British Heart Journal, 1976, **38**, 921–925.

Prognosis in unstable angina[1]

Ming-Kiat Heng, Robin M. Norris, Bramah N. Singh, and John B. Partridge

From the Departments of Cardiology, Coronary Care, and Radiology, Green Lane Hospital, and the Department of Medicine, University of Auckland, New Zealand

A retrospective study was made of 158 patients with unstable angina admitted to a coronary care unit over a 4-year period. Twenty patients (13 per cent) had myocardial infarcts while in hospital, and of these 3 died; three others died without preceding evidence of myocardial infarction. There was thus an acute mortality rate of 4 per cent. Patients with persisting angina after the first 24 hours and those without a previous history of myocardial ischaemia were more likely to develop a myocardial infarct or to die in hospital.

Follow-up information, ranging from 3 to 7 years, was available in 144 of 152 hospital survivors. Patients older than 60 years ($P<0.05$), with cardiomegaly ($P<0.01$) and with pulmonary venous congestion ($P<0.05$) were found to have significantly increased long-term mortality. Long-term mortality was also found to rise with increasing coronary prognostic index. The average mortality rate for the whole group of hospital survivors was about 5 per cent per annum. Of the 111 patients who were alive at follow-up, 19 (17%) had had a myocardial infarct after leaving hospital, and a similar number had moderate or severe angina.

Many patients with acute myocardial infarction describe a change in the character of angina before the event (Sampson and Eliaser, 1937); the symptom either deteriorates from a previously stable pattern, or recurs after a period of freedom from chest pain. Interest in this phenomenon has arisen because of the possibility that it may herald impending myocardial infarction, the consequences of which might be averted by prompt treatment. Thus, there have been previous trials with anticoagulation therapy (Nichol, Phillips, and Casten, 1959; Wood, 1961); more recently, attention has been directed at emergency myocardial revascularization (Dunkman *et al.*, 1974). At present, however, the place of surgery in unstable angina is uncertain, in part because the long-term prognosis of patients with the condition has not been well documented. Only one previous study has described a follow-up of over 5 years (Gazes *et al.*, 1973). In order to obtain more information on the short and long-term outlook of patients with unstable angina, and the clinical factors that might influence prognosis, we have retrospectively studied a group of such patients admitted to a coronary care unit.

Received 8 March 1976.

[1]This investigation was supported by the Auckland Medical Research Foundation, and the New Zealand Medical Research Council and National Heart Foundation.

Patients and methods

Hospital records of patients admitted to the Green Lane Hospital Coronary Care Unit (CCU) over a four-year period (March 1967 to March 1971) were examined for patients who satisfied our criteria for unstable angina.

Unstable angina was considered to be present if patients had ischaemic cardiac pain at rest or with minimal exertion occurring within 4 weeks before admission, either for the first time, or after a period of stable angina. In all patients, the symptoms had been sufficiently severe to warrant admission to the hospital, and were either crescendo in nature, or associated with one or more prolonged bouts of chest pain lasting up to 30 minutes. These patients were all admitted to the CCU. Patients with significant arrhythmias, severe valvular disease, or evidence of myocardial infarction occurring less than 4 weeks before admission or for up to 48 hours after admission were excluded. Myocardial infarction was diagnosed if, in addition to the characteristic ischaemic pain, at least one of the following two criteria were fulfilled: (a) pathological Q waves, ST segment elevation, or T wave inversion with

evolutionary changes; (b) rise in serum aspartate aminotransferase to over 40 units/ml. Patients who had had previous myocardial infarction or angina for more than 4 weeks were considered to have a previous history of ischaemic heart disease.

From the case notes of these patients details were noted of the following: previous history of ischaemic heart disease, cigarette smoking, hypertension, and diabetes; admission chest *x*-ray film; serial electrocardiograms; biochemical data; persistent chest pain in hospital; and details of medical treatment. The chest *x*-ray films, the majority of which were standard five-foot anteroposterior films taken using portable apparatus, were all obtained within 24 hours after admission, and were examined for heart size and presence of pulmonary congestion by one radiologist (J.B.P.) who had no knowledge of the clinical outcome of the patients in the study; the presence of cardiomegaly was assessed by a method described previously (Norris *et al.*, 1969). Persisting chest pain was considered present if the records indicated that chest pain was present for three or more days after the first 24 hours in hospital, despite adequate bed rest and in most cases administration of nitroglycerin and beta-adrenergic blocking drugs.

To obtain follow-up information, a standard questionnaire was sent to the referring doctors in June 1974 inquiring about the symptomatic status of the hospital survivors with particular regard to angina, or the date and cause of death. If this approach failed, either the patients or their relatives, friends, or neighbours were traced, and information obtained by either interviewing or writing to them. In cases where the details of death were incomplete, further information was obtained from death certificates at the Registry of Deaths in Auckland. Of the survivors who were traced in this manner, the median follow-up was 5 years, range 3 to 7 years.

Results were analysed statistically using the χ^2 test and differences were considered significant when $P < 0.05$ for the two-tailed test.

Results

There were 1757 admissions to the CCU during the four-year period; 158 patients (9%) had unstable angina by our criteria. Of these, 109 were men and 49 women; the average age was 55 years. Thirty-four patients had no previous history of ischaemic heart disease; of the 124 patients who had such a history, 40 had no past history of myocardial infarction, while 84 had had one or more myocardial infarcts in the past.

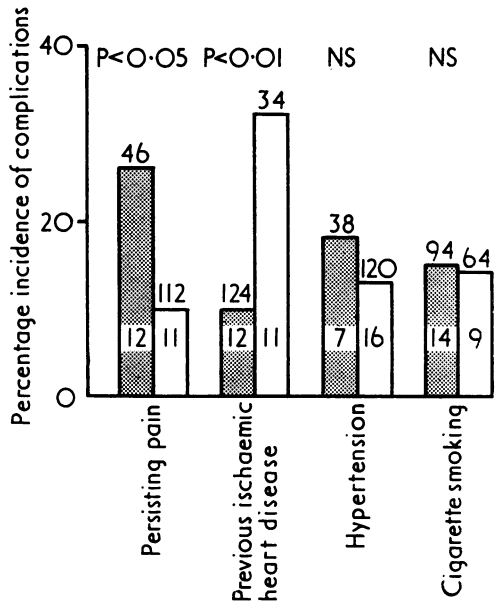

FIG. 1 *Clinical factors related to the occurrence of myocardial infarction or death in hospital. Shaded bars refer to patients with the factors under consideration, and unshaded bars to patients without these factors. The number of patients at risk are indicated above, and the number with complications inside each bar.*

TABLE *Serious complications in hospital*

Complications	*No. of cases*	*Deaths*
Myocardial infarction	20	3
Sudden death without preceding evidence of myocardial infarction	3	3

Complications in hospital

The incidence of myocardial infarction and death in hospital is shown in the Table. Twenty patients (13%) had myocardial infarcts occurring from 48 hours to 3 weeks after admission to hospital, and of these 3 died. Three other patients died without preceding evidence of myocardial infarction, 2 suddenly and 1 from pulmonary embolism. Necropsy of these 3 patients showed no evidence of fresh myocardial infarction in the first 2 patients, and confirmed massive pulmonary embolism in the third. The mortality rate in hospital was thus 4 per cent.

Fig. 1 examines some clinical factors which

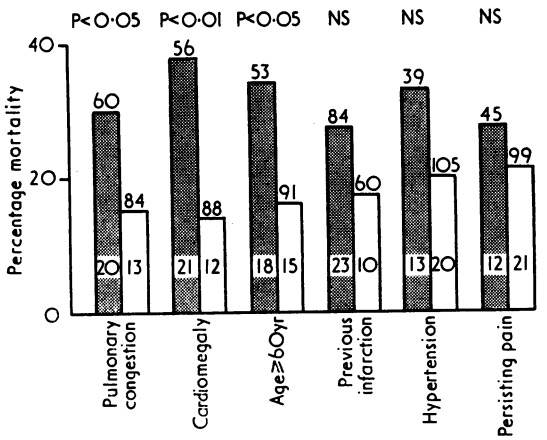

FIG. 2 *Clinical factors related to long-term mortality. Shaded bars refer to patients with the factors under consideration, and unshaded bars to patients without these factors. The numbers of patients at risk are indicated above each bar, and the number of patients who died after leaving hospital inside each bar.*

might be associated with the occurrence of either myocardial infarction or death in hospital. Patients who had persisting pain after the first 24 hours ($P < 0{\cdot}05$), and those without a previous history of ischaemic heart disease ($P < 0{\cdot}01$) were more likely to have a bad short-term prognosis. A history of hypertension or cigarette smoking, however, was not associated with increased risk.

Long-term follow-up

Follow-up information was available in 144 of 152 hospital survivors (95%). This was examined for the presence of factors which might influence the long-term prognosis (Fig. 2). The risk of dying after leaving hospital was found to be associated with age greater than 60 years ($P < 0{\cdot}05$), cardiomegaly ($P < 0{\cdot}01$), and pulmonary congestion ($P < 0{\cdot}05$) as judged from the admission chest *x*-ray film. A history of previous myocardial infarction, hypertension, and the presence of persistent chest pain in hospital were also associated with increased long-term mortality, but the differences did not reach statistical significance.

Since 4 of these factors (age, cardiomegaly, radiological evidence of pulmonary congestion, and a past history of myocardial infarction) are used in a previously described coronary prognostic index (CPI) for long-term survival (Norris *et al.*, 1970), it was of interest to relate the long-term mortality to the CPI of the hospital survivors. Fig. 3 shows the cumulative annual mortality rate for 3 groups of

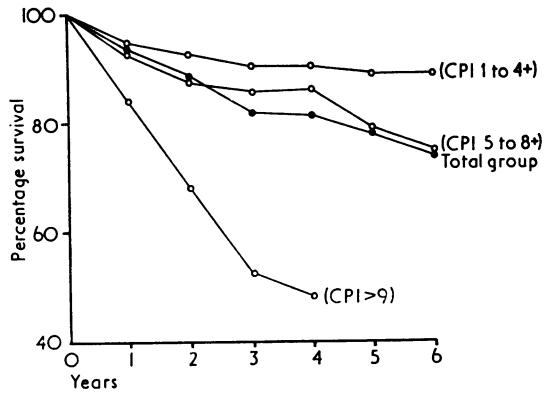

FIG. 3 *Follow-up of 144 hospital survivors, showing cumulative mortality rate related to the coronary prognostic index. The rate for the group with CPI > 9 was not plotted after 4 years, as the number of survivors was too small.*

patients with increasing CPI. It is apparent that mortality rises with increasing CPI. The cumulative mortality of the group with CPI greater than 9 ($n=25$) was significantly greater than that of the group with CPI 1 to 4+ ($n=65$) after 2 years ($P < 0{\cdot}01$) and that of the group with CPI 5 to 8+ ($n=54$) after 3 years ($P < 0{\cdot}005$). The difference in the cumulative mortality rates between the group with CPI 1 to 4+ and that with CPI 5 to 8+ did not reach statistical significance. The yearly mortality rate was about 2 per cent for patients with CPI 1 to 4+, 5 per cent for patients with CPI 5 to 8+, and 13 per cent for patients with CPI > 9. The average mortality rate for the whole group was about 5 per cent over the 6-year period of follow-up.

Of the 111 hospital survivors who were alive at the time of follow-up, 19 (17%) have had a subsequent myocardial infarct. Nineteen patients were found to have moderate to severe angina, i.e. angina occurring with mild exertion or interfering with work or normal activities.

Discussion

One of the particularly difficult areas in clinical cardiology today is the management of unstable angina. Recently, Fowler (1971) called for a widely acceptable objective definition of the condition, and stressed that this should include recent onset angina from a background of good health, a change in the symptomatic pattern of previously recognized ischaemic heart disease, and angiographic confirmation of coronary artery obstruction. The patients in our study satisfy the clinical criteria suggested,

but must be regarded as a selected group in that the nature of the symptoms was such that admission to the hospital was considered necessary. The lack of angiographic data in our study is a disadvantage, but many of these patients were admitted when coronary angiography was either not performed in Green Lane Hospital or was in its infancy there. Furthermore, we were interested in long-term follow-up information, and to have this in conjunction with angiographic data would obviously have required many more years to obtain.

For a number of years, interest in unstable angina has resulted from the possibility that the pattern of changing symptoms might be a warning of impending myocardial infarction. Four weeks after admission, 13 per cent of our patients had developed acute myocardial infarcts, and 4 per cent had died. These results are comparable with those reported recently by others (Fulton *et al.*, 1972; Krauss, Hutter, and De Sanctis, 1972; Gazes *et al.*, 1973) who observed an incidence of myocardial infarction varying from 6 to 17 per cent and an acute mortality rate from 1 to 8 per cent. Our study showed that patients without a previous history of ischaemic heart disease, and those with persisting angina in hospital, appeared to be at increased risk from either infarction or dying in hospital. The former finding was unexpected, and may be the result of a tendency in our centre for patients with known heart disease to be referred preferentially for admission. The observation that patients with persisting angina unrelieved by medical treatment form a high risk group has been made previously (Gazes *et al.*, 1973; Fischl, Herman, and Gorlin, 1973).

The mortality rate of patients with unstable angina in our study was about 5 per cent annually. This might have been higher if coronary angiography had been performed, and patients with normal coronary arteries excluded. The only other study with a long-term follow-up (Gazes *et al.*, 1973) reported an annual mortality of 8 per cent in the first 5 years, and 5 per cent over 10 years. The mortality rate for unstable angina is thus not dissimilar to the annual mortality of 4 per cent reported for patients with stable angina (Frank, Weinblatt, and Shapiro, 1973).

The results of the present study have shown that, as in the case of patients with completed infarction (Norris *et al.*, 1970), long-term survival of patients with unstable angina can be predicted by analysis of clinical factors measurable on admission to hospital. Thus, increasing age, cardiomegaly, and left ventricular failure significantly and adversely affected long-term prognosis, while there was also a tendency for a previous history of ischaemic heart disease and hypertension to predict an unfavourable outcome.

Despite minor differences in the definition of unstable angina, our results agree with those of recent studies (Fulton *et al.*, 1972; Krauss *et al.*, 1972; Gazes *et al.*, 1973) with regard to long-term mortality and incidence of myocardial infarction and death in the acute stage. These results indicate that in the context of ischaemic heart disease the prognosis of patients with unstable angina is not particularly grave. The mortality rate in the acute stage is also comparable with that described for patients treated surgically, which ranged from no mortality (Auer *et al.*, 1971; Bolooki *et al.*, 1974) to 10 per cent (Miller *et al.*, 1973). In studies where randomization of surgical and medical treatments was attempted (Bertolasi *et al.*, 1974; Kloster *et al.*, 1975), no significant difference in acute mortality between surgery and conservative manage- was noted. The effect of surgery on the long-term mortality of unstable angina, however, is at present uncertain, but compared with medical treatment a higher proportion of surgically-treated patients with unstable angina was reported to be symptomatically improved on follow-up in randomized (Bertolasi *et al.*, 1974; Kloster *et al.*, 1975) and non-randomized studies (Scanlon *et al.*, 1973; Conti *et al.*, 1973). These considerations suggest that there is no strong indication for emergency myocardial revascularization for such patients, and that elective surgery should be reserved for patients whose symptoms are unresponsive to medical treatment.

References

Auer, J. E., Johnson, W. D., Flemma, R. J., Tector, A. J., and Lepley, D. (1971). Direct coronary artery surgery for impending myocardial infarction. *Circulation,* **44,** Suppl. 2, 102.

Bertolasi, C. A., Trongé, J. E., Carreño, C. A., Jalon, J., and Vega, M. R. (1974). Unstable angina—prospective and randomized study of its evolution, with and without surgery. *American Journal of Cardiology,* **33,** 201.

Bolooki, H., Sommer, L., Kaiser, G. A., Vargas, A., and Ghahramani, A. (1974). Long-term follow-up in patients receiving revascularization for intermediate coronary syndrome. *Journal of Thoracic and Cardiovascular Surgery,* **68,** 90.

Conti, C. R., Brawley, R. K., Griffith, L. S. C., Pitt, B., Humphries, J. O., Gott, V. L., and Ross, R. S. (1973). Unstable angina pectoris; morbidity and mortality in 57 consecutive patients evaluated angiographically. *American Journal of Cardiology,* **32,** 745.

Dunkman, W. B., Perloff, J. K., Kastor, J. A., and Shelburne, J. C. (1974). Medical perspectives in coronary artery surgery—a caveat. *Annals of Internal Medicine,* **81,** 817.

Fischl, S. J., Herman, M. V., and Gorlin, R. (1973). The intermediate coronary syndrome—clinical, angiographic and therapeutic aspects. *New England Journal of Medicine,* **288,** 1193.

Fowler, N. O. (1971). 'Preinfarctional' angina: a need for an objective definition and for a controlled clinical trial of its management. *Circulation,* **44,** 755.

Frank, C. W., Weinblatt, E., and Shapiro, S. (1973). Angina pectoris in men. Prognostic significance of selected medical factors. *Circulation,* **47,** 509.

Fulton, M., Duncan, B., Lutz, W., Morrison, S. L., Donald, K. W., Kerr, F., Kirby, B. J., Julian, D. G., and Oliver, M. F. (1972). Natural history of unstable angina. *Lancet,* **1,** 860.

Gazes, P. C., Mobley, E. M., Jr., Faris, H. M., Jr., Duncan, R. C., and Humphries, G. B. (1973). Preinfarctional (unstable) angina—a prospective study—ten year follow-up. *Circulation,* **48,** 331.

Kloster, F., Kremkau, L., Rahimtoola, S., Griswold, H., Ritzmann, L., Neill, W., and Starr, A. (1975). Prospective randomized study of coronary bypass surgery for chronic stable angina. *Circulation,* **52,** Suppl. 2, 90.

Krauss, K. R., Hutter, A. M., Jr., and DeSanctis, R. W. (1972). Acute coronary insufficiency: course and follow-up. *Circulation,* **45-46,** Suppl. I, 66.

Miller, D. C., Cannom, D. S., Fogarty, T. J., Schroeder, J. S., Daily, P. O., and Harrison, D. C. (1973). Saphenous vein coronary artery bypass in patients with 'preinfarction angina'. *Circulation,* **47,** 234.

Nichol, E. S., Phillips, W. C., and Casten, C. G. (1959). Virtue of prompt anticoagulant therapy in impending myocardial infarction: experiences with 318 patients during a 10-year period. *Annals of Internal Medicine,* **50,** 1158.

Norris, R. M., Brandt, P. W. T., Caughey, D. E., Lee, A. J., and Scott, P. J. (1969). A new coronary prognostic index. *Lancet,* **1,** 274.

Norris, R. M., Caughey, D. E., Deeming, L. W., Mercer, C. J., and Scott, P. J. (1970). Coronary prognostic index for predicting survival after recovery from acute myocardial infarction. *Lancet,* **2,** 485.

Sampson, J. J., and Eliaser, M. (1937). The diagnosis of impending acute coronary artery occlusion. *American Heart Journal,* **13,** 675.

Scanlon, P. J., Nemickas, R., Moran, J., Talano, J. V., Amirparviz, F., and Pifarre, R. (1973). Accelerated angina pectoris: clinical, hemodynamic, arteriographic and therapeutic experience in 85 patients. *Circulation,* **47,** 19.

Wood, P. (1961). Acute and subacute coronary insufficiency. *British Medical Journal,* **1,** 1779.

Requests for reprints to Dr. R. M. Norris, Coronary Care Unit, Green Lane Hospital, Auckland 3, New Zealand.