British Heart Journal, 1974, **36**, 786–790.

Prognosis after myocardial infarction
Six-year follow-up

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The mortality pattern occurring 3 to 6 years after recovery from myocardial infarction is described in a group of 349 patients. Mortality in this group had been previously related to prognostic factors recorded prospectively at the time of admission to hospitals, and separate coronary prognostic indices for hospital and three-year survival had been formulated. The present follow-up shows that mortality between 3 and 6 years can still be related to factors dependent on the degree of myocardial damage sustained, and can be predicted by the coronary prognostic index for 3-year survival. Hypertension also had an adverse effect on survival, but the effect which emerges over the 3- to 6-year follow-up is apparent only in patients with an otherwise good prognosis.

We have previously reported on clinical factors, present on admission to hospital, which were associated with mortality in a group of 757 patients with myocardial infarction admitted to three hospitals in Auckland during one year (1966–67) (Norris *et al.*, 1969, 1970). We incorporated numerical weightings for these factors into coronary prognostic indices for survival in hospital (Norris *et al.*, 1969), and for 3 years after discharge from hospital (Norris *et al.*, 1970). The present paper reports progress of the 3-year survivors of this same group of patients at a median period of 6 years after discharge. It shows that the chances of survival between 3 and 6 years after recovery were, as in our shorter term surveys, associated with age and factors dependent on the severity of myocardial damage. These factors were radiological evidence of pulmonary venous congestion, pulmonary oedema, and cardiac enlargement at the time of the infarct.

Patients and methods

Data on all patients, taken prospectively at the time of admission to hospital, were held on punch cards as previously described (Norris *et al.*, 1969, 1970, 1968a; Norris, Caughey, and Scott, 1968b). Follow-up was carried out as previously (Norris *et al.*, 1970), mainly by letters to general practitioners who were caring for the patients, to the patients themselves, or to their relatives. Information requested was restricted to an inquiry as to whether the patient was working, well but not working, incapacitated, or dead. If death had occurred, the time, place, and circumstances of death were requested. Survival was correlated with risk factors (hypertension, diabetes, and obesity), recorded at the time of infarction, and with the coronary prognostic index for 3-year survival. The diagnosis of hypertension was based either on a positive history from the patient or his referring practitioner, or the finding of high blood pressure requiring treatment during hospital admission.

Received 22 October 1973.

Of 530 patients followed after discharge from hospital (Norris *et al.*, 1970), 357 were known to be alive at 3 years. Of these, 349 (98%) were traced at 6 years, comprising 66 per cent of those who were originally discharged from the hospitals in 1966–67.

Results

Seventy-eight patients had died between the 3- and 6-year follow-ups, this number being 22 per cent of the 357 three-year survivors, and 15 per cent of the original group of 530. Mortality at 3 years had been 33 per cent, so that the total 6-year mortality rate was 48 per cent of hospital survivors.

Mortality rates were related to the presence of the previously described clinical prognostic factors which had been present at the time of infarction 6 years before. Table 1 includes those factors which were included in the coronary prognostic index for 3-year survival. Table 2 includes those factors previously found not to influence long-term survival, and which were therefore not included in the prognostic index. In each Table, mortality rates are given for 0 to 3, 3 to 6, and 0 to 6 years. The significance of differences for mortality between grades of severity of the clinical prognostic factors are indicated in the Tables.

TABLE 1 *Mortality up to six years related to clinical factors included in long-term coronary prognostic index*

Prognostic factor and variations	*No. of patients*	*Mortality rate (%) (0–3 yr)*	*Mortality rate (%) (3–6 yr)*	*Total mortality rate (%) (0–6 yr)*
Age (yr)				
<50	83	14	14	26
50–59	167	26*	19	40*
60–69	163	38*	20	51*
70–79	91	43	42†	67*
80–89	26	58	40	75
Heart size				
Normal	306	23	19	38
Enlarged	224	46†	29*	62†
Lung fields				
Normal	322	23	17	36
Pulmonary congestion	103	32	30*	52†
Pulmonary oedema	105	64†	43	80†
History of previous ischaemia				
None	252‡	23	19	38
Previous angina, no infarct	129	31	26	49*
One or more previous infarcts	148	50†	28	64†
Total cases	530	33	22	48

Significance for differences in mortality rates (*P<0·05; †P<0·01) are calculated between successive gradations of severity of each factor as set out vertically in the table. Mortality after pulmonary oedema at 3 to 6 years was significantly greater than mortality with normal lung fields (P<0·01).
‡ History of ischaemia was not recorded in one patient.

TABLE 2 *Mortality up to 6 years related to clinical factors not included in long-term prognostic index*

Factor and variation	*No. of patients*	*Mortality rate (%) (0–3 yr)*	*Mortality rate (%) (3–6 yr)*	*Total mortality rate (%) (0–6 yr)*
Position of infarct				
Anterior transmural	156	35	27	53
Inferior transmural	152	28	19	42
Subendocardial	206	32	20	46
Left bundle-branch block	16	50	38	69
Admission systolic blood pressure (mmHg)				
>125	360	30	22	45
95–124	142	33	23	48
<95	28	54	23	65
Diabetes				
Present	52	44	24	57
Absent	478	31	22	46
Hypertension				
Present	102	36	32*	57*
Absent	428	32	20	46
Obesity†				
Obese	175	30	18	43
Normal	224	34	22	49
Thin	21	43	10	49
Not recorded	110	32	32	54
Total cases	530	33	22	48

* Mortality significantly different from mortality of normotensive patients (P<0·05). Other mortality differences in this table are not significant.
† Graded according to height-weight details provided by patients at time of hospital admission.

TABLE 3 *Mortality in hypertensive and normotensive patients related to long-term coronary prognostic index*

Coronary prognostic index for long-term survival	*Total cases*	*Hypertensive No. of cases*	*6-year mortality (%)*	*Normotensive No. of cases*	*6-year mortality (%)*
<3	170	28	39*	142	20
3–5	141	34	59*	107	39
6 or greater	211	39	69	172	71
Total cases†	522	101	57*	421	46

* Mortality significantly different from normotensive mortality rate ($P < 0.05$).
† Excludes 8 patients lost between the 3- and 6-year follow-ups.

Survival between 3 and 6 years was significantly reduced in patients over 70 years of age at the time of infarction, and in those who had pulmonary congestion, pulmonary oedema, or radiological evidence of cardiomegaly at the time of infarction. Survival was also reduced in patients who had had recurrent infarction, but in contrast to the figures from 0 to 3 years, the difference was not significant at 3 to 6 years.

When the total mortality of 0 to 6 years was considered (right side of Table 1), there was a progressive increase in mortality rate for each grade of severity of all four prognostic factors. Most striking was the 80 per cent mortality rate for hospital survivors who had suffered from pulmonary oedema or interstitial oedema at the time of the original infarct. Summation of these factors to the coronary prognostic index for 3-year survival (Fig.), showed a progressive increase in 6-year mortality rate from 23 per cent (coronary prognostic index less than 3) up to 100 per cent (coronary prognostic index 12 or greater).

Mortality rates for those factors previously found not to affect significantly the 3-year survival showed less striking differences (Table 2). However, mortality for hypertensive patients was significantly increased from the 3 to 6 years, and for the total 0 to 6-year period. This increase was less in degree than for any of the four original prognostic factors listed in Table 1.

The increased mortality for hypertensive patients became more striking when patients were grouped according to the presence of the prognostic factors listed in Table 1 (i.e. by the 3-year coronary prognostic index). Table 3 shows that the increased mortality rates occurred only in those patients who had an otherwise good prognosis (coronary prognostic index < 6). It appeared that the unfavourable prognosis associated with hypertension was overshadowed by the unfavourable late effects of advanced age, cardiomegaly, circulatory failure, or recurrent myocardial damage. When these adverse factors were absent, the ill-effects of hypertension became manifest, and inclusion of a weighting for hypertension at the time of the original calculations would have improved the predictive value of the coronary prognostic index for the more favourable prognostic groups.

A similar reduction in survival rate to that occurring in hypertensives occurred among diabetic patients, but did not attain significance because of the smaller number of diabetics. As with hypertensives, there was suggestive evidence that the increased mortality among diabetic patients occurred mainly in the most favourable prognostic group (coronary prognostic index < 3). However, the number of diabetic patients in this group (17) was

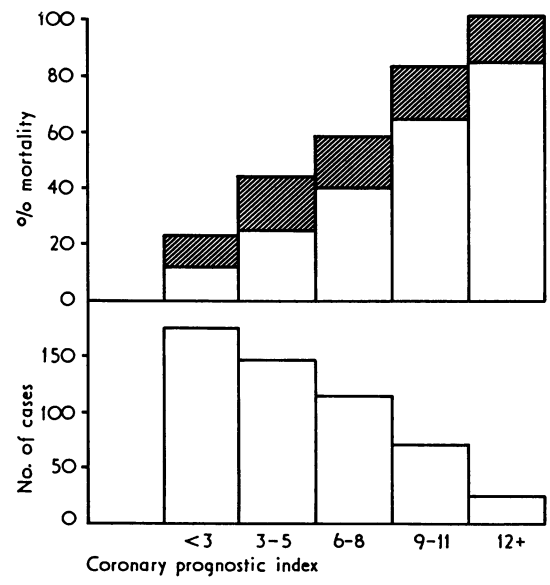

FIG. *Number of patients and percentage mortality rate in five groups of patients who had an increasingly poor prognosis as assessed by the long-term coronary prognostic index. Previously reported 3-year mortality rate is shown by the unshaded histograms, and 3 to 6-year mortality by the shaded histograms.*

too small for differences to attain significance. Obese patients did not fare differently from the non-obese in any prognostic group.

Mortality was higher among patients who had had anterior transmural infarction compared with those who had suffered inferior (posterior) or subendocardial infarction, but again the differences were not significant. Obesity, somewhat loosely defined at the time of admission to hospital (Norris *et al.*, 1969), had no effect on mortality rate.

Discussion

Studies on this original group of 757 patients have shown that survival for up to 6 years after myocardial infarction is related mainly to age, the presence or absence of myocardial ischaemia previous to the infarct, and factors associated with the severity of the infarct itself. Of these three, the last may be the most important. Of all patients who had pulmonary oedema, 45 per cent died in hospital (Norris *et al.*, 1969) and 80 per cent of hospital survivors were dead within 6 years. The total 6-year mortality rate among this subgroup was 89 per cent. This mortality rate was greater than the cumulative 6-year mortality for patients over 70 years of age (82%), or for patients with recurrent myocardial infarction (74%). Follow-up has shown that factors associated with severity of cardiac damage (pulmonary venous hypertension, pulmonary oedema, and cardiomegaly) still operate during the 3- to 6-year postinfarct period. The coronary prognostic index for 3-year survival is thus of value for predicting survival for up to 6 years.

It would be of particular interest to compare the long-term effects of these prognostic factors with those of primary risk factors for coronary artery disease. The Framingham study (Gordon and Kannel, 1971) and similar prospective surveys (Rosenman *et al.*, 1970; Epstein *et al.*, 1965; Keys, 1970) have shown that the major risk factors for cardiovascular mortality in apparently healthy populations are hypercholesterolaemia, hypertension, and cigarette smoking. Diabetic subjects also have an increased mortality (Ostrander *et al.*, 1965), while evidence for an adverse effect of obesity, though suggestive, is by no means conclusive (Rosenman *et al.*, 1970; Epstein *et al.*, 1965). Information is available from the present studies on the effects of hypertension, diabetes, and, less precisely, on obesity. Unfortunately, no data on cigarette smoking or serum cholesterol are available. It is unlikely, however, that serum cholesterol has much predictive value among patients with overt myocardial ischaemia (Shanoff, Little, and Csima, 1970; Frank, Weinblatt, and Shapiro, 1973).

The present follow-up has shown that hypertensive patients have a significantly increased mortality rate at 6 years after infarction. However, this effect is overshadowed by that of the previously described prognostic factors. When these factors are absent, the adverse effects of hypertension become apparent by the 6-year stage of follow-up. It is likely that this effect will become more pronounced among our surviving patients in the future. Of our 271 6-year survivors, 210 (78%) have a long-term coronary prognostic index of less than 6, and are thus in the group in whom hypertension is seen to have an adverse effect. It is of interest to speculate that other primary risk factors might act in this way. Our data gave suggestive, though inconclusive, evidence that diabetes might affect prognosis similarly, though no effect of obesity on either short- or long-term survival could be demonstrated.

It is evident that extensive myocardial damage at the time of infarction has an adverse effect on long-term prognosis which is at least as great as its effect on hospital or short-term mortality. It is possible that measures experimentally to reduce infarct size (Maroko *et al.*, 1971; Willerson *et al.*, 1972; Libby *et al.*, 1973) might have clinical application. If such agents are tested in controlled clinical trials, our studies suggest that long-term as well as short-term mortality rates should be followed in treated and control groups of patients.

Not included in these studies is the pathological factor which may have the greatest effect on prognosis in overt ischaemic heart disease – namely the extent and severity of the coronary atheroma itself (Friesinger, Page, and Ross, 1970; Bruschke, Proudfit, and Sones, 1973). More extensive atheroma might be expected in patients with recurrent myocardial infarction. We are at present studying, in conjunction with a trial of coronary saphenous vein graft surgery, a group of patients who have recovered from recurrent infarction. Survival will be correlated with the extent and distribution of atheroma assessed by arteriography together with the long-term coronary prognostic index, and primary risk factors.

This work has been supported by the Medical Research Council and the National Heart Foundation of New Zealand.

We are grateful to Dr. P. W. T. Brandt for interpretation of the chest *x*-rays.

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