Cardiac pain at rest

Management and follow-up of 100 consecutive cases

NICHOLAS BROOKS, CAROLE WARNES, MARTIN CATTELL,
RAPHAEL BALCON, MICHAEL HONEY, CLIVE LAYTON,
MARVIN STURRIDGE, JOHN WRIGHT

From the Cardiac Department, The London Chest Hospital, London

SUMMARY One hundred consecutive patients, admitted to the coronary care unit with cardiac pain at rest but no evidence of recent myocardial infarction have been followed up for nine to 26 (mean 14) months. They were treated initially with bed rest, beta-adrenergic blockade, and nitrates.

In 54 patients pain subsided within 24 hours. Coronary angiography was carried out in 46. Thirty-five had coronary artery lesions and three had spasm in normal coronary arteries. One had hypertrophic cardiomyopathy and seven had normal findings. Seventeen patients with previous angina and severe coronary disease were operated on, with one death and one perioperative infarction; two died late, 12 were symptom free, and two had angina. Seven of 18 patients treated medically had recurrent angina and underwent operation. Of the 11 unoperated patients, one died, three had angina, and seven were symptom free. Two of the eight patients who were not catheterised developed infarction, four had angina, and three were symptom free.

Recurrent pain continued for more than 24 hours in 46 patients, and all underwent angiography. Forty-three had coronary artery disease and 34 underwent early bypass surgery; there were two operative deaths and three perioperative infarctions. Twenty-six were symptom free at follow-up. Of the nine unoperated patients with coronary disease, four developed infarction, two were operated on for recurrent angina, two were symptom free, and one had mild angina.

Optimal management of patients with pain at rest can be determined only with knowledge of the coronary artery anatomy and of left ventricular function. Many respond initially to intensive medical treatment and coronary angiography can be performed electively. In those with continuing pain, urgent angiography is required and can be done safely.

Cardiac pain occurring at rest, without evidence of myocardial infarction, either as a presenting symptom or in a patient known to have ischaemic heart disease, is a clinical problem which has received much attention in recent years. Reports of the immediate and long-term prognosis vary widely,¹⁻³ however, and the most appropriate management has been uncertain. Encouraged by the low risk of coronary arteriography in patients with rest pain,^{4,5} the prognostic information obtained from knowledge of the coronary artery anatomy,^{6,7} and the undoubted effectiveness of surgery in the relief of "unstable angina",^{5,8,9} we have evolved a regimen of early investigation for all patients, with operation for those with certain unfavourable features. The policy became established by the end of 1976, and this paper describes the clinical course and follow-

up of 100 consecutive patients admitted to hospital from 1 January 1977.

Patients

Seventy-five patients were referred by their family doctors and 25 were transferred from other hospitals. They were admitted to the coronary care unit between January 1977 and May 1978. There were 85 men and 15 women aged between 36 and 73 (mean 55) years. All had experienced one or more recent episodes of prolonged chest pain at rest, which was thought by a cardiologist to be cardiac in origin. None had electrocardiographic or enzyme evidence of recent myocardial infarction. Patients who experienced only nocturnal, decubi-

tus, or emotionally-induced angina were not included, and we also excluded those with atypical pain in whom coronary arteriography was carried out to resolve diagnostic uncertainty. Thirty patients had had a myocardial infarction in the past, and the admission electrocardiogram was abnormal in 76 (pathological Q waves, ST segment or T wave changes, or left bundle-branch block) and normal in 24.

Patients were treated with bed rest, regular nitrates, and a beta-adrenergic blocking agent. All received oral isosorbide dinitrate 10 mg four hourly, with additional 5 mg doses sublingually during pain. More recently we have been giving hourly sublingual isosorbide in addition to the oral dose, whether or not pain was present. Propranolol was used unless there was a definite history of asthma, in which case metoprolol or acebutolol was prescribed. The starting dose of propranolol was 120 mg daily, and this was increased to 320 mg daily or until the pulse rate fell to less than 60 per minute. Those who continued to experience pain for more than 24 hours after admission were investigated early by coronary angiography and left ventriculography. Patients whose symptoms resolved within 24 hours had elective cardiac catheterisation, usually during the same hospital admission.

Significant coronary artery disease was considered to be present when at least one major vessel had its diameter reduced by more than 70 per cent. The terms single, double, or triple vessel disease are used to indicate disease within one, two, or three of the principal coronary artery systems (the right, left anterior descending, or circumflex). Left ventricular function was assessed from a single plane (RAO) ventriculogram with ejection fraction measured by the area-length method using a planimeter.

On the basis of the angiocardiographic findings and clinical course, a decision was made in each case either to continue with medical treatment or to refer the patient for aortocoronary bypass operation. In general those with continuing pain were treated by early operation, but if they had single vessel disease more time (up to 48 hours) was allowed to see if they would settle. In patients whose pain subsided, elective operation was usually advised for those with multiple vessel or left main coronary disease, particularly if they had a history of previous angina.

Operation was carried out on cardiopulmonary bypass using a bubble oxygenator, with mild hypothermia. Reversed saphenous vein was used as the bypass graft in all cases, with aortic cross-

clamping during performance of the distal anastomosis.

Perioperative myocardial infarction was diagnosed electrocardiographically by the occurrence of new pathological Q waves, loss of R wave height in the praecordial leads, or the development of left bundle-branch block.

All surviving patients have been followed up for between nine and 26 months (mean follow-up period 14 months).

Results

We have considered the patients in two groups: those whose symptoms resolved within 24 hours of admission to hospital, and those who continued to have pain after this time despite intensive medical treatment.

PATIENTS RESPONDING TO MEDICAL TREATMENT

Angina subsided within 24 hours in 54 patients.

Cardiac catheterisation was not carried out in seven because of advanced age, poor general condition, or because they refused investigation. One of these patients was readmitted with a myocardial infarction four days after discharge from hospital. At late follow-up three had exertional angina, one continued to have intermittent rest pain, and the remaining three (including the patient readmitted with infarction) were symptom free.

One patient had a myocardial infarction five days after admission. He made an uncomplicated recovery and was readmitted for coronary angiography and operation two months later. Though reinvestigation has shown the presence of three satisfactory grafts, he had mild exertional angina at follow-up.

Cardiac catheterisation was carried out in the other 46 patients, in 43 during the same hospital admission, and in the remaining three within 12 weeks. No complications resulted from the procedure.

Seven patients had normal findings. Another four had no evidence of fixed obstructive coronary disease, but one of these had hypertrophic cardiomyopathy, one developed spontaneous coronary artery spasm, and two developed spasm in response to intravenous ergometrine.¹⁰ All three patients with spasm had associated chest pain and ST segment elevation on the electrocardiogram. Of these 11 patients without fixed obstructive coronary artery disease, 10 were symptom free at follow-up, and one with spasm had intermittent chest pain.

The remaining 35 patients had significant coronary artery obstructions. Six had single vessel

disease, 13 had double vessel disease, and 16 had stenosis or occlusion of all three major coronary arteries; one had an additional stenosis of the left main coronary artery.

It was decided to treat 18 patients medically, but seven were readmitted within seven months with severe angina (four with recurrent rest pain) and underwent operation. Of these seven surgical patients, none died, but one had a perioperative myocardial infarction. At follow-up four were symptom free and one had mild angina. Two had severe recurrent angina resulting from occlusion of their grafts; both have had a second operation and were symptom free at the time of discharge from hospital. At follow-up of the 11 unoperated patients, one died from a myocardial infarction, three continued to have angina, and seven were symptom free.

It was decided to treat 17 patients by elective surgery. One was readmitted before the planned date of operation with chest pain and a small rise in cardiac enzymes; because of continuing pain he had an emergency triple vein graft, and at follow-up he had mild exertional angina. Of the remaining 16 patients, one died during operation: an elderly

diabetic patient with hypertension and poor left ventricular function (ejection fraction 15%). She had a prolonged operation requiring four grafts and extensive endarterectomy; and failed to regain consciousness. One patient had a perioperative myocardial infarction. There were two late deaths, neither of which could be attributed with certainty to coronary disease: one was from a stroke and the other from a road accident. At follow-up of the 13 survivors 12 were symptom free and one had recurrent angina.

PATIENTS WHO DID NOT RESPOND TO MEDICAL TREATMENT

Forty-six patients continued to experience recurrent rest pain after 24 hours of medical treatment, and all underwent coronary angiography within 48 hours of admission. No complications resulted from the procedure.

Three patients had normal findings, with no evidence of coronary artery spasm, either spontaneous or provoked by ergometrine. At follow-up two are symptom free and one has intermittent chest pain.

Forty-three patients had significant coronary

Fig. 1 Summary of the clinical course of 54 patients whose pain subsided within 24 hours of admission to hospital. CAD, coronary artery disease; 1VD, single vessel disease; 2VD, double vessel disease; 3VD, triple vessel disease; MI, myocardial infarction; Reop, reoperation; Periop, perioperative; HCM, hypertrophic cardiomyopathy.

artery disease. Seven had single vessel disease, 10 had double vessel disease, and 26 had triple vessel disease; five also had stenosis of the left main stem. Thirty-four patients were referred for early vein graft operation. In four the operation was preceded by intra-aortic balloon pumping, either because of severe impairment of left ventricular function (two patients with ejection fractions of 30%), or because of continuing severe pain at a time when the operating theatre was not available (two patients). There were two perioperative deaths, both in patients with poor left ventricular function (ejection fractions 30 and 42%), one of whom had been treated with the balloon pump. There were three perioperative myocardial infarctions. At follow-up of the 32 survivors, 26 were symptom free, four had mild, and one had severe angina. Another patient with severe recurrent angina had had a second operation for graft occlusion.

Two patients initially declined surgical treatment, but were later readmitted with recurrent rest pain and underwent operation. At follow-up one was symptom free and one had angina.

Three patients, all with single vessel disease, were treated medically, and at follow-up two were symptom free and one had mild angina.

Four patients developed myocardial infarction between two and five days after admission. One

had single vessel disease and infarction occurred four days after coronary angiography during a trial of medical treatment. In the others it was difficult to determine the precise timing of infarction in relation to recurrent attacks of pain, and angiography was carried out in all. One subsequently underwent elective operation and became symptom free. Of the other three who developed infarction, two had persistent angina and one was symptom free.

Discussion

Unlike many investigations of "unstable angina" our study was restricted to patients with cardiac pain at rest, because they constitute a relatively well-defined clinical group with a worse prognosis than those with recent onset or progressive effort angina.^{9 11 12} Their management was based on guidelines derived from previous experience, and since the choice of medical or medical and surgical treatment was determined by the clinical and angiographic findings in each case, we did not attempt to compare results in the two groups of patients. It might be argued that in not all cases could the pain be ascribed with certainty to myocardial ischaemia. Because this was a retrospective study, information on whether or not electro-

Fig. 2 Summary of clinical course of 46 patients who did not respond to medical treatment within 24 hours. Abbreviations are as in Fig. 1.

cardiographic changes occurred during pain was not always available, particularly in those who responded promptly to medical treatment. In some of the 10 patients with normal angiographic findings, the diagnosis may, therefore, have been incorrect, but since we excluded those with atypical clinical features, the absence of repolarisation changes during pain would not have affected their management, or precluded the need for angiography.

Rest pain can usually be controlled by bed-rest, nitrates, and beta-adrenergic blockade,¹³⁻¹⁵ and the risk of infarction and death in the first few days of medical treatment is said to be low.^{1 5 12} One reason for the comparatively high proportion of "medical failures" among our patients may be that they were selectively referred to us from other hospitals, but it is interesting to note that of 80 patients admitted to a hospital in Boulogne with rest pain, a similar proportion (37/80) developed recurrent angina within 30 days of starting medical treatment,¹⁶ and of 124 patients with rest pain reported by Wiles *et al.*,¹⁷ 71 failed to respond to "maximal medical therapy". The somewhat arbitrary time limit of 24 hours between admission to hospital and assessment of the response to conservative measures is, however, less than in most previous studies, and had a longer period been allowed to lapse, it is likely that the proportion of patients failing to respond to treatment would have been smaller.

Intra-aortic balloon counterpulsation usually results in the prompt relief of ischaemic pain, and its use has been advocated to stabilise patients unresponsive to medical treatment in preparation for angiography and operation.^{18 19} We have not adopted this practice because it introduces an additional source of complications, and in our experience cardiac catheterisation and operation can be carried out safely without it. We did, however, use the balloon pump in four instances: in two patients after coronary angiography because of continued and frequent attacks of pain at a time when the operating theatre was not available for immediate use, and in two patients with severe left ventricular failure.

We believe that knowledge of the presence, localisation, and extent of coronary disease and of left ventricular function is essential for optimal management of patients with rest pain, and we carry out cardiac catheterisation on all but the elderly, those with other life-shortening disease, and those who refuse investigation. This policy can be justified only if the incidence of complications from the procedure is negligible, as it was in our patients.

Though initially controversial, the place of aortocoronary bypass in the management of "unstable angina" has now become more clearly defined. While in early studies a high operative mortality (10 to 25%) and incidence of perioperative infarction was reported,^{4 20 21} there has been a striking improvement in recent years, with operative mortality consistently below 10 per cent, and sometimes as low as 2 per cent.^{5 9 19 22} In a study of patients with recurrent rest pain randomised to either medical or surgical treatment, there were no deaths and two infarctions in 19 medical patients and one death and three infarctions in the 21 surgically treated.⁸ In a more recent randomised trial of medical and surgical treatment for patients with all categories of "unstable angina" by the National Co-operative Study Group,²² mortality was similar in the two groups of patients (3 and 5%, respectively), and while the overall incidence of myocardial infarction was higher in those treated surgically (17 vs 8%), during the last four years of study the perioperative infarction rate fell to a level similar to that of spontaneous infarction in the medically treated patients. By contrast, the preliminary report of a randomised study from Buenos Aires⁹ showed a clear advantage for surgical treatment in patients with rest pain, with mortality at a mean follow-up period of eight months of 5 per cent in the operated and of 35 per cent in the unoperated patients. Hultgren *et al.*,⁵ in a non-randomised but carefully matched trial of 118 patients with "unstable angina", also observed a lower mortality and incidence of infarction in the surgical patients. In all these comparisons of treatment, surgically treated patients had a significantly better exercise capacity at follow-up, with less angina, than those treated medically.

From these studies certain principles have emerged. Patients with rest pain should be treated medically in the first instance, and if this is successful the question of emergency surgery does not arise. We operated electively on those thought most likely to have further complications, that is patients with severe coronary disease and those with previous angina,^{1 2} and the surgical results were comparable to those described in other reports of elective vein graft procedures. A consistent observation,^{5 9 22} confirmed by our own experience, is that a significant proportion of patients who present with rest pain and who initially respond to medical treatment, will, if not operated on, have further episodes of severe angina necessitating admission to hospital. This happened in seven of the 18 patients in whom medical treatment had been thought most appropriate, and all were operated on during the second admission.

Unfortunately it is not easy to predict which patients will relapse; while it might be expected that single vessel disease would be a favourable feature, three of our patients with this finding had further pain and one developed infarction, while on the other hand, of 11 patients with double or triple vessel disease who were treated medically, five were symptom free at follow-up. There does, however, seem little doubt that patients with disease isolated to the right coronary artery have an excellent prognosis.¹⁶ Another important finding, emphasised by others and itself a justification for carrying out angiography in all these patients, is that nearly a quarter (11/46) of those who responded to medical treatment (and underwent angiography), and a few (3/46) of those not responding, did not have atherosclerotic coronary disease.

In the patients with pain unresponsive to medical treatment who are thought to be particularly at risk of subsequent infarction and death^{1 2} it is clear that operation can be carried out with a mortality little higher than for elective procedures, and equal to or possibly lower than in patients treated conservatively. No less important, however, is the consistent demonstration that aortocoronary bypass grafting is the best available method for producing immediate and long-term pain relief. Referral for surgical treatment thus presents the patient with a clear plan of action, removing the uncertainty associated with prolonged medical treatment, and in many cases shortening the hospital stay. We, therefore, operated on patients with continuing pain unless infarction had already occurred, and the results in 34 patients (two deaths, three peri-operative infarctions, and 26 symptom free at follow-up) are comparable to the results of operation in similar patients in other reports. Both operative deaths were in patients with poor left ventricular function, and one occurred despite treatment with the balloon pump. The value of operating on such patients might be questioned, but another, with an ejection fraction of 30 per cent, survived operation and was symptom free at follow-up.

A progressive decline in mortality of patients with rest pain has been reported over the past decade.

While this may in part be attributable to the difficulty in defining comparable groups of patients, we believe that our results, in line with this trend are because of careful selection of high risk patients for surgical treatment. This selection, though imperfect, can be made only if all patients with rest pain are investigated early in their clinical course by coronary angiography.

References

- 1 Krauss KR, Hutter A JMr, De Sanctis RW. Acute coronary insufficiency. Course and follow-up. *Circulation* 1972; suppl I: 66-71.
- 2 Gazes PC, Mobley EM Jr, Faris HM Jr, Duncan RC, Humphries GB. Preinfarctional (unstable) angina—a prospective study—ten year follow-up. *Circulation* 1973; **48**: 331-7.
- 3 Duncan B, Fulton M, Morrison SL, *et al.* Prognosis of new and worsening angina pectoris. *Br Med J* 1976; **i**: 981-5.
- 4 Miller DC, Cannom DS, Fogarty TJ, Schroeder JS, Daily PO, Harrison DC. Saphenous vein coronary artery bypass in patients with "preinfarction angina". *Circulation* 1973; **47**: 234-41.
- 5 Hultgren HN, Pfeifer JF, Angell WW, Lipton MJ, Bilisoly J. Unstable angina: comparison of medical and surgical management. *Am J Cardiol* 1977; **39**: 734-40.
- 6 Bruschke AVG, Proudfit WL, Sones FM Jr. Progress study of 590 consecutive non-surgical cases of coronary disease followed 5-9 years. I. Arteriographic correlations. II. Ventriculographic and other correlations. *Circulation* 1973; **47**: 1147-62.
- 7 Cohen MV, Gorlin R. Main left coronary artery disease. Clinical experience from 1964-1974. *Circulation* 1975; **52**: 275-85.
- 8 Selden R, Neill WA, Ritzmann LW, Okies JE, Anderson RP. Medical versus surgical therapy for acute coronary insufficiency. A randomized study. *N Engl J Med* 1975; **293**: 1329-33.
- 9 Bertolasi CA, Trongé JE, Carreño CA, Jalon J, Ruda Vega M. Unstable angina—prospective and randomized study of its evolution, with and without surgery. *Am J Cardiol* 1974; **33**: 201-8.
- 10 Cattell MR, Stone DL, Brooks NH, Balcon R. Ergometrine-induced spasm in normal or minimally diseased coronary arteries. In: Kaltenbach M, Lichtlen P, Balcon R, Bussmann WD, eds. *Coronary heart disease. 3rd international symposium Frankfurt*. Stuttgart: Thieme, 1978: 147-51.
- 11 Cairns JA, Fantus IG, Klassen GA. Unstable angina pectoris. *Am Heart J* 1976; **92**: 373-86.
- 12 Hultgren HN. Medical versus surgical treatment of unstable angina. *Am J Cardiol* 1976; **38**: 479-86.
- 13 Mizgala HF, Khan AS, Davies RO. The effect of propranolol in acute coronary insufficiency: a preliminary report (abstract). *Clin Res* 1969; **17**: 637.
- 14 Papazoglov NM. Use of propranolol in preinfarction angina (letter). *Circulation* 1971; **44**: 303-4.
- 15 Fischl SJ, Herman MV, Gorlin R. The intermediate coronary syndrome. Clinical, angiographic and therapeutic aspects. *N Engl J Med* 1973; **288**: 1193-8.
- 16 Huret JF, Agier B, Rosier SP, *et al.* Delayed semi-elective coronary bypass surgery for unstable angina pectoris. *J Thorac Cardiovasc Surg* 1978; **75**: 476-82.
- 17 Wiles JC, Peduzzi PN, Hammond GL, Cohen LS, Langou RA. Preoperative predictors of operative mortality for coronary bypass grafting in patients with unstable angina pectoris. *Am J Cardiol* 1977; **39**: 939-43.

- 18 Gold HK, Leinbach RC, Buckley MJ, Mundth ED, Daggett WM, Austen WG. Refractory angina pectoris: follow-up after intra-aortic balloon pumping and surgery. *Circulation* 1975; **54**, suppl III: 111–46.
 - 19 Weintraub RM, Voukydis PC, Aroesty JM, *et al.* Treatment of preinfarction angina with intra-aortic balloon counterpulsation and surgery. *Am J Cardiol* 1974; **34**: 809–14.
 - 20 Scanlon PJ, Nemickas R, Moran JF, Talano JV, Amirparviz F, Pifarre R. Accelerated angina pectoris. Clinical, hemodynamic, arteriographic and therapeutic experience in 85 patients. *Circulation* 1973; **47**: 19–26.
 - 21 Conti CR, Brawley RK, Griffith LSC, *et al.* Unstable angina pectoris: morbidity and mortality in 57 consecutive patients evaluated angiographically. *Am J Cardiol* 1973; **32**: 745–50.
 - 22 Russell RO, Resnekov L, Wolk M, *et al.* Unstable angina pectoris: national co-operative study group to compare surgical and medical therapy. 11. In-hospital experience and initial follow-up results in patients with one, two and three vessel disease. *Am J Cardiol* 1978; **42**: 839–48.
- Requests for reprints to Dr N Brooks, Cardiac Department, The London Chest Hospital, Bonner Road, London E2 9JX.