ORIGINAL ARTICLE

Rescue percutaneous coronary intervention for failed thrombolysis: results from a district general hospital

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Objective: To assess the outcome of a policy of emergency percutaneous coronary intervention (PCI) in patients with acute myocardial infarction and electrocardiographic (ECG) evidence of failed reperfusion after thrombolysis.

Design: Observational study.

Setting: District general hospital.

Patients: A total of 109 consecutive patients with acute myocardial infarction who underwent emergency angiography and angioplasty for failed reperfusion diagnosed on the basis of standard ECG criteria.

Main outcome measures: In-hospital mortality; death, infarct territory reinfarction, and reintervention by PCI or coronary artery bypass graft (CABG) during follow up; in-lab resource utilisation.

Results: At initial angiography, 76 patients had Thrombolysis in Myocardial Infarction (TIMI) trial 0/1 flow and 33 had TIMI 2/3 flow. Fourteen patients were in cardiogenic shock. TIMI 3 flow was established or maintained in 93 patients (85%). Overall in-hospital mortality was 9%. It was 3% in non-shock patients, 50% in shocked patients, and 40% when the procedure was unsuccessful (TIMI 0/1 flow post-procedure). Over a mean follow up of 30 months (>12 months of follow up in all patients) there were 19 further events (one death, five reinfarctions, and 13 revascularisations (nine CABG and four PCI)). The cost of rescue PCI was not significantly higher than comparable elective interventions.

Conclusion: A policy of emergency angiography and PCI for failed reperfusion in acute myocardial infarction can be carried out in a hospital without on-site surgical backup with good medium term clinical outcomes.

Between 30% and 50% of patients with acute myocardial infarction fail to reperfuse (Thrombolysis in Myocardial Infarction (TIMI) trial 3 flow) at 90 mins after the initiation of thrombolytic treatment. The prognosis of these patients is significantly poorer compared with those who do reperfuse, irrespective of age, sex, area of the myocardium involved, and the thrombolytic agent used.¹ The application of percutaneous coronary intervention (PCI) as a mode of "rescue" for failed thrombolysis may offer significant benefit, at least for patients with large myocardial infarctions.² Some patients thought to have failed reperfusion by standard electrocardiographic (ECG) criteria are shown to have "normal" antegrade flow at angiography. Previous studies of angioplasty in this group have failed to demonstrate benefit.^{3,4} All of these studies were performed before the availability of stents and platelet 2b3a receptor antagonists, both of which can dramatically improve the outcome of PCI.^{5,6} The Lanarkshire Cardiac Catheterisation Laboratory has been providing emergency "rescue" PCI since January 1996. We report the procedural and clinical outcomes and in-lab resource utilisation in 109 consecutive patients who underwent rescue PCI from January 1996 to January 2000.

METHODS

The Lanarkshire Cardiac Catheterisation Laboratory serves the district general hospitals of Hairmyres, Monklands, and Law (total population ~ 580 000). A policy of rescue angioplasty was instituted in January 1996, although referrals from Law Hospital did not begin until November 1998. The service is provided between 0800 and 2200 hours seven days a week and is generally offered to patients presenting within 12 hours of the onset of chest pain. However the time limit is flexible and clinical parameters of failed reperfusion (persisting ST elevation and ongoing ischaemic chest pain) are considered before

rejecting patients who present beyond 12 hours. There is no age limit. Cardiac surgery is available in either of two centres in Glasgow and we comply with the British Cardiovascular Intervention Society's guidelines for "time to bypass" in the event of a need for emergency surgery arising.

Procedural data were collected prospectively and clinical outcomes were assessed retrospectively by review of the case records and telephone contact by research nurses. The diagnosis of failed reperfusion was based on the previously described ECG criteria of failure of the ST segment elevation to resolve by more than 50% in the lead with maximum elevation at 90 mins after the initiation of thrombolytic treatment.⁷ The clinical status of the patients at 90 mins including ongoing chest pain and haemodynamic instability were considered before proceeding to rescue PCI. The chest pain to thrombolysis time and the thrombolysis to PCI time were recorded in all patients. Coronary angiography and angioplasty were performed from the femoral artery with standard guide catheters and guide wires. If TIMI flow 0-2 was present PCI was performed. In patients with TIMI 3 flow despite ECG features of failed reperfusion, PCI was performed if the morphology of the culprit lesion suggested a high risk of reocclusion (usually residual stenosis $\geq 90\%$). The decision to proceed to coronary artery stenting was left to the discretion of the attending cardiologist. Abciximab was used when the angiogram suggested a heavy thrombus burden and particularly if there was

Abbreviations: CABG, coronary artery bypass graft; ECG, electrocardiographic; PCI, percutaneous coronary intervention; rtPA, recombinant tissue plasminogen activator; TAMI, Thrombolysis and Angioplasty in Myocardial Infarction; TIMI, Thrombolysis in Myocardial Infarction (trial)

Table 1 Demographics, clinical details, and outcomes (n=109); values are number unless otherwise stated

Cardiogenic shock	14
Mean (SD) age	61 (11)
Males/females	80/29
Site of infarction	
Anterior	56
Inferior	48
Posterior	5
Thrombolytic agent	
Tissue plasminogen activator	55
Streptokinase	49
Both	5
Median pain to needle time (min)	143
Median thrombolysis to PCI time (min)	240
Median time to reperfusion (min)	380
In-hospital mortality (non-shock group) (%)	3.2
In-hospital mortality (shock group) (%)	50
In-hospital mortality (failed PCI) (%)	40
Combined in-hospital mortality (%)	9.2
Follow up data (mean 30 months)	
Death	1
Reinfarction	5
Reintervention	13
Total event rate (%)	26.6

persisting ECG evidence of failed reperfusion despite a good angiographic result. Intra-aortic balloon pump counterpulsation was used only in patients who were severely hypotensive or who had other evidence of cardiogenic shock. Ticlopidine or clopidogrel was used for two to four weeks post-procedure if a stent was deployed. TIMI flow was recorded before and after PCI in each patient and was based on the observation of the attending cardiologist. The end points recorded were death, non-fatal myocardial infarction, and repeat revascularisation over a mean follow up of 30 months (range 12–48 months) with ≥ 12 months of follow up available in all patients. In addition the in-lab cost of 50 consecutive emergency procedures was compared with 50 consecutive elective single vessel PCI during the same period.

RESULTS (TABLE 1)

In this four year period, 109 patients underwent emergency PCI after failed thrombolytic treatment. Fourteen patients were in cardiogenic shock. Sixty five patients (60%) were from Hairmyres, 26 (24%) from Monklands, and 18 (16%) from Law. The average transfer time was 35 mins from Monklands Hospital (11 miles) and 45 mins from Law Hospital (13 miles). There were no deaths during transfer. The mean age of the patients studied was 61 years and the male to female ratio was 3:1. Five patients had received a full second dose (rescue

Figure 1 Individual pain to needle and needle to PCI times for 50 consecutive patients undergoing rescue or adjunctive PCI.**Table 2** Angiographic and procedural details; values are number or number (%)

Coronary artery disease	
Left main	3
1 vessel	49
2 vessel	33
3 vessel	24
Infarct related artery	
Left main	1
Left anterior descending	51
Right	50
Circumflex	7
Abciximab	55 (50)
Stents	49 (45)
Intra-aortic balloon pump	14

thrombolysis) due to either failure to reperfuse or early reocclusion after initially successful thrombolysis. The median pain to needle time was 143 mins with 95 patients (87%) receiving thrombolysis within six hours of the onset of pain. There was wide interindividual variation in the thrombolysis to PCI time (fig 1) but none the less 92 patients (85%) had PCI performed within 12 hours of the onset of their pain with a median time to reperfusion in all patients of 380 mins. The patterns of coronary artery disease and procedural details in both groups of patients are summarised in table 2.

Pain to reperfusion time

The median pain to reperfusion time (pain to completion of the procedure) was 380 mins in the whole cohort and 570 mins in the 16 patients who either had an in-hospital death or a failed procedure.

Procedural outcomes

TIMI flows before and after PCI for patients with and without cardiogenic shock are reported in table 3. In one patient with TIMI 2 flow and a mid-right coronary artery lesion the vessel occluded after PCI and despite repeated balloon dilatations and abciximab, failed to reopen. This patient, who subsequently died, was the only patient in whom flow was TIMI 0/1 after PCI having been TIMI 2/3 before PCI. Overall TIMI 3 flow was achieved and/or maintained in 90% of patients in the non-shock group and 57% of patients in the shock group.

In-hospital and medium term (≥ 12 months) clinical outcomes

Non-cardiogenic shock (n=95)

In this group there were three deaths in-hospital. One patient died after an unsuccessful procedure (noted above). A second

Table 3 TIMI flows before and after PCI for patients with and without cardiogenic shock (see learning points)

		TIMI after PCI			
		0	1	2	3
Before PCI					
No cardiogenic shock (n=95)					
0	54	5	0	3	46
1	11	0	0	0	11
2	17	1	0	0	16
3	13	0	0	0	13
Cardiogenic shock (n=14)					
0	11	3	0	3	5
1	0	0	0	0	0
2	2	0	0	0	2
3	1	0	0	0	1

died due to cardiac rupture, which occurred in the catheterisation laboratory after successful PCI. This patient had failed rescue thrombolysis and abciximab. A third patient died suddenly in electromechanical dissociation 24 hours after a technically successful procedure. Cardiac tamponade was excluded and death was presumed to be due to reinfarction. No patients underwent emergency bypass surgery. There were four non-fatal reinfarctions. One patient reinfarcted 72 hours after balloon angioplasty of an occluded left posterior descending artery. He underwent repeat PCI and stenting to the same segment. Two patients reinfarcted due to subacute stent thrombosis. A fourth patient reinfarcted one month after discharge after an unsuccessful procedure. There were an additional nine reinterventions—one repeat PCI and eight coronary artery bypass graft (CABG). One of the patients who proceeded to CABG was already on the waiting list at the time of his infarction and was operated on two days after rescue PCI. Four patients had multivessel disease and underwent elective CABG. One patient underwent elective repeat CABG after a successful PCI to a saphenous vein graft supplying the left anterior descending artery. Symptomatic restenosis occurred in three patients with two requiring CABG and one repeat PCI. Overall 79 patients (83%) remained event-free for the end points considered.

Cardiogenic shock (n=14)

In this group seven patients died in-hospital (50%) including two who died in the catheterisation laboratory before PCI could be completed. One patient had left main stem occlusion and died 11 days post-procedure despite TMI 3 flow after PCI and continued patency having been demonstrated by repeat angiography on day 7. Two patients with successful PCI (TIMI 3 flow) and two others with partially successful PCI (TIMI 2 flow) died due to persistent cardiogenic shock. One patient with failed rescue thrombolysis died due to gastrointestinal haemorrhage. No patients underwent emergency bypass surgery. Of the seven survivors, one patient who had a successful PCI to a saphenous vein graft to the left anterior descending artery reinfarcted in the same territory four months later, again failed to reperfuse with thrombolytic treatment, and underwent a second successful rescue PCI. Elective CABG was performed in a patient who had a partially successful procedure to the circumflex artery. Overall five patients (36%) remained event-free for the end points considered.

All patients

The overall in-hospital mortality was 9% (10 deaths) but rose to 40% (four deaths) in the 10 patients who had a failed procedure. Event-free survival rate at ≥ 12 months of follow up was 77%.

Bleeding complications

The patient who died from gastrointestinal bleeding had received rescue thrombolysis and had also received abciximab and heparin after a failed rescue PCI. Significant bleeding (systemic bleeding from any site and/or groin haematoma with a haemoglobin fall of > 30 g/l) occurred in 12 patients (25%) who received streptokinase and nine patients (16%) who received recombinant tissue plasminogen activator (rtPA). The use of abciximab was associated with an increased risk (27% v 6%)

Procedural costs

The mean (SD) in-lab cost (consumables only) of 50 consecutive rescue PCIs was £1349 (728). In comparison the mean cost of 50 consecutive elective single vessel PCIs was £1105 (715). This difference did not reach statistical significance ($p=0.10$).

DISCUSSION

In the GUSTO Angiographic Substudy, the 90 mins TIMI 3 flow rate in the infarct related artery was 54% in the accelerated rtPA group. The 30 day mortality was 9.8% in patients with TIMI 0 or 1 flow, 7.9% in patients with TIMI 2 flow, and 4.3% in those with TIMI 3 flow.⁸ Similar results were obtained in the TIMI 4 trial which randomised patients presenting within six hours to receive either front loaded rtPA, anisoylated plasminogen streptokinase activator complex, or a combination of a reduced dose of both.⁹ These trials have confirmed that up to 50% of patients with acute myocardial infarction fail to achieve early and complete reperfusion after thrombolytic treatment.

Previous studies of rescue PCI

TAMI

The outcomes of 607 patients with thrombolysis mediated and 169 patients with patency achieved by rescue angioplasty were compared in the course of the five Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) trials. Despite higher left ventricular ejection fraction, better infarct zone functional recovery and less reocclusion in the thrombolysis group, successful rescue angioplasty was associated with the same low in-hospital and long term mortality rate as initially successful thrombolysis.¹⁰

Mayo Clinic

In an observational study, Holmes *et al* reported excellent four year survival rates in 63 patients after rescue angioplasty for failed thrombolysis with streptokinase, despite depressed pre-discharge ejection fraction. Patency of the culprit artery was achieved in 80% and the in-hospital mortality was less than 3%.¹¹

TIMI

A substudy of the TIMI 1 and 2 trials compared outcomes in 33 consecutive patients with occluded infarct related arteries treated by rescue PCI with 100 consecutive patients with occluded infarct related arteries treated conservatively. No benefit of rescue PCI could be demonstrated.¹² A similar analysis from the TIMI 4 trial showed that although successful rescue PCI resulted in superior TIMI grade flow than successful thrombolysis, the incidence of adverse events in the rescue PCI group was not different to the no PCI group.¹³

GUSTO

In a substudy of the GUSTO-I trial, successful rescue PCI resulted in superior left ventricular function and 30 day mortality outcomes compared with patients treated conservatively despite more impaired initial left ventricular function in patients offered rescue angioplasty.¹⁴

RESCUE

Probably the best study comparing the two modalities of treatment for failed thrombolysis is the RESCUE trial. One hundred and fifty one patients with first anterior wall infarction treated with any accepted intravenous thrombolytic regimen and angiographically demonstrated to have an occluded infarct related vessel within eight hours of the onset of chest pain were randomised to either conservative treatment or to balloon angioplasty. At 30 days there was a statistically significant reduction in the combined end points of death, severe heart failure, and ventricular tachycardia in favour of the rescue PCI group.² A similar trend towards lower mortality with rescue PCI was reported by Belenkie *et al* in a smaller randomised trial involving 28 patients.¹⁵

South Cleveland Study

Sutton *et al* recently reported the results of rescue PCI in 156 patients treated in a regional cardiothoracic unit in the UK. The diagnosis of failed reperfusion was made at 120 mins by

standard ECG criteria and unlike our series, patients with cardiogenic shock were excluded. The mean time to reperfusion exceeded 470 mins. TIMI 3 flow was established in 124 patients (79%). Twenty one patients (13%) had a failed procedure and as in our study the mortality was very high in this group (45%). In-hospital mortality was 5.9% in patients with a successful procedure and 10.5% for the whole cohort.¹⁶

In-hospital mortality in our non-cardiogenic shock group was 3%. Possible reasons for this apparent better outcome include patient selection, earlier diagnosis of failed reperfusion (90 v 120 mins), shorter time to reperfusion (380 v ≥470 mins), higher procedural success in patients with TIMI 1–2 flow (97% v 73% achieving TIMI 3 flow), and greater use of 2b3a blockers (50% v 21%).

We have achieved similar rates of infarct artery patency and in-hospital mortality to those reported from the large American cardiothoracic centres. The Cleveland Clinic Foundation reported 92% infarct artery patency and 5% in-hospital mortality in the rescue PCI arm of the RESCUE trial.² The impressive results from the Mayo Clinic have been referred to earlier.¹¹

Time window for rescue PCI

The median pain to needle time in our patients was 143 mins with 86% presenting within six hours of the onset of chest pain. This suggests that the failed reperfusion was due to true thrombolytic failure rather than delayed presentation. Median delay before rescue PCI was another four hours giving a median time to reperfusion of slightly over six hours. The median time to reperfusion in the RESCUE trial was four and a half hours. This period was significantly longer in the cohort who either had an in-hospital death or a failed procedure (over nine hours). Our data suggest that the time to reperfusion influences both procedural success and in-hospital outcomes with best results obtained when this period is less than eight hours.

Transferring patients for rescue PCI

Some cardiologists remain concerned about transferring unstable patients for rescue PCI. The average transfer time to our unit was less than 45 mins and there were no deaths in transit in the 44 patients referred from other sites. In the PRAGUE study there were no deaths during 200 transfers with an average transfer time of one hour.¹⁷ The Maastricht group have reported a study in which 149 patients were transferred from hospitals without angioplasty facilities to an interventional centre without any severe complications occurring in transit.¹⁸ Our data and existing evidence suggest that patients with an acute myocardial infarction can be safely transferred to an interventional centre but all effort must be made to minimise transfer times so that myocardial salvage can be optimised.

Stents and 2b3a blockers in rescue PCI

The use of intracoronary stents was at the discretion of the operator but suboptimal results after balloon angioplasty and severe dissections were the usual indications. Observational studies reported good angiographic and clinical outcomes with stents in rescue PCI.^{19, 20} The use of abciximab as adjunctive therapy to primary and rescue angioplasty in the EPIC trial was associated with a statistically significant reduction in ischaemic events (reinfarction and repeat intervention) at six months.⁶

Risks of bleeding during rescue PCI

Percutaneous intervention in patients with who have recently received thrombolytic treatment is clearly associated with a risk of bleeding, particularly from arterial puncture sites. However this problem has largely been resolved by a variety of groin closure devices. None of the patients in this study

received a groin closure device but it is our normal practice now to close the puncture site at the end of the procedure. The use of 2b3a blockers after full dose thrombolysis increases the risk of bleeding even further and not surprisingly, significant bleeding events were higher in the abciximab treated group. There is no available data on the use of abciximab in the setting of a failed rescue thrombolysis but our experience indicates that this combination should be avoided.

Rescue PCI in cardiogenic shock

In the SHOCK trial survival at six months was significantly better in the interventional arm despite no mortality benefit at 30 days (50.3% v 63.1%; $p=0.027$).²¹ Both 30 day and one year survival benefit was evident in patients treated with early aggressive intervention compared with medical treatment in the GUSTO-I study.^{22, 23} As such we should be offering emergency percutaneous and where appropriate surgical revascularisation to patients presenting in cardiogenic shock. However, in the UK healthcare system thrombolytic treatment is still the most widely offered reperfusion treatment to these patients and as such there is likely to be a continuing demand for rescue PCI.

PCI in patients with TIMI 3 flow

The decision to proceed with PCI in a patient who already has TIMI 3 flow is a difficult one. Continuing clinical and ECG evidence of failed reperfusion and/or a severe residual stenosis of the infarct related artery are the usual reasons to proceed. The GUSTO data clearly indicate that at least after thrombolytic treatment TIMI 3 flow is better than TIMI 2 flow. Ito *et al* have also shown that even patients with TIMI 3 flow do not always have adequate myocardial perfusion at the tissue level.²⁴ Concerns that a failed procedure will result in a reduction in flow in patients with TIMI 3 before PCI were raised by a number of studies conducted in the 1980s. However this is less of an issue in the stent era particularly with the added protection of 2b3a receptor blockade.⁴ In our series all patients with TIMI 3 flow before PCI maintained TIMI 3 flow after PCI.

CONCLUSION

This observational study confirms that emergency PCI can be carried out in hospitals without on-site cardiac surgery. There was no systematic assessment of myocardial salvage or long term patency of the infarct related artery but follow up is ongoing. Outcome assessment is complicated by undoubted selection bias. In our centres, patients in whom the area of infarction is considered small by ECG criteria and are haemodynamically stable are not considered for rescue PCI. We restrict our efforts to patients with large infarctions, do not exclude cardiogenic shock, but only rarely proceed beyond 12 hours after the onset of pain. In this series the mortality of rescue PCI in the non-cardiogenic shock group is comparable to successful thrombolytic treatment. However there were significant delays between the diagnosis of failed thrombolysis and rescue PCI being performed due in part to non-availability of the catheterisation laboratory after 2200 hours. Reduction of these delays may further improve outcomes.

We believe our results can be replicated in other district general hospitals with cardiac catheterisation facilities provided an experienced team is available. Emergency surgery is not indicated for patients who fail to reperfuse with thrombolysis and hence surgical cover for “rescue” PCI is in our opinion not a prerequisite for a successful programme.

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Learning points

A. TIMI grading of coronary flow

- 0: Occluded artery with no penetration of dye.
- I: Occluded artery with minimal penetration of dye beyond lesion.
- II: Open artery with slow flow beyond lesion.
- III: Open artery with normal flow beyond lesion.

B. Rescue percutaneous coronary intervention

- The only randomised trial (RESCUE trial) demonstrated a significant reduction in the combined end point of death and heart failure in the rescue arm in patients with large anterior infarctions treated by PCI within eight hours of the onset of pain.
- Successful intervention in non-shock patients is associated with mortality rates comparable to successful thrombolysis.
- Failed intervention is associated with poor outcomes and high mortality.
- The heavy thrombus burden in these patients suggests glycoprotein 2b3a blockers may be of benefit but this must be weighed against the risks of increased bleeding.
- The British Heart Foundation sponsored REACT trial has been set up to compare conservative treatment versus "rescue" thrombolysis with reteplase versus rescue PCI.

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