Primary angioplasty

The optimal reperfusion strategy in the United States?

Limitations to thrombolytics have included the inability to restore normal flow in most patients, recurrent ischaemia, reocclusion, and restricted recovery of left ventricular function. In an attempt to overcome these limitations, in early studies angioplasty was applied immediately after intravenous thrombolysis. However, these studies failed to show a benefit of immediate percutaneous transluminal coronary angioplasty (PTCA) and there was a suggestion that it worsened the outcome compared with a more conservative approach.¹⁻⁵ Subsequent studies showed that thrombolytic therapy aggregates platelets,⁶⁻⁸ extends coronary dissection planes,^{9,10} and increases the cardiac event rate after coronary angioplasty.^{11,12} Thus the current focus has been on primary PTCA. "Direct" or "primary" PTCA refers to angioplasty that is undertaken as a primary reperfusion strategy without prior thrombolytic therapy. Observation series showed high patency rates and a favourable prognosis in patients treated with primary PTCA.¹³⁻¹⁸ However, until recently there were no prospective randomised data to compare primary PTCA with thrombolysis.

PROSPECTIVE TRIALS

To test whether PTCA results in greater myocardial salvage than thrombolysis, Gibbons randomised 47 patients to primary PTCA and 56 patients to tissue plasminogen activator (t-PA, alteplase).¹⁹ Infarct size as assessed by acute and predischARGE Sesta ⁹⁹Tc methoxy-isobutyl isonitrile scans was similar in the two groups, however, with an average time to reperfusion of 4.5 hours it would be difficult to show any difference in infarct size. Moreover, patients assigned to the t-PA arm had a significant reduction in recurrent ischaemia (15 v 36%, $P = 0.02$), shorter length of hospital stay (7.7 v 10.6 days), and a trend toward reduced hospital costs (\$16 811 v \$21 400, $P = 0.09$). At 6 months there were fewer readmissions in the PTCA group (4 v 18%, $P = 0.04$) and lower follow up costs.

Zijlstra *et al* randomised 142 patients to receive either intravenous streptokinase or primary PTCA.²⁰ Acute patency was achieved in 98% of patients randomised to PTCA. Patients assigned to the PTCA arm had lower rates of recurrent ischaemia (9 v 38%, $P = 0.001$) and reinfarction (0 v 13%, $P = 0.003$). The mean (SD) predischARGE ejection fraction was higher in the PTCA group (51 (11) v 45 (12)%, $P = 0.004$). Late follow up catheterisation showed a patent vessel in 91% of PTCA patients compared with 68% of streptokinase patients ($P = 0.001$).

The Primary Angioplasty in Myocardial Infarction (PAMI) trial was a multicentre trial in which 395 patients of any age who presented with acute myocardial infarction (MI) were treated with heparin and aspirin and then randomised to primary PTCA or t-PA followed by conservative care.²¹ Time from randomisation to treatment was longer in the PTCA group (60 v 32 minutes). However, once the PTCA procedure was initiated, reperfusion was quickly established, resulting in earlier resolution of chest pain. Among the patients randomised to PTCA, 90% had PTCA attempted and procedural success was achieved in 97%. No patient required emergency

coronary artery bypass grafting (CABG) after attempted PTCA. A patent vessel was achieved by PTCA or spontaneous reperfusion in 98% of patients randomised to PTCA. The table shows that patients randomised to PTCA had a lower rate of recurrent ischaemia, fewer intracranial bleeds, a shorter length of hospital stay, and a trend for fewer reinfarctions and lower mortality. Patients who met the thrombolysis in myocardial infarction (TIMI 2B)²² criteria of "not low risk" (age >70 years, anterior MI, heart rate >100 beats/min) had a significant reduction in mortality with PTCA (2.0 v 10.4%, $P = 0.01$). For the patients considered to be at low risk, mortality in the PTCA and t-PA groups was similar. The primary end point of recurrent myocardial infarction or death occurred less frequently in the PTCA group by the time of hospital discharge (5.1 v 12.0%, $P = 0.02$) and at 6 months (8.5 v 16.8%, $P = 0.02$). Left ventricular function acutely and at 6 weeks was similar in the two groups. The in-hospital charges, which included physician fees, were similar in the two groups.

Results of the primary angioplasty in myocardial infarction (PAMI) trial

	PTCA (n = 195) (%)	t-PA (n = 200) (%)	P
Death overall:	2.6	6.5	0.06
Not low risk*	2.0	10.4	0.01
Low risk	3.1	2.2	0.69
Reinfarction	2.6	6.5	0.06
Death or non-fatal reinfarction	5.1	12.0	0.02
Death or non-fatal reinfarction (6 mth)	9	17	0.02
Haemorrhagic stroke	0	2	0.05
Ventricular fibrillation	7	2	0.02
Vascular surgical repair	2	0	0.05
Ejection fraction (mean (SD)) (%)	53 (13)	53 (13)	0.52
Length of hospital stay (days)	7.5	8.4	0.03

*Not low risk: age >70, anterior MI, heart rate >100 beats/min.

CONCLUSIONS

In conclusion, the three published randomised trials each showed a significant reduction in recurrent ischaemia when PTCA was compared with thrombolysis. In addition, pooled data from these trials show that primary PTCA is associated with significantly lower rates of reinfarction, stroke, and death than thrombolysis (figure). The less complicated hospital course after PTCA significantly reduced the length of hospital stay in all three randomised trials and combined hospital and professional charges for PTCA treated patients were less than or equal to those for the thrombolytic group.

It has now been established that TIMI 3 flow is an important determinant of left ventricular functional recovery and survival.²³ A meta-analysis of angiographic trials²⁴ and the GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) angiographic substudy²⁵ report acute patency rates after thrombolysis of from 50% (with streptokinase) to 80% (after accelerated t-PA) with normal antegrade flow in only 40–52% of patients. The strategy of primary PTCA resulted in acute patency rates of 98–99%, normal flow in 93–94% of vessels, and <50% stenosis in 93–97% patients.^{17,19-22} In addition, primary angioplasty does not seem to delay the time to reperfusion

Pooled data from the three published randomised trials indicate that primary PTCA is associated with reduced rates of reinfarction, death, and stroke.¹⁸⁻²⁰

as assessed angiographically^{20 25} or by resolution of chest pain.^{19 21} Therefore, the available data suggest that primary PTCA is superior to intravenous thrombolytic drugs at quickly establishing a patent infarct vessel.

Until recently, it was thought that reocclusion after thrombolysis occurred primarily in the first few days of infarction. Paired early and late coronary arteriograms were obtained in only two thrombolytic trials. In the TAMI-6 trial angiography was performed 48 hours and 6 months after myocardial infarction.²⁶ Patients treated with t-PA had patency rate of only 59% at 6 months which was no different from patients who had received placebo. The Antithrombotics in the Prevention of Reocclusion in Coronary Thrombolysis (APRICOT) trial randomised 300 patients who had a patent vessel 48 hours after streptokinase to receive aspirin, coumadin (with continuation of heparin until a therapeutic prothrombin time was achieved), or neither.²⁷ At 3 month follow up catheterisation all three groups had high rates of reocclusion, with a late patency rate of only 71%. In contrast, patency rates after PTCA remained high (87-91%) 3-6 months after myocardial infarction.^{12 20 28}

Therefore, there are several advantages to PTCA when used as a primary reperfusion strategy. An emergency diagnostic catheterisation with early definition of coronary anatomy allows the treatment to be individually tailored; indeed, in the PAMI trial, 10% of patients randomised to PTCA did not undergo the procedure because they had severe multivessel or left main disease requiring emergency bypass surgery (5%) or spontaneous reperfusion with no high grade stenosis (5%). Acute and late patency rates are higher than those achieved with thrombolysis, the rates of recurrent ischaemia and intracranial bleeding are reduced, and the length of hospital stay shortened. Importantly, primary angioplasty also seems to reduce rates of reinfarction and death, particularly in high risk patients. These data suggest that when the facilities and trained personnel are available, primary angioplasty is the preferred reperfusion strategy.

CINDY L GRINES

WILLIAM W O'NEILL

William Beaumont Hospital,

Division of Cardiology, Royal Oak, Michigan, USA

- Rogers WJ, Baim DS, Gore JM, *et al*, for the TIMI II-A Investigators: Comparison of immediate invasive, delayed invasive and conservative strategies after tissue-type plasminogen activator. *Circulation* 1990;81:1457-76.
- Topol EJ, Califf RM, George BS, *et al*, and the Thrombolysis and Angioplasty in Myocardial Infarction Study Group. A randomized trial of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. *N Engl J Med* 1987;317:581-8.
- Simoons ML, Arnold AER, Betric A, *et al*. Thrombolysis with tissue plasminogen activator in acute myocardial infarction: no additional benefit from immediate percutaneous coronary angioplasty. *Lancet* 1988;i:197-202.
- The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction: results of the Thrombolysis in Myocardial Infarction (TIMI) phase II trial. *N Engl J Med* 1989;320:618-27.
- SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group. SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. *Br Med J* 1991;302:555-60.
- Fitzgerald DJ, Roy L, Wright F, *et al*. Functional significance of platelet activation following coronary thrombolysis. *Circulation* 1987;76:IV-153.
- Kerins DM, Roy L, Fitzgerald GA, *et al*. Platelet and vascular function during coronary thrombolysis with tissue-type plasminogen activator. *Circulation* 1989;80:1718-25.
- Bennett WR, Yawn DH, Migliore PJ, *et al*. Activation of the complement system by recombinant tissue plasminogen activator. *J Am Coll Cardiol* 1987;10:627-32.
- Castaneda-Zuniga WR, Sibley R, Amplatz K. The pathologic basis of angioplasty. *Angiology* 1984;35:195-205.
- Kohchi K, Takebayashi S, Block PC. Arterial changes after percutaneous transluminal coronary angioplasty: results at autopsy. *J Am Coll Cardiol* 1987;10:592-99.
- Ambrose JA, Sharma S, Sabino T, *et al*. Thrombolysis and Angioplasty in Unstable Angina (TAUSA) Trial [abstr]. *Circulation* 1993;88:1-208.
- O'Neill WW, Weintraub R, Grines CL, *et al*. A prospective, placebo-controlled, randomized trial of intravenous streptokinase and angioplasty versus lone angioplasty therapy of acute myocardial infarction. *Circulation* 1992;86:1710-7.
- O'Keefe JR Jr., Rutherford BD, McConahay DR, *et al*. Early and late results of coronary angioplasty without antecedent thrombolytic therapy for acute myocardial infarction. *Am J Cardiol* 1989;64:1221-30.
- Rothbaum DA, Linnemeier TJ, Randin RJ, *et al*. Emergency percutaneous transluminal coronary angioplasty in acute myocardial infarction: a 3 year experience. *J Am Coll Cardiol* 1987;10:264-72.
- Miller PF, Brodie BR, Weintraub RA, *et al*. Emergency coronary angioplasty for acute myocardial infarction. *Arch Intern Med* 1987;147:1565-70.
- Perrigo ES, Leguizamón E. Management of Acute Myocardial Infarction (AMI) using Immediate Percutaneous Transluminal Angioplasty (I-PTCA) [abstr]. *Med Sci Sports Exerc* 1989;21:S-55.
- O'Neill WW, Brodie BR, Ivanhoe R, *et al*. Primary Coronary Angioplasty for Acute Myocardial Infarction (The Primary Angioplasty Registry). *Am J Cardiol* 1994;73:627-34.
- O'Neill WW. Angioplasty therapy of cardiogenic shock: are randomized trials necessary? *J Am Coll Cardiol* 1992;19:915-7.
- Gibbons RJ, Holmes RJ, Reeder GS, *et al*. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. *N Engl J Med* 1993;328:685-91.
- Zijlstra F, DeBoer MJ, Hoorntje JCA, *et al*. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. *N Engl J Med* 1993;328:680-4.
- Grines CL, Browne KR, Marco J, *et al*. A comparison of primary angioplasty with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1993;328:673-9.
- The TIMI Study Group. Comparison of invasive and conservative strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction. Results of the thrombolysis in myocardial infarction (TIMI) Phase II Trial. *N Engl J Med* 1989;320:618-27.
- The GUSTO Angiographic Investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function, and survival after acute myocardial infarction. *N Engl J Med* 1993;329:1615-22.
- Granger CB, Ohman EM, Bates E. Pooled analysis of angiographic patency rates from thrombolytic therapy trials [abstr]. *Circulation* 1992;86:I-269.
- DeWood MA, Fisher MJ. Direct PTCA vs rt-PA in acute myocardial infarction: preliminary results from a prospective, randomized trial [abstr]. *Circulation* 1989;80:II-418.
- Topol EJ, Califf RM, Vandormael M, *et al*, and the Thrombolysis and Angioplasty in Myocardial Infarction (TAMI-6) Study Group. A randomized trial of late reperfusion therapy for acute myocardial infarction. *Circulation* 1992;85:2090-9.
- Meijer A, Werter CJ, Freek WA, *et al*. The APRICOT study: aspirin versus coumadin in the prevention of recurrent ischaemia and reocclusion after successful thrombolysis, a placebo-controlled angiographic follow-up study [abstr]. *J Am Coll Cardiol* 1992;19:91A.
- Brodie B, Grines C, Ivanhoe R, *et al*. Six month clinical and angiographic follow-up after direct angioplasty for myocardial infarction: final results from the Primary Angioplasty Registry. *Circulation* 1994;25:156-62.