The role of coronary angioplasty and stenting in acute myocardial infarction

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Summary

Despite the improvements in the pharmacological treatment of acute myocardial infarction, it is recognised that thrombolysis fails to reproduce reperfusion in a significant proportion of patients. Coronary interventional techniques have been shown to offer an alternative reperfusion strategy. There is increasing evidence that mechanical reperfusion may offer significant advantages over established thrombolytic therapy.

Keywords: angioplasty; stenting; myocardial infarction; percutaneous transluminal coronary angioplasty; thrombolysis

The mortality from acute myocardial infarction (AMI) has been steadily decreasing and according to some estimates,^{1 2} about 40% of the fall in mortality until the late 1980s was due to coronary care units, pre-hospital resuscitation and newer medical treatments. It is the latter which has contributed to the continued decline in case fatality rates to the present day.³ Nevertheless, the in-hospital and early mortality from AMI remains unacceptably high, approximately 20% in Scotland in the MONICA project.⁴

The use of aspirin,⁵ β -blockers,⁶ and more recently angiotensin-converting enzyme inhibitors⁷ and statins,⁸ have contributed to the reduction in mortality after AMI. However, none of these measures directly address the underlying cause of the AMI, namely thrombosis. Restoration of normal blood flow in an infarct-related coronary artery is the 'holy grail' of modern cardiology. Significant reductions in mortality of 20–30% were achieved by early attempts at thrombus dissolution using intravenous thrombolytic agents.^{9 10} More recently the use of the more specific agent recombinant tissue plasminogen activator (rtPA) when used in an 'accelerated' approach in the GUSTO I trial has produced further benefits, especially in high-risk groups, when compared with streptokinase.¹¹ Despite these improvements, coronary angiographic substudies have shown that reperfusion rates are less impressive. Restoration of normal thrombolysis in myocardial infarction (TIMI grade 3, box 1) flow in the infarct related artery at 90 minutes after commencement of thrombolytic therapy has been found in only 29–54% of culprit vessels.^{10 12} Initially, indirect evidence from experimental studies suggested that an 'open' infarct-related vessel confers a better outcome irrespective of any myocardial salvage.¹³ The Western Washington trial of intracoronary streptokinase showed that patients with restoration of vessel patency had significantly improved long-term prognosis when compared to those with partial or no reperfusion, without any improvement in myocardial function.¹⁴ These observations lead to the logical conclusion that thrombolysis should ideally be followed by immediate coronary angiography and angioplasty if appropriate. Early angiography also has the added benefit of accurately defining coronary anatomy allowing early triage to surgery.

The principal question which has to be answered is on whom, if any, should coronary intervention be performed following thrombolysis. The approaches vary between angioplasty in those with satisfactory reperfusion but a residual stenosis, restricting intervention to only those with evidence of reduced perfusion (less than TIMI grade 3), or even more selectively dealing only with those who have failed to reperfuse, so called 'rescue angioplasty'.

A further obvious question is when should any intervention take place, immediately or shortly after the initiation or completion of thrombolysis, after some hours, after a few days, or only if the patient has further evidence of cardiac ischaemia.

Angioplasty following thrombolysis

There was initial optimism when two early trials showed an apparent benefit from early angioplasty following either intracoronary or intravenous streptokinase.^{15 16} This led to the organisation of larger scale trials to confirm these results. The European Co-operative Study Group compared rtPA and conservative therapy versus rtPA and immediate angioplasty randomised patients with TIMI grade 0 or 1, and patients with a higher TIMI grade but with a residual stenosis of >60% in the infarct-related vessel.¹⁷ The trial, however, was terminated early after the ethical review committee found there was no difference in the primary end points of infarct size and left ventricular function and a non-significant trend towards increased mortality in the invasive group (15 *vs* 6 deaths) (table 1). These discouraging results were supported by the similar TIMI IIA study which reported higher rates of bypass surgery and bleeding complications in the invasive group.¹⁸

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Thrombolysis in myocardial infarction (TIMI) flow grading

Grade 0: No flow of contrast beyond the point of occlusion

Grade 1: Penetration with minimal perfusion (contrast fails to opacify the entire coronary bed distal to the stenosis for the duration of the investigation)

Grade 2: Partial perfusion (contrast opacifies the entire distal coronary artery, but the rate of entry or clearance, or both, is slower in the stenosed or previously blocked artery than in nearby normally perfused vessels)

Grade 3: Complete perfusion (contrast filling and clearance are as rapid in the stenosed or previously blocked vessel as in normally perfused vessels)

Box 1

The TAMI (Thrombolysis for Acute Myocardial Infarction) group of investigators performed a series of trials looking at various thrombolytic regimes and specifically addressed the issue of 'rescue angioplasty'. In a review of the first five TAMI trials 169 of 776 patients had angioplasty of infarct-related vessels to achieve patency after failed thrombolysis, the remainder having achieved patency by thrombolysis.¹⁹ The successful thrombolysis group had greater acute and 7–10 day left ventricular ejection fractions, better infarct zone recovery, and less re-occlusion. However, in-hospital and long-term mortality rates were similar in both groups (table 1).

In the angiographic substudy of the GUSTO trial²⁰ the angiographic success rate of 'rescue angioplasty' was 90%, a figure similar to that achieved by other groups.^{21–23} The principal finding was a marked difference in 30-day mortality in those patients in whom rescue angioplasty was unsuccessful (30.4%) compared to successful rescue angioplasty (8.6%) or successful thrombolysis (5.2%). This has also been observed in the second GUSTO study.²⁴ It must be stressed that the rescue procedure were not randomised and therefore only give inferential information on the clinical usefulness of this procedure. The randomised trial conducted by Ellis and co-workers suggested a borderline benefit in the combined clinical endpoint of death or severe heart failure in favour of rescue angioplasty (table 1).²¹ However only exercise and not resting left ventricular ejection fraction was significantly improved (43% *vs* 38%, *p* = 0.04). Preliminary data suggests that the results of rescue angioplasty may be improved by the adjunctive use of potent antiplatelet agents. In the GUSTO 3 trial analysis of a small subgroup who underwent angioplasty for failed thrombolysis appeared to show that the non-randomised use of the antiplatelet glycoprotein IIb/IIIa antibody abciximab, reduced 30-day mortality (3.7% *vs* 9.8%).²⁵

Thus, information on angioplasty following thrombolysis is limited but from what is currently available its use can only really be advocated in selected subgroups, specifically those in which thrombolysis has failed. Even in this group of patient the extent of benefit needs further defining. One problem is accurately defining those patients who have failed to reperfuse with thrombolytic therapy without recourse to angiography. Abrupt cessation of chest pain predicts reperfusion with a sensitivity of 66–84% but this occurs in only 30–50% of patients.²⁶ ST segment assessment is more promising but also has its limitations. ST segment resolution (ie 25–50% fall in ST segment elevation in either a sum of all leads or in the single worst lead) and establishment of patency of the infarct related artery yield varying sensitivities of 52–97% with specificities of 43–88%.²⁷ In the GUSTO I trial substudy, ST segment monitoring revealed a predictive ability of 70–82% for vessel patency and 58–64% for occlusion.²⁸

An issue which has yet to be addressed is whether there are any alternatives to rescue angioplasty or conservative treatment when thrombolysis fails. Can repeat thrombolysis be just as effective as rescue angioplasty? At present there are no data from randomised studies. However, the Rescue Angioplasty versus Conservative treatment or repeat Thrombolysis (REACT) trial, which is due to start enrolling patients in 1999, will compare the outcome in patients with failed thrombolysis when they are randomised to rescue angioplasty, further thrombolysis or conservative treatment (intravenous heparin for 24 hours). Results should be available in December 2001.

Primary angioplasty versus thrombolysis

The primary angioplasty debate was commenced by the simultaneous publication of three trials in 1993 comparing primary angioplasty with thrombolytic therapy for the treatment of AMI.^{29–31} Each of these trials had relatively small numbers making definite conclusions on mortality benefit difficult. However, two of the trials^{29–30} did reach positive conclusions regarding the benefits of the procedure. Grines' group²⁹ showed that primary percutaneous

PTCA in acute myocardial infarction

- is more complicated than elective PTCA
- achieves higher rates of reperfusion than thrombolytic agents
- achieves lower mortality and non-fatal reinfarction rates than thrombolysis
- has a lower incidence of stroke than thrombolysis
- should be considered for all those with contraindications to thrombolysis
- should only be used following thrombolysis where there is evidence of failed reperfusion or on-going ischaemia

Box 2

Table 1 Results of rescue PTCA and conservative treatment in failed thrombolysis

Reference	Number of patients	PTCA	Success rate (%)	Mortality of PTCA (%)	Mortality of conservative treatment (%)
22	72	72	92	4	—
17	367	183*	92	8.2	3.3
21	151	92	92	5.1	9.6**
20	214	214	90	8.6	5.2
19	776	169	—	5.9	4.6

Success was generally defined as restoration of TIMI grade 2–3 and residual stenosis <50%; *only 168 of those randomised had PTCA performed; ***p* < 0.05.

transluminal coronary angioplasty (PTCA) produced a significant reduction in the combined rates of recurrent ischaemia, haemorrhagic strokes, non-fatal reinfarction and death. Zijlstra's group³⁰ had the advantage of angiographic assessment in both arms of the study, and found higher rates of patency in the angioplasty group. Repeat angiography 3 months later in the PTCA group showed patency rates of 91% *vs* 68% at 3 weeks ($p = 0.001$). They also reported lower rates of reinfarction, unstable angina, less severe residual stenotic lesion and marginally better left ventricular ejection fractions in the angioplasty group. These investigators enrolled further patients in an extension to the original study.³² The combined results showed significant reductions in in-hospital mortality, reinfarction and more impressive improvements in left ventricular ejection fraction in the angioplasty group.

Since the publication of these studies there have been several more trials of primary angioplasty compared to thrombolytic therapy. The problem of small patient numbers has to some extent been circumvented by a comprehensive meta-analysis³³ of all the randomised studies comparing primary angioplasty with thrombolysis up to the end of 1997.^{24 29–32 34–38} In total, 2606 patients were randomised; 1316 received thrombolytic therapy, of whom 307 received streptokinase, 300 a 3–4 hour infusion of tPA or alteplase and 709 received 'accelerated' tPA. Not surprisingly in a 'trial setting' there was only a mean 26-minute delay to treatment by angioplasty.

The combined meta-analysis results showed the risk of death was 4.4% in the PTCA group and 6.5% in the thrombolytic group ($p = 0.002$). This translates into an additional 21 lives saved by PTCA per 1000 patients treated. When looking at the combined end points of death or non-fatal reinfarction there was a significant reduction in favour of PTCA (7.2% *vs* 11.9%, $p < 0.001$). This represents 46 fewer events per 1000 patients treated by PTCA. There was a trend for the 'accelerated' tPA treatment group to be better than the other thrombolytic regimes but this did not reach significance levels. Total stroke rates were significantly better in the PTCA group (0.7% *vs* 2.0%, $p < 0.007$), as were the rates of haemorrhagic stroke (0.1% *vs* 1.1%, $p < 0.001$). This difference was most marked in the 'accelerated' tPA trials. The risk of major bleeding was similar between all groups with 8.8% of PTCA patients and 8.4% of thrombolytic patients having at least one major bleeding episode.

Should these results make us all want to throw away our syringes of thrombolytic agents and reach for our angioplasty balloons? Apart from the obvious lack of availability of cardiac catheterisation facilities in most hospitals there are many issues which still need addressing.

Firstly, the patients recruited to the primary angioplasty trials were highly selected, as shown by the low mortality rate (6.5%) in the thrombolytic group. In one reported study the unselected mortality rate for all anterior myocardial infarction patients treated by primary PTCA within 6 hours of symptoms was considerably higher at 16.4%, than in the previously mentioned randomised trials.³⁹ Secondly, are the beneficial effects of PTCA maintained for longer than the short-term (30-day) follow-up used in most trials? Evidence from the GUSTO IIB trial²⁴ which included 6 months follow-up suggested in fact that there was no difference in end-points by this time. In this study, however, only 82% of patients randomised to the angioplasty arm actually underwent the procedure and only 73% of these achieved TIMI 3 flow compared with 92–97% in the other, albeit, smaller studies.^{29–32} A further issue is whether angioplasty should be specifically reserved for those patients judged to be at higher risk? However, even in 'low risk' groups, PTCA has been shown to significantly reduce rates of death, nonfatal reinfarction and stroke.³² Additional larger studies are required before conclusive recommendations in this area can be made.

Many patients with AMI may be ineligible for thrombolytic therapy because of contraindications. Paradoxically, it is often this group of patients who have most to gain from reperfusion therapy. They are more likely to be female, older, present late, have had previous infarcts, multivessel disease, lower ejection fraction, and higher in-hospital mortality (18.7% *vs* 3.9%, $p < 0.001$).⁴⁰ Analysis of data from patients who historically would have been excluded from or considered ineligible for the early thrombolytic trials (namely, presentation more than 6 hours after onset of chest pain) appears to show a significantly lower rate of repeat AMI or death achieved by PTCA versus thrombolysis (tPA). There is, however, a significant increase in procedure-related mortality due to co-morbid disease when compared to thrombolytic eligible patients (14% *vs* 3%).⁴¹ In patients who are considered ineligible for thrombolytic therapy because of a significantly increased bleeding risk then this may still be a problem to an extent with primary PTCA because of adjunctive antithrombotic therapy that may be used (heparin, ticlopidine, glycoprotein IIb/IIIa antagonists).⁴² It has to be remembered that these trials have, on the whole, been performed in centres with

Stenting in acute myocardial infarction

- can be safely performed in the setting of AMI
- achieves lower composite rates of target vessel revascularisation, repeat AMI and death than PTCA alone
- use in every patient having PTCA for AMI has not yet been proven
- sub-acute thrombosis rates are significantly reduced by ticlopidine
- results can be improved further by the use of glycoprotein IIb/IIIa inhibitors

Box 3

high levels of expertise and dedication to provision of primary angioplasty facilities. Thus it may not be appropriate to try and extrapolate these results to the wider population of hospitals in the US,²⁴ let alone the UK. Primary angioplasty is a more technically demanding procedure than elective angioplasty and is associated with an operator-dependent morbidity and mortality that varies with the skill and experience of the operator.⁴³ There has been a suggestion that primary angioplasty procedures could be carried out in centres without surgical backup, thereby potentially allowing more hospitals to offer this service.⁴⁴ In the trials mentioned above significant numbers of patients assigned to angioplasty actually had coronary artery by-pass grafting (CABG) performed instead, and generally more of the patients undergoing angioplasty required CABG than the thrombolysis arm. Given that the trials were generally analysed on an 'intention-to-treat' basis and that the CABG patients generally had good results this may have improved the benefits noted in the angioplasty arm. The single factor which may affect the extension of provision of primary angioplasty facilities is that of increased cost. Some of the studies mentioned above did carry out cost comparisons and found similar or marginal benefits with angioplasty. However, until definitive data on long-term outcomes are available, such comparisons are not valid.

Stenting in AMI

In all the previously mentioned trials there was no use of intracoronary stents and antithrombotic regimes comprised mainly aspirin and heparin. It is also interesting to note that in all trials angiographic success was defined as a residual diameter stenosis of less than 50%. It has been shown that the degree of residual stenosis following angioplasty correlates with re-stenosis rates.⁴⁵⁻⁴⁶ The implantation of intracoronary stents has revolutionised the practice of interventional cardiology in stable patients,⁴⁷ but can such successes be translated into the unstable situation of AMI? Concern has always existed regarding the implantation of 'thrombotic' metallic stents in a vessel where occlusion might have dire consequences.⁴⁸⁻⁴⁹ In AMI, unstable plaques, thrombus and circulating activated platelets are known to be present, thereby potentiating the thrombotic environment. However, if the concerns of possible thrombosis are laid aside for a moment, the reasons why stent implantation in these circumstances might be useful are obvious. Stents are well known to seal dissection planes and improve post-PTCA residual vessel stenosis in elective stenting. In AMI this could reduce recurrent ischaemia and re-occlusion, thereby reducing rates of death and re-infarction. In addition, stents are able to produce a larger lumen than PTCA alone and this, in elective stenting, has resulted in improved clinical and angiographic outcomes.⁵⁰⁻⁵²

Bail-out stenting in AMI

Stents were initially used cautiously in AMI and tended to be used as a 'bail-out' measure for acute or threatened closure. However, evidence supporting this approach in the form of randomised controlled trials is lacking, due no doubt to lack of ethical alternatives, given that the only other alternatives to stent placement are perfusion balloon PTCA, conservative care or emergency CABG. In a comprehensive review of the subject Stone⁵³ identified 12 studies of 'bail-out' stenting in AMI where this was performed in at least 70% of patients and with at least 50 patients included.⁵⁴⁻⁶⁵ These studies were very heterogeneous with differences in enrolment and procedures, and thus direct comparisons between them are not, strictly speaking, valid. Average success rates were reported at 96% with a rate of sub-acute thrombosis of 3.4%. There was 5.4% early mortality, 1.2% reinfarction rate and 7.0% need for target vessel revascularisation (TVR). Long-term follow-up data are once again not comprehensively reported, perhaps somewhat surprisingly, given that this is the area where stents would be expected to produce significant additional benefits over PTCA alone. There are seven studies with 10 patients or more reporting long-term follow-up for an average of 8.5 months⁵⁸⁻⁶⁰⁻⁶¹⁻⁶⁴⁻⁶⁶⁻⁶⁸ but even these data are not complete. TVR rates at 8 months were reported as 10.8%, with a composite rate of death, re-infarction or TVR of 13.3%, data which seem to represent a significant improvement over PTCA. The angiographic re-stenosis rate (defined as diameter reduction of greater than 50%) in a subset was found to be 26% at 6 months.

Primary stenting versus PTCA

The safety and feasibility of a primary stent approach, where stents are implanted in all patients irrespective of angioplasty result, has been evaluated by

Requirements for a primary PTCA strategy

- dedicated and fully staffed cardiac catheter laboratory 24 h/day
- experienced interventional cardiologists
- cardiac surgery on-site or near-by
- higher levels of investment than are generally currently available

Box 4

a number of non-randomised studies, although there are a growing number of randomised studies, either on-going or recently published, looking at this area. A review⁷³ of six non-randomised studies including 10 or more patients reporting the outcome of a primary stent strategy in AMI^{69–74} has recently been published. A total of 544 patients were included, with a success rate of 98%. The combined rate of subacute thrombosis was low at 1.8% as were the short-term (<3 months) rates of death (0.9%), re-infarction (1.3%), CABG (1.8%) and repeat TVR (2.1%). The combined end-point of death, re-infarction or TVR was 6.1%. These results would seem to be a significant improvement over PTCA alone, but selection bias cannot be ruled out. Long-term results have only been reported to a limited extent and suggest a re-stenosis rate of between 15–25% at 6 months.^{69 73}

Having demonstrated that a primary stenting strategy was safe the next priority was to compare its efficacy to angioplasty in AMI in randomised trials of AMI management. We will briefly review six randomised trials which have either recently presented their results or are on-going (table 2).^{53 75–78} In the Florence Randomised Elective Stenting in Acute Coronary Occlusions (FRESCO) trial,⁷⁵ 150 patients were randomised to stenting or no further therapy following a successful angioplasty (restoration of TIMI III flow and residual stenosis <30%). The 30-day results showed significantly fewer recurrent ischaemic events in the stented group (3% *vs* 15%) resulting in a significant excess of TVR in the angioplasty group (12% *vs* 1%). The 6-month results also showed a significant reduction in recurrent ischaemia rates and repeat TVR. The incidence of re-stenosis or re-occlusion was 17% in the stent group and 43% in the angioplasty group. The ESCOBAR trial⁷⁶ randomised 204 patients to primary stenting or PTCA but there was a 15% 'cross-over' to stenting in the PTCA group. The results showed significantly fewer TVR (2 *vs* 10%, *p* = 0.03) in the stented group at 30 days. The Primary Angioplasty *vs* Stent Implantation in AMI (PASTA) trial⁷⁷ enrolled 142 patients and preliminary incomplete results show a reduced composite endpoint of in-hospital death, reinfarction and TVR in the stented group. The Gianturco Roubin II Stent in AMI (GRAMI) trial⁷⁸ randomised 104 patients following crossing of the lesion with a guide wire. There was a much higher 'cross-over' rate of 25% of PTCA patients, a fact that may explain the failure to demonstrate differences in 1 year TVR or re-stenosis rates, although in the stented group there was a significant improvement in freedom from the composite rate of death, re-infarction or TVR both in-hospital and at 1 year. These latter results were primarily due to a decreased death and reinfarction in patients who presented in Killip class III-IV and were stented. The Second Stent in AMI (Stentim) trial and the PRISAM trial⁵³ have not yet reported but preliminary results appear to be similar to the trials above.

All these trials have the problem of having insufficient numbers of patients to be able to demonstrate any reduction in mortality or re-infarction alone with a primary stent strategy in AMI, but they do seem to suggest that the main disadvantage of primary PTCA, namely late re-stenosis and occlusion, can be significantly improved by the insertion of a stent in the majority of cases. The results of larger scale trials are awaited.

However, the limited evidence available at the present moment would suggest that after an excellent ('stent-like') angioplasty result, routine stent placement is probably unnecessary.⁷⁹ Nevertheless, in situations of significant vessel recoil or flow-limiting dissection, stenting can be unequivocally be recommended. It is the 'middle ground' patient group (those with residual diameter stenosis post-PTCA of 30–50% or non-flow-limiting dissections) in whom it is unclear at the present time which individuals would gain additional benefit from stenting. Ongoing trials should hopefully provide some answers.

Table 2 Results of randomised trials of primary stenting (quoted first) versus primary PTCA

	Ref 75	Ref 76	Ref 77	Ref 53	Ref 78
Number of patients	150	204	142	220	104
Mortality (%)	1 <i>vs</i> 0	0.5 <i>vs</i> 1.5	3.3 <i>vs</i> 8.2	4.1 <i>vs</i> 3.9	—
Re-infarction (%)	1 <i>vs</i> 3	0.5 <i>vs</i> 1.5	—	2.1 <i>vs</i> 6.1	—
TVR (%)	7 <i>vs</i> 25***	2 <i>vs</i> 10–	5 <i>vs</i> 13.1	2.1 <i>vs</i> 12.2#	11.5 <i>vs</i> 15.5
Combined end-point (%)	9 <i>vs</i> 28–	3 <i>vs</i> 13*	5 <i>vs</i> 21.3**	8.2 <i>vs</i> 21.6#	17 <i>vs</i> 35*

#*p* < 0.05, –*p* = 0.03, **p* = 0.02, ***p* = 0.008, ****p* = 0.002.

Crossover rates: crossover from PTCA to stent; TVR: target vessel revascularisation; combined end-point: total of target vessel revascularisation, re-infarction or death.

Ref 76: 30-day results; ref 75: 6-month results; ref 78: 1-year results; ref 77: incomplete in-hospital results; ref 53: in-hospital results.

Heparin-coated stents

The use of stents with a special coating of heparin has been investigated as a way of reducing stent thrombosis and avoiding the complications of systemic intravenous heparin. In the PAMI Heparin Coated Stent Randomised Trial, 900 patients with AMI were randomised to receive a new heparin-coated stent and no peri-procedural heparin versus primary PTCA and a 60-hour tapering heparin regimen. The 30-day results were presented at the American College of Cardiology meeting in Atlanta in 1998 and showed non-significant reductions in death, recurrent AMI and disabling stroke, but a significant reduction in ischaemia-driven TVR (0.6% *vs* 2.5%). The 6-month results were reported at the 1998 Transcatheter Cardiovascular Therapies conference in Washington and the improvements in TVR are maintained (7.5% *vs* 17%). This approach, using a regime in primary stenting which does not require heparin, is likely to reduce further vascular complications and facilitate earlier discharge.

Adjunctive therapy with coronary stenting

Initially it was thought necessary to institute an intensive anticoagulation regime with aspirin, heparin and a coumadin in the immediate post-procedure period when a stent is implanted. This regime was associated with a stent thrombosis rate of 1–9% but also led to a significant increase in haemorrhagic and vascular access site complications, with the latter varying between 10–30%, resulting in a substantial prolongation in hospital stay.⁸⁰ Antiplatelet agents have proved to be more attractive than anticoagulants in this situation, particularly as platelets are rapidly deposited on newly implanted stents.⁸¹ Ticlopidine is the only true antiplatelet agent other than aspirin routinely used in interventional cardiology. Recently a newer ticlopidine-like agent, clopidogrel has become available and its use in interventional cardiology is currently being investigated. The exact mode of action of ticlopidine is not known but it appears that it inhibits ADP activation of glycoprotein IIb/IIIa receptors on the platelet surface. Activation of these receptors mediates platelet-to-platelet interaction and thus aggregation.⁸² Several trials have shown a significant reduction in the primary end-points of death, myocardial infarction, or revascularisation, together with a reduction in haemorrhagic complications when aspirin plus ticlopidine has been compared to aspirin plus anticoagulation (Stent Anticoagulation Regimen Study, data presented at the American Heart Association Scientific Sessions, November 1996).^{61–83} The only disadvantage with the use of ticlopidine is its side-effect profile, which includes the minor effects of rashes and gastrointestinal upset and the more important risk of neutropenia. The latter was reported as severe in 0.8% of cases, but usually with prolonged (2–3 month) therapy and is reversible on discontinuation of therapy.^{84–85} The current recommended duration of therapy is 1 month following stenting.

More recently specific glycoprotein IIb/IIIa receptor antagonists, including the antibody abciximab, have been used to further reduce complications following interventional procedures. Results from a series of angioplasty trials have shown that the use of these agents in the peri-intervention period can reduce the incidence of death, AMI or revascularisation in the short and long term.^{86–91} In a recently published randomised study of a glycoprotein IIb/IIIa inhibitor in elective stenting (EPISTENT), significant benefit was evident with a reduction in the composite end point of death, MI or urgent revascularisation at 30 days (5.3% *vs* 10.8%).⁹² In theory glycoprotein IIb/IIIa antagonists when used in primary angioplasty and primary stenting should have even greater efficacy. However, large ongoing trials such as the CADILLAC study have still to report.⁵³

Stenting in thrombus-containing lesions

Conventional guidelines consider the presence of intracoronary thrombus to be an absolute contraindication to stenting.^{48–49} However as discussed previously, primary stenting consistently gives a better result than PTCA alone in AMI, a situation in which it is well known that the underlying pathological substrate frequently includes thrombus.^{93–94}

In a non-randomised trial the safety of stenting in visible thrombus-containing lesions has been demonstrated.⁹⁵ The results show low rates of subacute thrombosis (1%), death (6%) and non-Q wave myocardial infarction (6%), with acceptable re-stenosis rates (33%) in thrombus-containing target vessels. More work in this area is required to overcome the reluctance to stent in this situation, but undoubtedly the increasing use of glycoprotein IIb/IIIa inhibitors will help to assuage the doubts.

Conclusion

Primary PTCA does appear to produce consistently better reperfusion rates than thrombolytic therapy with better short- and medium-term outcomes in selected groups. Long-term benefits, however, have not been convincingly demonstrated. This may relate to a relatively high rate of coronary re-occlusion after primary PTCA, noted in serial angiographic studies.⁹⁶ The results from primary PTCA may be further improved by stent implantation in selected cases which can help prevent many of the complications associated with primary PTCA alone. The optimal antithrombotic regime includes short-term intravenous heparin which needs to be weight-adjusted especially if a glycoprotein IIb/IIIa receptor inhibitor is given, and ticlopidine if a stent is to be implanted.

Routine PTCA following thrombolysis has no place in AMI care, but for those with evidence of failed thrombolysis, ongoing ischaemia or contraindications to thrombolysis, further benefits can be achieved by mechanical intervention, provided this can be carried out quickly and by personnel skilled in this particular area.

The cost effectiveness of the newer and often very expensive developments has to be carefully weighed in each patient population before routine use is encouraged. For many hospitals the option of primary mechanical treatment of AMI is not feasible and the mainstay of therapy will remain thrombolytic agents. In the majority of settings thrombolytic therapy still provides significant improvements in morbidity and mortality. It is difficult to envisage how a therapy with such ease and speed of administration will ever lose its place at the top of the therapeutic ladder for AMI.

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