this study dP/dV was evaluated from the quotient $\Delta P/\Delta V$ as an approximation of dP/dV according to Diamond and Forrester (1972).

$$\frac{\Delta P}{\Delta V} = \frac{LVDEP - LVESP}{SV} \frac{\text{mmHg}}{\text{ml}}$$

with LVDEP = left ventricular end-diastolic pressure; LVESP = left ventricular end-systolic pressure; SV = stroke volume.

In all patients a shock index (Bleifeld *et al.*, 1973) appropriate for the early recognition of cardiogenic shock and derived from

$$\frac{(SAP - PAEDP) \cdot CI}{PAEDP \cdot AVDO_2}$$

¹ Boehringer Mannheim, Mannheim, West Germany.

TABLE I Haemodynamic data in each group

Parameter	Group I mean ± I SEM	Group II mean ± I SEM	Group III mean ± I SEM	Significance (P <)		
				I-II	I-III	II-III
Left ventricular filling pressure (mmHg)	8.4 ± 0.6 (n = 8)	16.3 ± 1.9 (n = 20)	26.8 ± 1.3 (n = 13)	0.001	0.001	0.001
Pulmonary artery end-diastolic pressure (mmHg)	8.9 ± 0.3 (n = 19)	15.4 ± 0.4 (n = 35)	28.3 ± 1.1 (n = 28)	0.001	0.001	0.001
Mean pulmonary artery pressure (mmHg)	13.1 ± 0.4 (n = 19)	22.2 ± 0.9 (n = 35)	35.5 ± 1.3 (n = 28)	0.05	0.001	0.01
Cardiac index (l./min/per m ²)	2.7 ± 0.3 (n = 13)	2.5 ± 0.1 (n = 22)	1.9 ± 0.2 (n = 17)	NS	0.05	0.02
Stroke volume index (ml/m ²)	37.5 ± 2.9 (n = 13)	31.0 ± 1.7 (n = 22)	21.1 ± 1.9 (n = 17)	NS	0.05	0.01
Left ventricular stroke work index (g m/m ²)	60.6 ± 15.1 (n = 10)	51.4 ± 4.7 (n = 19)	27.5 ± 5.7 (n = 14)	NS	0.01	0.001
Mean arterial pressure (mmHg)	96.8 ± 5.5 (n = 10)	95.6 ± 4.1 (n = 23)	95.1 ± 3.7 (n = 14)	NS		
Mean left ventricular diastolic stiffness (mmHg/ml)	0.11 ± 0.02 (n = 4)	0.26 ± 0.03 (n = 12)	0.36 ± 0.04 (n = 8)	0.01	0.01	0.05
Shock index	0.97 ± 0.14 (n = 8)	0.73 ± 0.12 (n = 20)	0.23 ± 0.06 (n = 13)	0.1	0.001	0.001

was calculated: SAP=systolic arterial pressure; CI= Cardiac output index; AVDO₂=arteriovenous oxygen difference.

Patients with cardiogenic shock had an index below 0.3.

Determination of infarct size

As recently described by Sobel *et al.* (1972), the mass of a myocardial infarct (I) in man can be estimated from serial determinations of creatine phosphokinase concentration using the equation:

$$I(g) = \frac{CPK_D (IU)}{CPK_N - CPK_I (IU/g)}$$

with CPK_D=total amount of depleted CPK in the infarct area (IU); CPK_N=CPK activity in the normal human myocardium (IU/g); CPK_I=CPK activity in the homogenized infarct tissue (IU/g).

CPK_D is obtained from the amount of CPK released (CPK_R) into the circulation (CPK_D=CPK_R/0.3). CPK_R is obtained by multiplying the volume of the CPK distribution space with the peak value of the amount of CPK that invades one millilitre of the distribution space (according to Sobel *et al.* (1972) 11.4% of the body weight). The maximal amount of CPK that invades the distribution volume can be evaluated from CPK serial determinations as follows (Fig. 1): the actual CPK concentration in serum is the result of two contrary mechanisms, namely invasion from the destructed myocardium and elimination. If the rate constant of elimination k is known, the invasion curve can be calculated from the CPK serum curve, by addition of the eliminated CPK E_{el}(t) to the actual concentration of CPK E(t). It is accordingly (Gładtke and Hattingberg, 1973)

$$E_1(t) = E(t) + E_{el}(t) \tag{1}$$

E_{el}(t) depends on the rate constant of elimination k and

the area limited by the CPK serum curve, i.e. the integral $\int_0^t E(t) (dt)$. Thus equation (1) changes into:

$$E_1(t) = E(t) + k \cdot \int_0^t E(t) dt \tag{2}$$

Equation (2) was calculated by using a Fortran programme. CPK values as a function of time were plotted by the computer. The values were approximated by the mathematically best fitting curve. This approximated curve was used for the calculation of equation (2). The values of equation (2) as a function of time, the so-called invasion curve, were plotted by the computer as well.

The rate constant of elimination k was calculated from the CPK serum curve. It proved to be necessary to determine k for each of the approximated curves and to use the value k thus obtained for the calculation of the invasion curve. In group I, k was 0.053 h⁻¹; in group II, 0.054 h⁻¹; and in group III, 0.075 h⁻¹. Further details of the methods used are described elsewhere (Mayiopoulos *et al.*, 1974).

Results

Haemodynamic alterations

Table I summarizes the haemodynamic results in 82 patients. Excluding mean arterial pressure and heart rate, highly significant differences were observed between the 3 groups.

In group I with pulmonary artery end-diastolic pressure < 12 mmHg the 19 patients had normal pressures in the pulmonary circulation. The mean pulmonary artery pressures were 13.1 ± 0.4 mmHg. Pulmonary artery end-diastolic pressure ranged from 7 to 11 mmHg (mean: 8.9 ± 0.3 mmHg). Cardiac index and left ventricular stroke work index were not significantly decreased.

There was a slight increase of left ventricular

TABLE 2 *Mean maximal serum values of CPK, GOT, LDH, and α -HBDH*

Serum enzyme	Group I mean \pm 1 SEM	Group II mean \pm 1 SEM	Group III mean \pm 1 SEM	Significance ($P <$)		
				I-II	I-III	II-III
CPK (mU/ml)	315 \pm 47.4 (n=19)	443.9 \pm 39.4 (n=34)	874.7 \pm 125.4 (n=20)	0.05	0.001	0.01
GOT (mU/ml)	69.4 \pm 7.8 (n=19)	98.3 \pm 10.2 (n=35)	316.3 \pm 129.2 (n=21)	0.1	0.001	0.01
LDH (mU/ml)	490.3 \pm 33.3 (n=19)	710.7 \pm 41.5 (n=33)	867.6 \pm 99.7 (n=21)	0.001	0.001	NS
α -HBDH (mU/ml)	315.1 \pm 22.5 (n=17)	543.2 \pm 44.1 (n=29)	646.4 \pm 78.8 (n=17)	0.001	0.001	NS

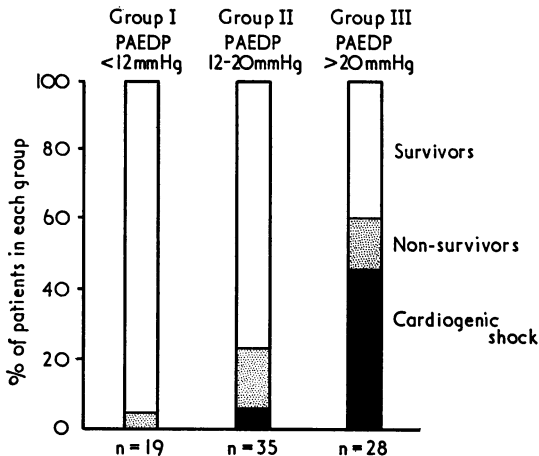


FIG. 2 Note the increasing proportion of non-survivors from group I to group III. Fifty per cent of the patients in group III died in cardiogenic shock.

stiffness with 0.11 ± 0.02 mmHg/ml compared to normal (0.07 mmHg/ml). According to the slight impairment in left ventricular haemodynamics no clinical signs of left heart failure were observed. Only one patient died on the 5th day from heart rupture.

Group II consisted of 35 patients with moderately increased pressures in the pulmonary artery. The mean pulmonary artery end-diastolic pressure was 15.4 ± 0.4 mmHg, significantly higher ($P < 0.001$) than in group I. Slight but not significant decreases of cardiac index (2.5 ± 0.1 l./min per m^2) and left ventricular stroke work index (51.4 ± 4.7 g m/m^2) were observed compared to the patients in group I. Left ventricular stiffness was further increased to 0.26 ± 0.03 mmHg/ml ($P < 0.01$). Nineteen patients (55%) in group II had pulmonary rales. Mean pulmonary end-diastolic pressure in these patients was 16.6 mmHg; 20 per cent of group II died, two after cardiogenic shock (Fig. 2).

In the 18 patients included in group III with pulmonary artery end-diastolic pressures > 20 mmHg there was a significant impairment of left ventricular function. The mean pulmonary artery

end-diastolic pressure was significantly greater (28.3 ± 1.1 mmHg) as compared with group I and II ($P < 0.001$), and left ventricular end-diastolic pressure was raised to 26.8 ± 1.3 mmHg. Cardiac index (1.9 ± 0.2 ml/min/ m^2) and left ventricular stroke work index (27.5 ± 5.7 g m/m^2) were significantly reduced ($P < 0.001$). The mean shock index was 0.23 ± 0.6 ($P < 0.001$), which was below 0.3, the upper limit of patients with cardiogenic shock previously observed in our department (Bleifeld *et al.*, 1973). In 73 per cent there was clinical evidence of left heart failure. Fifty per cent of these patients died in cardiogenic shock and mortality was very high in 85 per cent of group III (Fig. 2).

Enzymes

The mean maximal values of the rise of the different enzymes are summarized in Table 2. There were significant differences between the three groups. The peak value of the CPK in group I was 315 ± 47 mU/ml, significantly less ($P < 0.05$) than in group II with 444 ± 39 mU/ml. A further increase was observed in group III to 875 ± 125 mU/ml, which was 22 times the normal ($P < 0.001$). CPK peaked in the mean 24 hours after the first signs of infarction.

The concentration of GOT in the serum was found to rise in group I to 69 ± 8 mU/ml, and in group II to 98 ± 10 mU/ml. The peak value of group III was 316 ± 130 mU/ml, which was 26 times the normal value ($P < 0.001$ compared to groups I and II). The mean maximal value of GOT was measured 42 hours after the infarction.

Significant differences were also observed between the three groups for LDH and α -HBDH. The constant quotient LDH/ α -HBDH of 1.4 indicates that the LDH originated in all three groups from the heart muscle that had been destroyed. In group III both enzymes were raised to 4 times the normal (LDH 867 ± 99.7 , α -HBDH 646 ± 79 , $P < 0.001$ compared to group I). Maximal values of LDH and α -HBDH were on the third day.

Mean peak values of CPK and GOT differed considerably not only between the three groups, but there was also, in the individual patient, a rough

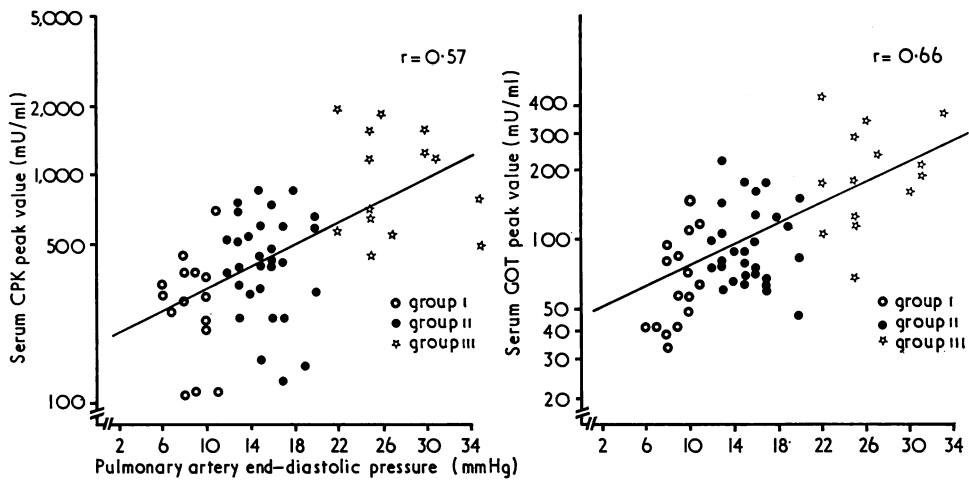


FIG. 3 The maximal serum enzyme concentrations of CPK and GOT are plotted against the pulmonary artery end-diastolic pressure. In the individual patient there is only a rough correlation, as both parameters may be influenced by variables other than infarct size.

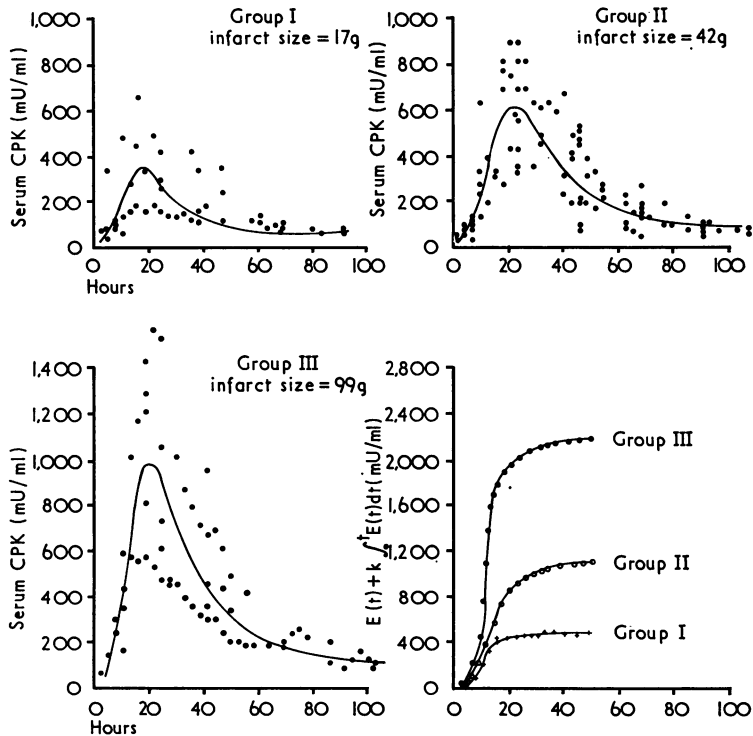


FIG. 4 This figure summarizes the CPK serial values of each group approximated by the mathematically best-fitting curve, which was used for the calculation of the average infarct size of each group. The right lower quadrant shows the CPK invasion curves which differ in their height and rate of rise.

correlation between pulmonary artery end-diastolic pressure and enzyme rise ($r=0.57$ for CPK and $r=0.66$ for GOT). This is shown in Fig. 3.

CPK serial determinations of each group are shown in Fig. 4. The enzyme values were approximated by the mathematically best-fitting curve. From this curve mean infarct size was calculated according to the equation mentioned above. Mean infarct size in group I was 17 g. In group II the value rose to 42 g. Patients of group III had a mean infarct size of 99 g. As shown in the right lower quadrant of Fig. 4, the maximal amount of CPK that invaded the distribution space increased from group I to III. Besides this there was also an accelerated enzyme invasion with augmenting infarct size, as can be seen from the increasing slope of the invasion curves.

Discussion

Experimental myocardial infarctions in dogs after coronary artery ligation or coronary embolization revealed that infarct size was related to the rise in serum GOT and LDH (Nydic, Wroblewski, and LaDue, 1955; Lemley-Stone *et al.*, 1955; Ruegsegger *et al.*, 1959). Bang and LaDue (1962) thought that, in man also, serum enzyme activity correlated with the infarct size. They showed that the maximal enzyme rise in patients who survived their infarction was half that of those who died. Kluge (1969) suggested that patients should be divided into a high risk group, with maximal CPK serum values greater than 600 mU/ml, and a low risk group with CPK peak values below 600 mU/ml, as mortality was 50 per cent in those whose CPK values were greater than 600 mU/ml. Recently Chapman and Gray (1973) proposed a prognostic index for acute myocardial infarction, which among other parameters was based on serum GOT increases. In these studies serum enzyme changes were related to clinical data. As clinical signs in acute myocardial infarction may be unreliable, the present study was carried out to compare left ventricular haemodynamic data with serum enzyme changes. Within this context pulmonary artery pressure measured at end-diastole enabled the patients to be divided into three groups, because of the excellent correlation of this with left ventricular end-diastolic pressure ($r=0.93$) (Merx *et al.*, 1973) and the safety of the procedure involved in measuring it. (Swan *et al.*, 1970; Bleifeld, 1973.)

Although none of the enzymes studied specifically has its origin in cardiac muscle, it can be assumed from the uniform behaviour of all enzymes that the increase after myocardial infarction has to be attributed to myocardial damage. Only in the case of the

high concentration of GOT in group III may an additional source, probably the liver, be supposed. The haemodynamic impairment of left ventricular function correlated well with the average maximum serum enzyme activity. As peak values of enzyme rise may be affected not only by the infarct size but also by some other variables, such as the rate of biliary and renal excretion, the presence of plasma activators or inhibitors, maximal serum enzyme concentration may not necessarily be an index of infarct size (Cohen and Morgan, 1973). These variables can be neglected, if the infarct size is calculated from the amount of enzyme released into the distribution space.

In group I serial measurements of CPK revealed a mean myocardial necrosis of 17 g which was significantly less than in groups II and III. These patients had a normal left ventricular end-diastolic pressure, a normal stroke work index (61 ± 15 g m/m²), and a normal cardiac index (2.7 ± 0.3 l./min per m²). No clinical signs of left ventricular failure were observed. With the exception of one patient, who died from acute cardiac rupture, all patients survived.

About 50 per cent of all patients studied belonged

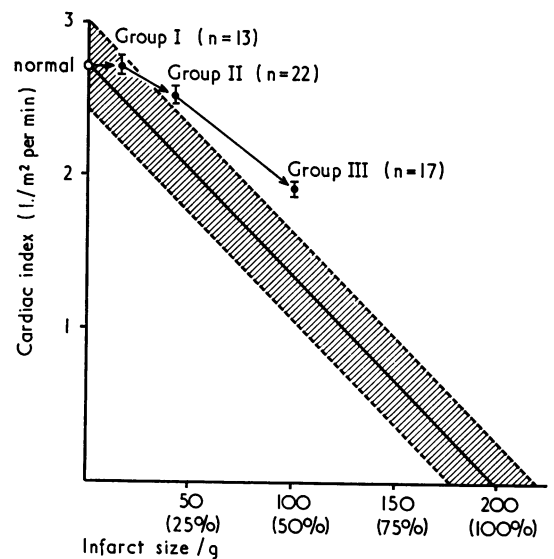


FIG. 5 This figure illustrates the relation between cardiac index and infarct size. The normal value of cardiac index according to the mean age of the whole patient population was estimated to be 2.7 l./min per m² (Guyton, Jones, and Coleman, 1973) and an average left ventricular weight of 200 g was assumed (Harnarayan *et al.*, 1970). Cardiac index decreased with increasing infarct size but remained above the theoretically expected reduction.

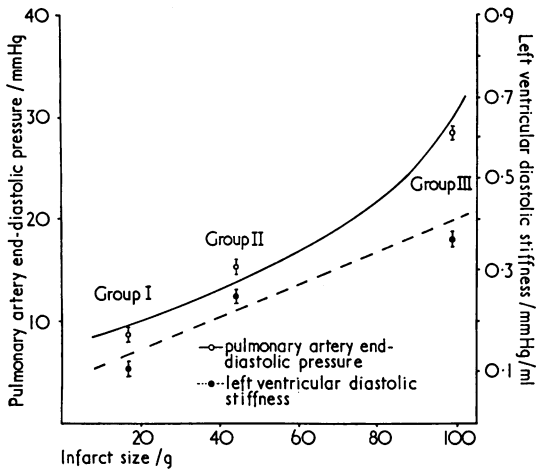


FIG. 6 Left ventricular diastolic stiffness is probably directly related to the infarct size. With increasing infarct size and diastolic stiffness pulmonary artery end-diastolic pressure is likewise raised.

to group II. Their average loss of myocardium was 42 g. Left ventricular filling pressure ranged between 12 and 20 mmHg with a mean of 16.3 ± 0.4 mmHg. In contrast to this increase in the end-diastolic pressure in the left ventricle there was no corresponding decline in stroke work index and cardiac index, indicating the involvement of some compensatory mechanisms.

The largest infarcts as estimated from the CPK concentrations with an average of 99 g were observed in group III with pulmonary artery end-diastolic pressures > 20 mmHg. Stroke work index (27.5 ± 5.7 g m/m²) and cardiac index (1.9 ± 0.2 l./min per m²) were significantly reduced compared to groups I and II. Complicated infarctions belonged to this group and 87 per cent of patients with cardiogenic shock were in group III.

The clear-cut difference in enzyme rise between the 3 groups demonstrates that on a statistical mean the degree of impaired cardiac function is primarily based on the amount of recent myocardial necrosis. This loss of contractile mass may be expected to result in a reduction of cardiac index directly related to the size of the infarct, if there were no compensatory mechanisms and the infarct area were completely stiff (Swan *et al.*, 1972). Fig. 5 shows, that, in fact, the cardiac index declined with increasing infarct size. However, in all 3 groups the cardiac index remained above the theoretical decrease which would have been expected with infarction of 9, 21, and 50 per cent of the left ventricle. From the compensatory mechanisms which affect cardiac index, heart rate and afterload can be excluded, because in the groups under discussion no change from normal was observed. Several studies in animals (Hood *et al.*, 1970) and estimation of left ventricular volume by ultrasound in humans (Broder and Cohn, 1972) have shown that there is no essential increase of

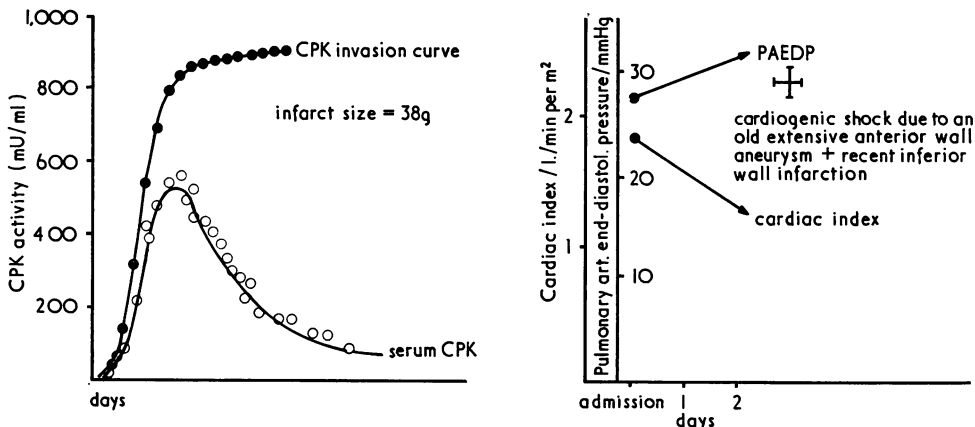


FIG. 7 The CPK serial values and the CPK invasion curve in a patient with an acute inferior wall infarction of 38 g are shown in the left part of Fig. 7. At the time of admission his cardiac index was 1.9 l./min per m² and his pulmonary artery end-diastolic pressure was 28 mmHg (right part of Fig. 7). The patient died on the 3rd day in cardiogenic shock. The discrepancy between the relatively small infarct size and the severe haemodynamic changes was explained by an old anterior wall aneurysm in addition to the acute myocardial infarction.

left ventricular end-diastolic volume immediately after myocardial infarction. Accordingly, the relative maintenance of cardiac index above the theoretical reduction seems not to be due to the Starling mechanism. The behaviour of the cardiac index as illustrated in Fig. 5 may be explained by two mechanisms. First, the stiffening of the infarct area results in an increase of stroke volume and cardiac output as compared to a more compliant infarction, since the contraction of the non-infarcted myocardium can only lead to an optimal pressure build-up, when a stiff infarction area serves as a firm resistance. Secondly, contractility of the non-infarcted myocardium was not diminished, but rather was increased. Even in patients of group III with an average infarct weight of 99 g (50% of the left ventricle) the non-infarcted myocardium does not fail to compensate. In considering these points it should be noted that the haemodynamic data were obtained at the time of admission and that in the course of the illness haemodynamic values, especially those of group III, often worsened considerably.

As mentioned above, the elastic properties of the infarct area play an important role in cardiac performance. Previous studies from our laboratory indicated a fourfold increase of mean left ventricular diastolic stiffness after infarction (Bleifeld *et al.*, 1974a,b), caused by a regional increase of wall stiffness restricted to the infarct area and not affecting the viable myocardium. Therefore the increase of stiffness after infarction should be dependent on the extent of myocardial necrosis. Fig. 6 shows that mean diastolic left ventricular stiffness is probably linearly correlated to the infarct size. Left ventricular filling pressure is raised likewise. At present, it is only speculation as to whether the rise in left ventricular end-diastolic pressure in the early phase of acute myocardial infarction is exclusively due to the stiffening of the infarct area or whether it may in addition be affected by an increase in left ventricular end-diastolic volume. In the animal experiments of Hood *et al.* (1970) left ventricular filling pressure increased after coronary artery ligation in the presence of an unaltered left ventricular end-diastolic volume. Recent studies from Broder and Cohn (1972) in the acute phase of human myocardial infarction showed no change in end-diastolic volume in the left ventricle compared to normal as calculated from echocardiograms. The increased left ventricular filling pressure seems to be mainly caused by changes in the wall stiffness.

Another aspect of our study is the possibility of separating the consequences of the recent necrosis from previous changes. The actual haemodynamic alterations measured in an individual patient are the

combined result of old and recent loss of myocardium, whereas serial enzyme changes only reflect the amount of recent necrosis. This is shown in Fig. 7, which summarizes the haemodynamic and CPK serial values of a patient with acute inferior wall infarction who died on the 3rd day in cardiogenic shock. At the time of admission pulmonary artery end-diastolic pressure was 28 mmHg and the cardiac index was 1.9 l./min per m², indicating the poor prognosis. However, infarct size was only 38 g, which is usually too small to cause cardiogenic shock. Besides the relatively small acute inferior wall infarction necropsy revealed a 5 × 7 cm old aneurysm of the anterior wall. The case illustrates that serial determinations of CPK and haemodynamic studies can be combined to separate old from recent myocardial changes.

In conclusion then, it can be stated that haemodynamic and serial enzyme evaluations give useful information for assessing the immediate and long-term prognosis.

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