EMERGENCY CORONARY ANGIOPLASTY IN REFRACTORY UNSTABLE ANGINA

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Abstract We performed percutaneous transluminal coronary angioplasty as an emergency procedure in 60 patients with unstable angina pectoris that was refractory to treatment with maximally tolerated doses of beta-blockers, calcium antagonists, and intravenous nitroglycerin. The initial success rate for angioplasty was 97 per cent (56 patients). There were no deaths related to the procedure, although total occlusion occurred in four patients. Despite emergency bypass grafting, all four sustained a myocardial infarction. All the patients were followed for at least six months. Late cardiac death occurred in one patient, whereas eight had recurrent angina pectoris. There was no progression to myocardial infarction. The restenosis rate was 28 per cent (13 of 46) in the patients with initially successful coronary angioplasty who had repeat angiography. Improved cardiac functional status after sustained successful coronary angioplasty was demonstrated by an almost normal capacity on bicycle exercise testing and the absence of ischemia during thallium isotope studies in 80 per cent.

We conclude that emergency percutaneous transluminal coronary angioplasty may be useful for the treatment of selected patients with unstable angina pectoris who are unresponsive to intensive pharmacologic treatment. (N Engl J Med 1985; 313:342-6.)

The clinical syndrome of unstable angina causes great concern to clinicians because of the perceived high risk of progression to myocardial infarction or cardiac death.1-6 Given the heterogeneous coronary pathoanatomy, the variations in time and severity of clinical presentation among patients with unstable angina, and uncertainty about the extent of threatened or actual necrosis of the myocardium, it is unlikely that any one therapeutic approach will be appropriate for all such patients. The various options among pharmacologic treatments and surgery have led to a consensus.3-6 It is now common practice to stabilize the acute ischemic symptoms initially with intensive medical treatment and to reserve bypass surgery for patients refractory to such treatment.3-4 Since percutaneous transluminal coronary angioplasty has gained acceptance as an alternative form of revascularization,7 patients with unstable angina pectoris, although initially not thought suitable as candidates because of their instability, have successfully undergone this procedure.8-10 Now that investigator experience has grown and important advances have been made in catheter techniques, we considered that it would be timely to review our experience with emergency coronary angioplasty, using a steerable dilatation catheter, as an alternative to coronary artery bypass grafting. The following specific issues were addressed: (1) Can coronary angioplasty relieve ischemic symptoms and prevent progression to myocardial infarction or death in patients not responding to intensive pharmacologic therapy lasting for at least 24 hours? (2) What is the incidence of major complications of the procedure? and (3) What is the rate of recurrence of symptoms or of the occurrence of major cardiac events during at least six months of follow-up?

Methods

During the period January 1983 to April 1984, 1283 patients were admitted to our coronary care unit. Unstable angina pectoris was diagnosed in 217. The extent of coronary artery disease in these patients is shown in Table 1. In 109 patients the disease was...
refractory to intensification of treatment. Of these, 60 patients with unstable angina pectoris satisfied all the following criteria: (1) chest pain at rest for at least 15 minutes, accompanied by reversible electrocardiographic ST-T changes without such signs of cardiac necrosis as a rise in creatine kinase to twice the normal level or the development of Q waves; (2) hospitalization for at least 24 hours in an intensive care unit, with continuous electrocardiographic and hemodynamic monitoring; (3) optimal medical therapy, including adequate administration of beta-adrenergic blocker to achieve a resting pulse of less than 60 beats per minute, nifedipine, and intravenous nitroglycerin to optimize preload (pulmonary capillary wedge pressure <14 mm Hg) and afterload (systolic arterial pressure <110 mm Hg) in an effort to increase the coronary blood supply to the jeopardized myocardium; (4) continuation of ischemic attacks, despite such therapy; (5) adequacy of the lesion for surgical intervention or the presence of a coronary artery lesion suitable for treatment by percutaneous transluminal coronary angioplasty. Patients were considered suitable for angioplasty if they had localized disease in one vessel and, in case of multivessel disease, the vessel selected for attempted dilatation did not give off collateral vessels and if left main stem disease was absent; and (6) normal or slightly abnormal left ventricular function.

Sixty patients fulfilled these criteria. Their clinical characteristics are shown in Table 2. The procedure was attempted in 39 patients with a lesion of the left anterior descending artery, 10 with a lesion of the right coronary artery, 10 with a lesion of the circumflex artery, and 1 with a lesion of a graft. In five patients the artery, thought to be technically suitable for angioplasty, was found at the time of angioplasty to be totally occluded; in two patients the artery was already totally occluded at the time of the diagnostic angiogram. The mean (±S.D.) time from admission to angiography was 2.7±5.6 days, and from angiography to angioplasty, 3.6±5.6 days. Coronary angioplasty was performed in 32 patients (53 per cent) during normal working hours and in 28 (47 per cent) at night or during the weekend.

The procedure was performed according to the technique of Grünzig,1 with a steerable balloon catheter manufactured either by Schneider–Grünzig (Zürich, Switzerland) or by Meditech (Wate- rdown, Mass., U.S.A.) inserted by femoral route. After the procedure, 250 mg of aspirin dissolved in 5 ml of normal saline and 100 mg of intravenous heparin were given; during the procedure a continuous drip of low-molecular-weight dextran was given. A Zuckar pacing electrode was positioned in the right ventricle. To prevent coronary artery spasm, nifedipine (0.2 mg) or nitroglycerin (isosorbide dinitrate, 1 to 3 mg) was given into the coronary artery, and this was repeated when necessary.13 Only the ischemia-related lesion was dilated in cases in which multivessel disease was present. The ischemia-related lesion was determined by localizing the recorded electrocardiographic changes. Electrocardiographic changes in leads V₁ to V₅ were associated with lesions of the left anterior descending artery; changes in I, aVL, and V₆ with the marginal branch of the circumflex artery or the diagonal branch of the left anterior descending artery; changes in inferior leads, with either the right coronary artery or the circumflex artery. The transmural pressure gradient was measured before and after each dilation. The inflation pressure varied from 2 to 12 atm for a period of 10 to 60 seconds; on the average the pressure applied was 9.8±1.8 atm, for a total period per dilation of 218±111 seconds.

An angioplasty procedure was considered successful when it resulted in clinical relief of acute ischemic symptoms, with a reduction in the size of the lesion to less than 50 per cent of the luminal diameter or a reduction of the transmural pressure gradient to less than 0.30 (the pressure gradient normalized for mean aortic pressure).14

After the procedure, all the patients were monitored for 24 hours in the coronary care unit, where electrocardiography was performed and enzyme levels were measured. The patients were usually discharged three days after the procedure. They continued to receive treatment with nifedipine (40 to 60 mg daily) and aspirin (300 mg daily) for six months, with the aim of preventing spasm or platelet aggregation. During the procedure a surgical team was available in case of need. A periprocedural myocardial infarction was diagnosed when a new Q wave developed in the 12-lead electrocardiogram.

Clinical follow-up information was obtained at 3, 6, and 12 months, either during a visit by the patient to the outpatient clinic or from the referring physician. Cardiac deaths, myocardial infarctions, and recurrences of angina pectoris were tabulated. The majority of patients underwent an exercise test with thallium scintigraphy and repeat angiography. The patients performed symptom-limited exercise on the bicycle, with stepwise increments in load of 20 W every minute. The three orthogonal leads X, Y, Z of the Frank lead system were recorded and analyzed. A horizontal ST-wave depression of 0.1 mV or more during exercise was considered a positive response.

Exercise thallium scintigraphic imaging was performed in the anterior and left anterior oblique 45° and 65° views, immediately after injection of 1.5 mCi of thallium-201 at peak stress. The redistribution images were obtained four hours later. Images were obtained with a gamma camera (Searle Radiographics, Des Plaines, Ill.) and processed with a computer interface as previously described.15 Defects with redistribution were considered to represent exercise-induced ischemia. Persistent defects without redistribution were considered to represent scabs. Repeat angiograms were obtained in multiple views, including hemisaxial angulation, and were interpreted by observers without knowledge of the patient’s clinical status. Restenosis was defined as an increase in narrowing of the luminal diameter of the dilated lesion to more than 50 per cent. The severity of the stenosis before and after angioplasty and at control was calculated with the help of a computer-based system for coronary angiography analysis.16 Data are expressed as means ±S.D.

**RESULTS**

Percutaneous transluminal coronary angioplasty was initially successful in 56 of the 60 patients (93 per cent). The initial success rate in patients with a totally occluded vessel was 86 per cent (six of seven patients). The mean gradient before coronary angioplasty was 61±13 mm Hg; after the procedure it was 18±12 mm Hg. The diameter stenosis before angioplasty was 69±13 per cent; after successful angioplasty it was 28±10 per cent. The success rate for the left anterior descending artery was 95 per cent (37 of 39 patients), for the right coronary artery 90 per cent (9 of 10), for
Table 2. Clinical Characteristics of 60 Patients with Unstable Angina Pectoris and Emergency Percutaneous Transluminal Coronary Angioplasty.

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Male sex</td>
<td>51 (85)</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>59 (range, 36–73)</td>
</tr>
<tr>
<td>Previous coronary bypass grafting</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>23 (38)</td>
</tr>
<tr>
<td>New onset of angina pectoris at rest</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Worsening of preexisting stable angina</td>
<td>20 (33)</td>
</tr>
<tr>
<td>Angina within 4 wk after myocardial infarction</td>
<td>11 (18)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (mean ± S.D.)</td>
<td>0.60 ± 0.09</td>
</tr>
</tbody>
</table>

the left circumflex artery 90 per cent (9 of 10), and for the bypass 100 per cent (1 of 1). In four patients the procedure was complicated by total occlusion of the vessel; all four had a myocardial infarction (pathologic Q waves developed in three, and one had a marked rise in the creatine kinase level) despite emergency coronary artery bypass grafting. There were no deaths related to the procedure.

All the patients were followed for at least 6 months after successful angioplasty, half of them for 12 months (Table 3). One patient died from a myocardial infarction. Seven patients had recurrent angina, all within six months after angioplasty; six were treated either by repeat angioplasty or by bypass grafting. The four patients with unsuccessful coronary angioplasty and emergency bypass surgery were all followed for 12 months; one had a recurrence of angina pectoris.

Table 3. Late Results after Initially Successful Percutaneous Transluminal Coronary Angioplasty (PTCA) in 56 Patients with Refractory Unstable Angina.

<table>
<thead>
<tr>
<th>FOLLOW-UP PERIOD</th>
<th>3 MO</th>
<th>6 MO</th>
<th>12 MO</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>56</td>
<td>55</td>
<td>27</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Recurrence of angina pectoris</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Repeat PTCA</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Coronary bypass grafting</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

asymptomatic patients was 33 per cent (three of nine patients), whereas two other patients later became symptomatic and then had restenosis.

Repeat angiograms were available in 46 of the 56 patients (82 per cent) who had an initially successful angioplasty. In 10 patients, angiography was not repeated; one had recurrent angina, eight were free of symptoms, and one had a fatal myocardial infarction. The angiography was performed 2.3 ± 1.8 months after coronary angioplasty.

Restenosis occurred in 13 patients (28 per cent), of whom 7 were free of symptoms. All six patients with recurrent angina pectoris had restenosis. On repeat angiography, the diameter stenosis in asymptomatic patients was 34 ± 18 per cent; in the symptomatic patients it was 68 ± 8 per cent.

**DISCUSSION**

The management of unstable angina pectoris is first of all directed toward the relief of acute ischemic symptoms and secondly to the prevention of progression to myocardial infarction.4,6 Unstable angina is nearly always associated with high-grade, fixed coronary narrowing13–17 leading to restricted antegrade flow. Other factors, such as generalized increased vasomotor tone, severe localized spasm of the healthy wall in eccentric lesions, or platelet deposition progressing to complete thrombosis, also have a role.18–22 Pharmacologic treatment therefore aims either to decrease the myocardial demand for oxygen by reducing the heart rate (bed rest, beta-blockers), adjusting preload and afterload pressures (nitrates, calcium antagonists), and protecting the stunned myocardium (calcium antagonists with beta-blockers), or to increase the oxygen supply more directly by coronary vasodilation (calcium antagonists, nitrates), or by the inhibition of platelet deposition and thrombus formation (aspirin). Although the conditions of most patients will stabilize with optimal medical treatment, consisting of hospitalization and a combination of beta-blockade, calcium antagonists, and intravenous nitroglycerin18,23–26 adjusted during continuous electrocardiographic and hemodynamic monitoring and administered in maximally tolerated doses, a subgroup of patients will continue to have pain and presumably ischemia. Previous studies have indicated that high rates of mortality and cardiac events occur in this subset of patients.3,4,23–26 Coronary artery bypass grafting has been suggested as the treatment of choice.

Percutaneous transluminal coronary angioplasty has been shown to improve coronary blood flow by reducing the severity of the obstruction in selected patients with stable angina pectoris.7 Therefore, the rationale for its use in patients who do not respond to medical treatment lies in its potential to provide revascularization of the jeopardized myocardium without the need for coronary bypass surgery, with its attendant risks of perioperative myocardial infarction or death.27 However, coronary angioplasty often causes
vasospasm in patients with stable angina, and if vasospasm is a frequent and important factor in unstable angina, then intracoronary instrumentation may be unduly hazardous. The study by Williams et al.⁸ and more recently those by Meyer et al.⁹ and Faxon et al.¹⁰ have shown that coronary angioplasty could be performed safely and successfully in unstable angina.

The patients who underwent emergency coronary angioplasty in our study constitute a small subgroup of the large spectrum of patients with unstable angina. Our selection process required that the patients had to be refractory to intensive medical therapy after at least 24 hours of hospitalization and to have coronary lesions technically suitable for bypass surgery. From this group we were ultimately selected for emergency coronary angioplasty those who had a lesion of the ischemia-related vessel suitable for the procedure, no left main stem disease, and a normal or only slightly abnormal left ventricular function.

In our study, coronary angioplasty was successful in 93 per cent of the patients in whom the procedure was attempted. This success rate is higher than the 61 to 76 per cent reported by the three studies cited above but is comparable to the 85 to 90 per cent reported in series of patients with stable angina pectoris.²⁸-³⁰ It should be emphasized here that the procedure in our study was performed with a steerable dilatation catheter, which has been shown to increase the initial success rate to 10 per cent above that achieved with a nonsteerable dilatation catheter, as was used in the other studies. The National Heart, Lung, and Blood Institute’s percutaneous transluminal coronary angioplasty registry³⁰ reported that acute coronary events associated with coronary angioplasty occurred more frequently in patients with unstable angina.

In our study the procedure resulted in progression to coronary artery occlusion in four patients (7 per cent). In two patients the vessel became occluded during the attempts to cross the lesion, apparently because of damage to the vessel by the guide wire at the site of the lesion. In two patients the dilation resulted in dissection with total occlusion. These patients were promptly revascularized with bypass grafting, yet all had a myocardial infarction. Although the prognosis for such patients with coronary bypass surgery is uncertain, we believe that these cases show again that immediate surgical standby remains a requirement to ensure patient safety. There were no deaths related to the coronary angioplasty procedure. These results compare favorably with the complication rates for hospital mortality and myocardial infarction of 0.9 and 9 per cent, respectively, reported by the National Heart, Lung, and Blood Institute’s percutaneous transluminal coronary angioplasty registry.¹⁰

During a follow-up of at least six months after successful coronary angioplasty, there was clinical progression of the disease in 8 of 56 patients (14 per cent), with fatal myocardial infarction in 1 patient (2 per cent) and recurrence of angina pectoris in 7 (13 per cent). The patient who died was free of symptoms for one week after the procedure and died after recurrent infarction. At autopsy the initially successfully dilated lesion was totally occluded by a fresh thrombus. The recurrence of symptoms after dilation was corroborated by an angiographically determined restenosis in all asymptomatic patients. The angiographic restenosis rate was 28 per cent (including 10 per cent that were asymptomatic). This rate is similar to that reported in stable angina pectoris (20 to 30 per cent)⁷ and unstable angina pectoris (22 per cent).⁹

The results of electrocardiographic exercise testing and thallium scintigraphy indicated that in asymptomatic patients after percutaneous transluminal coronary angioplasty, the exercise capacity became virtually normal, although there was an 8 per cent incidence of an abnormal electrocardiographic response and a 19 per cent incidence of reversible perfusion defects. These abnormal responses occurred to the same extent in patients with one-vessel disease as in patients with multivessel disease in whom only the ischemia-related vessel was dilated. These results support our opinion that angioplasty of the ischemia-related vessel in patients with multivessel disease with refractory unstable angina pectoris is an attractive approach, at least for the short term.

Thus, at an acceptable risk and with a high initial success rate, percutaneous transluminal coronary angioplasty can restore coronary blood flow in refractory unstable angina, although these results must compete with those of emergency coronary artery bypass grafting. A recent nonrandomized study¹⁰ compared the rates of myocardial infarction and death in a comparable group of patients with one-vessel disease and unstable angina pectoris who underwent either coronary bypass surgery or coronary angioplasty. From these data it appears that angioplasty compares favorably with bypass surgery. The procedure is associated with similar mortality and morbidity rates, but a more marked improvement in symptoms can be expected after coronary angioplasty. Unfortunately, the data available from that study do not contain information about patients with refractory unstable angina, but

<table>
<thead>
<tr>
<th>Extent of CAD*</th>
<th>No. of Patients</th>
<th>Exercise Capacity (% of normal value)</th>
<th>ST-Segment Depression &gt;1 mm</th>
<th>Thallium-Reversible Perfusion Defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-vessel disease</td>
<td>34</td>
<td>99±17</td>
<td>2 (6)</td>
<td>6 (30 (20)</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>13</td>
<td>93±15</td>
<td>2 (15)</td>
<td>2 (12 (17)</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>97±16</td>
<td>4 (9)</td>
<td>8 (42 (19)</td>
</tr>
</tbody>
</table>

*CAD denotes coronary artery disease.
Values are expressed as means ± S.D.
Thallium scintigraphy data were available for only 42 patients.
Includes patients with multivessel disease in whom only the ischemia-related vessel was dilated.
support our opinion that percutaneous transluminal coronary angioplasty, as an emergency procedure in selected patients with unstable angina refractory to medical treatment, is very efficacious.

We are indebted to Gusta Koster for assistance in the preparation of the manuscript.

REFERENCES