

Correlation of mortality rate and serum enzymes in myocardial infarction

Test of efficiency of coronary care

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In patients with acute myocardial infarction treated in a coronary care unit, there was a linear relation between the mortality rate, and the serum aspartate aminotransferase (SGOT) and lactic dehydrogenase (LDH) levels. The degree of correlation was highly significant. Practically all the variation in mortality rate was explained by variation in the height of these enzymes, and hence in the extent of infarction. Furthermore, there was no mortality over and above that described by the regression coefficients. It was concluded that treatable arrhythmias, independent of the severity of infarction, did not contribute significantly to the death rate. The regression of mortality rate on serum enzyme levels is proposed as a test of the efficiency of a coronary care unit.

The efficacy of coronary care units in reducing the mortality rate of acute myocardial infarction is hard to determine (Oliver, Julian, and Donald, 1967; Rockwell, 1969; Lown, Klein, and Hershberg, 1969). Furthermore, there are difficulties in assessing the efficiency of an individual unit (Klaus *et al.*, 1970). It was shown previously that in patients treated in the coronary care unit of the Royal Newcastle Hospital, an increase of the SGOT above 200 Sigma-Frankel units/ml or of the LDH above 2,000 Berger-Broida units/ml was associated with a significantly increased mortality rate (Chapman, 1971). It is now suggested that the correlation of mortality rate and serum enzyme levels provides a test of a unit's efficiency.

Patients and methods

There were 536 admissions to the coronary care unit in the 16 months from its opening on 20 August 1968. Acute myocardial infarction, according to previously defined criteria (Chapman, 1970), was present in 376 cases. Details of management have been given (Chapman, 1970, 1971). The mortality rate refers to the whole time in hospital. The mean time in hospital was 21 days.

For the SGOT and LDH estimations, blood was taken at approximately 24 hours and 3 days,

respectively, after infarction. Many patients had multiple specimens taken, especially if the exact time of infarction was not known, or if reinfarction was suspected. The highest reading was the one analysed. Some patients died before the enzymes were due to be estimated. In some other cases, specimens were taken at the wrong time, were not taken at all, or proved unsatisfactory for analysis. If an alternative cause for increase was present at the same time, the result was discarded. The result of a 24-hour SGOT was available in 262 cases, and of a 3-day LDH in 315 cases.

The study was prospective. It is part of a larger analysis being carried out with the aid of an NCR 500 computer (Chapman, 1971). The regression constants, the coefficients of correlation and of determination, and the significance of the correlation coefficients were calculated using standard statistical methods (Yeomans, 1968). Similar analyses were performed by the present author on data published by Kibe and Nilsson (1967).

Results

The mortality rate was 16.2 per cent for the 376 cases. For patients in whom the SGOT was estimated, the rate was higher, but not significantly (Table). It was lower in those for whom the LDH was estimated, because these were the survivors of the first 48 hours, when the greatest death rate applied.

The mortality rate increased, overall, in proportion to the levels of the enzymes (Table). When the values were plotted, a

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TABLE Distribution of cases according to SGOT and LDH levels, with associated mortality

	No. of cases	No. of deaths	Mortality rate (%)	
*SGOT	1-40	45	4	8.9
	41-50	37	2	5.4
	51-100	72	9	12.5
	101-150	45	4	8.9
	151-200	27	4	14.8
	≥201	36	24	66.7
	Total	262	47	17.9
†LDH	1-350	5	0	0
	351-550	24	0	0
	551-1,000	136	9	6.6
	1,001-1,500	56	4	7.1
	1,501-2,000	42	5	11.9
	≥2,001	52	21	40.4
	Total	315	39	12.4

* In Sigma-Frankel units/ml.

† In Berger-Broida units/ml.

linear relation was found (Fig. 1 and 2)¹. The coefficients of linear correlation were very high. The coefficient for each enzyme differed from zero, to a highly significant degree. The coefficient of determination (r^2) was 0.933 for the SGOT, and 0.956 for the LDH. That is to say, 93 per cent of the variation in mortality rate was explained by variation in the SGOT level, and 96 per cent by variation in the LDH level. With low values of both enzymes, the regression lines passed close to zero on the Y axis. Thus, there was no mortality over and above that which was related to the enzyme levels, and which was described by the regression coefficients.

Discussion

These data suggest that, in cases treated in the coronary care unit, mortality was related almost exclusively to extent of myocardial infarction. For both enzymes, there was a highly significant linear correlation between mortality rate and enzyme level. Ninety-three per cent of the variation in the mortality rate was explained by variation in the level of the SGOT, and 96 per cent by variation in that of the LDH. The height to which these enzymes rise is proportional to the volume of the infarct (West, Eshchar, and Zimmerman, 1966; Killen and Tinsley, 1966; Kibe and Nilsson, 1967; Whitby, 1968).

There appear to be two components to the mortality of acute myocardial infarction

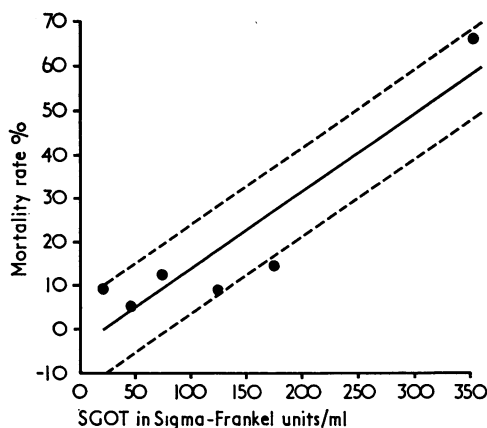


FIG. 1 Correlation of mortality rate and SGOT level ($r = 0.966$; $P < 0.0002$; $Y = 0.178 \times - 3.745$). Exact values for readings above 200 units/ml were not reported; an upper limit of 500 units was assumed. The distance of each dotted line from the regression line is twice the standard error of estimate.

Co-ordinates of points: 20.5, 8.9; 45.5, 5.4; 75.5, 12.5; 125.5, 8.9; 175.5, 14.8; 350.5, 66.7.

Co-ordinates of ends of regression line: 20.5, -0.1; 350.5, 58.6.

Co-ordinates of ends of dotted lines:

Upper: 20.5, 10.1; 350.5, 68.8. Lower: 20.5, -10.3; 350.5, 48.4.

FIG. 2 Correlation of mortality rate and LDH level ($r = 0.976$; $P < 0.0002$; $Y = 0.012 \times - 5.075$). Exact values for readings above 2,000 units/ml were not reported; an upper limit of 5,000 units was assumed. The distance of each dotted line from the regression line is twice the standard error of estimate.

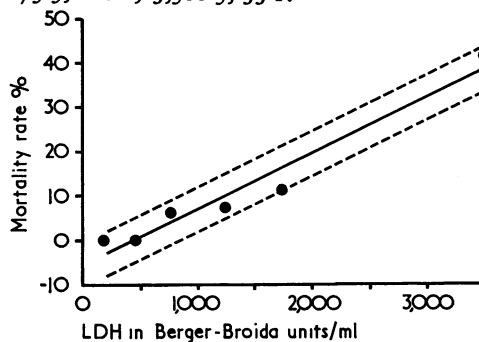
Co-ordinates of points: 175.5, 0.0; 450.5, 0.0; 775.5, 6.6; 1,250.5, 7.1; 1,750.5, 11.9; 3,500.5, 40.4.

Co-ordinates of ends of regression line:

175.5, -2.9; 3,500.5, 38.4.

Co-ordinates of ends of dotted lines:

Upper: 175.5, 2.4; 3,500.5, 43.7. Lower: 175.5, -8.2; 3,500.5, 33.1.



¹ Each point on the graph represents a number of patients. The position of the regression lines is modified accordingly.

treated outside coronary care units. The first is directly related to the size of the infarct. Thus, a significant linear correlation between mortality and serum enzyme levels can be found in the series of Kibe and Nilsson (1967). The second component is an increment which is unrelated to the severity of infarction. It presumably results from the primary arrhythmias which may occur even with small infarcts (Stock, Goble, and Sloman, 1967; Adgey *et al.*, 1969). The latter therefore have a mortality rate out of proportion to their size (Robinson, Sloman, and McRae, 1964; Lown *et al.*, 1967; Whitby, 1968; Isacsson, Westerlund, and Wingstrand, 1969). In the series of Kibe and Nilsson (1967) there was an additional mortality, cut off on the Y axis, over and above that described by the regression coefficient and hence accounted for by the size of infarction. The increment was 21 per cent in the case of the SGOT, and 11 per cent in that of the LDH. It was presumably due to arrhythmias. The different rates for the two enzymes probably reflect the fact that, for any arrhythmia, at least 75 per cent of patients developing it first do so within 72 hours of infarction (Chapman, unpublished observations).

Coronary care cannot be expected to influence the mortality directly related to severity of infarction. It is believed, however, to reduce that resulting from arrhythmias (Lown *et al.*, 1967; Restieaux *et al.*, 1967; MacMillan *et al.*, 1967; Day, 1968; Kimball and Killip, 1968; Norris, Brandt, and Lee, 1969).

In the present series, there was no evidence that primary arrhythmias, unrelated to severity of infarction, contributed significantly to the death rate. Practically all of the variation in the mortality rate was explained by variation in the serum enzyme levels, and hence in the extent of infarction. Furthermore, the regression lines cut off no additional mortality on the Y axis.

It is suggested that the regression of mortality rate on serum enzyme levels provides a test of the efficiency of a coronary care unit. If there is a statistically significant linear correlation coefficient, and the regression line cuts off no mortality on the Y axis, then the mortality rate is related only to the extent of infarction, and the number of patients dying from treatable arrhythmias is insignificant. On the other hand, if there is some mortality in addition to that described by the regression coefficient, patients may be dying of such arrhythmias. For this test to be valid, the enzymes must be estimated at the correct time intervals after infarction.

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