Optimal reperfusion strategy for acute myocardial infarction

Primary percutaneous coronary intervention has proved to be a superior intervention strategy for acute myocardial infarction than pre-hospital thrombolysis. Both strategies are being used in the UK in parallel, and time to intervention is crucial with both strategies. The Myocardial Infarction National Audit Project registry is showing a gradual move towards percutaneous coronary intervention as the strategy of choice when available.

The main goal of early reperfusion therapy is to achieve full coronary blood flow in the infarct-related artery. Reopening an acutely occluded coronary artery saves myocardium, reduces mortality, reduces reinfarction and stroke, and improves outcomes in acute myocardial infarction. Both interventional and pharmacological therapy have their place in the management of patients with acute myocardial infarction but there is still debate about what kind of reperfusion therapy is optimal and what is immediately available. There are two parallel initiatives in England and Wales aiming at fast reperfusion in acute myocardial infarction: pre-hospital thrombolysis and primary percutaneous coronary intervention. All myocardial infarcts are now audited as part of the Myocardial Infarct National Audit Project (MINAP). At present approximately 80% of infarcts are dealt with by thrombolysis (either pre-hospital or in-hospital). This percentage is just beginning to fall as the primary percutaneous coronary intervention workload and workforce expand (MINAP Steering Group, 2006).

Thrombolytic therapy

Publication of the ISIS II trial established the value of thrombolysis in reducing myocardial infarction mortality. Early administration of the thrombolytic agent was vital and Boersma et al (1996) emphasized that the maximum efficacy of thrombolytic therapy is achieved when treatment is initiated within the first hour of symptom onset. Very early thrombolysis in the first hour after symptom onset could save up to 65 lives/1000 treated: the concept of 'the golden hour'. In the second hour after the onset of symptoms, this benefit is reduced by 50%.

More recently, a substudy of the second Assessment of the Safety and Efficacy of a New Thrombolytic Trial (ASSENT-2) showed an independent association between 1-year mortality and ST-segment resolution on a 24-hour electrocardiogram as well as a prognostic association between time-to-treatment and ST-segment resolution. Almost 56% of patients treated within 2 hours from pain onset had ST-segment resolution, compared with 52% of patients treated within 2–4 hours, and only 43% of patients treated between 4 and 6 hours (Fu et al, 2001).

Dr Ewa Dzielicka *is Clinical Fellow in Cardiology and* **Dr Howard Swanton** *is Consultant Cardiologist at The Heart Hospital, London W1G 8PH*

Correspondence to: Dr H Swanton

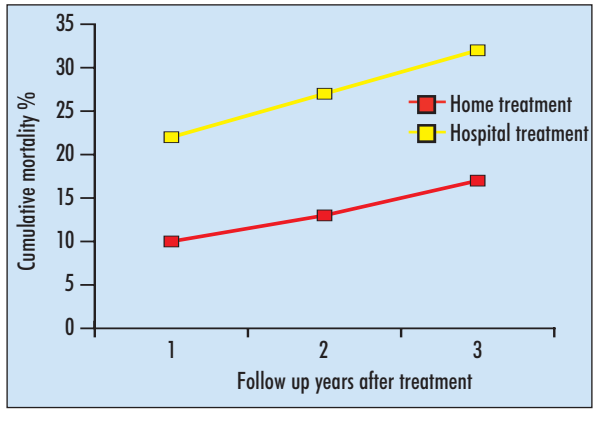
Pre-hospital thrombolysis

Pre-hospital thrombolysis was first tried in the UK in the GREAT trial in Scotland where the results of pre-hospital thrombolysis were compared with in-hospital thrombolysis. Although the study showed a reduced mortality with pre-hospital thrombolysis the results did not quite reach statistical significance. However, follow up for 1 year after thrombolysis showed a remarkable benefit from pre-hospital treatment (*Figure 1*).

A subsequent meta-analysis in 2000 of 6434 patients in six trials (*Figure 2*) showed a relative risk reduction in mortality of 17% and an absolute risk reduction of 2% in those patients receiving pre-hospital thrombolysis. A median 1 hour was saved by pre-hospital treatment and an estimate of one life saved/62 treated (Rawles, 1994; Morrison et al, 2000).

Pre-hospital thrombolysis is a rapidly expanding initiative in England and Wales with almost all ambulance services able to deliver thrombolysis by trained paramedics. Reteplase and tenecteplase were approved for use by paramedics in 2003, and changes to the prescriptions only

Figure 1. Late follow up of GREAT trial. Long-term benefit of pre-hospital thrombolysis (home treatment) over in-hospital thrombolysis. Absolute relative risk 15%, confidence interval 6–25% P=0.0014. From Rawles (1994).



medicines (human use) legislation were passed by parliament in 2004. A rigorous check list of indications and contraindications is used by the paramedics (*Table 1*), and early data from MINAP show substantial reductions in mortality in those patients receiving pre-hospital thrombolysis compared with in-hospital thrombolysis. Pre-hospital thrombolysis accounts for 18% of all thrombolysed patients in the UK with a median door-to-needle time of 38 minutes. A total of 7005 patients had been treated by pre-hospital thrombolysis by the end of December 2006, and 3035 in 2006 alone (253/month). In 88% of hospitals in-hospital thrombolysis was delivered to 75% of patients within 30 minutes of their arrival at hospital (MINAP Steering Group, 2006). In contrast in 2006, in the UK, 1647 patients were treated with primary percutaneous coronary intervention in preference to a fibrinolytic strategy, compared with 1087 in 2005.

Failed thrombolysis

Maintaining arterial patency remains a challenging task for fibrinolytic therapy. Although thrombolysis is easy to perform, normal TIMI (Thrombolysis In Myocardial Infarction) grade 3 flow is restored in only 40–50% of patients whereas primary percutaneous coronary intervention is associated with normal epicardial flow in more than 90% of patients (GUSTO Investigators, 1993). Patients who fail reperfusion by thrombolysis (continuing pain, or persistent ST elevation) must be treated with immediate coronary angioplasty (rescue percutaneous coronary intervention). The REACT trial has convincingly shown that rescue percutaneous coronary intervention is far superior to conservative management with heparin or a repeat dose of a thrombolytic agent.

Table 1. Paramedic check list for use of pre-hospital thrombolysis in England and Wales

Indications	Age <80 years old	
	Pain <6 hours	Typical distribution
		Onset rapid but not abrupt
		Not influenced by breathing
	Signs	Heart rate 40–180 bpm
		Systolic blood pressure >80–180 mmHg
		Diastolic blood pressure <110 mmHg
	Electrocardiogram	ST elevation >2 mm in two or more leads
		No bundle–branch block
Contraindications	Atrioventricular block	
	Pregnancy or delivery	
	Peptic ulcer in the last 6 months	
	Stroke in last year	
	Bleeding tendency	
	Warfarin	
	Surgical operation in last month	
	Head injury or brain disorder	
	Streptokinase or previous lysis	
	Cardiopulmonary resuscitation	
	Organ failure	

From Joint Royal Colleges Ambulance Liaison Committee (jrcalc.org.uk/)

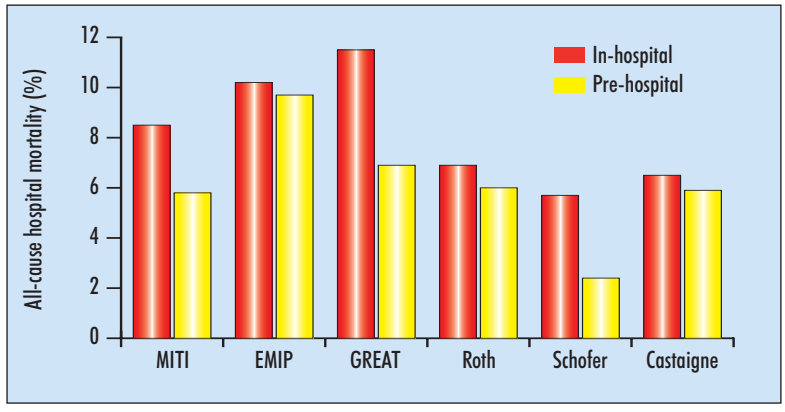


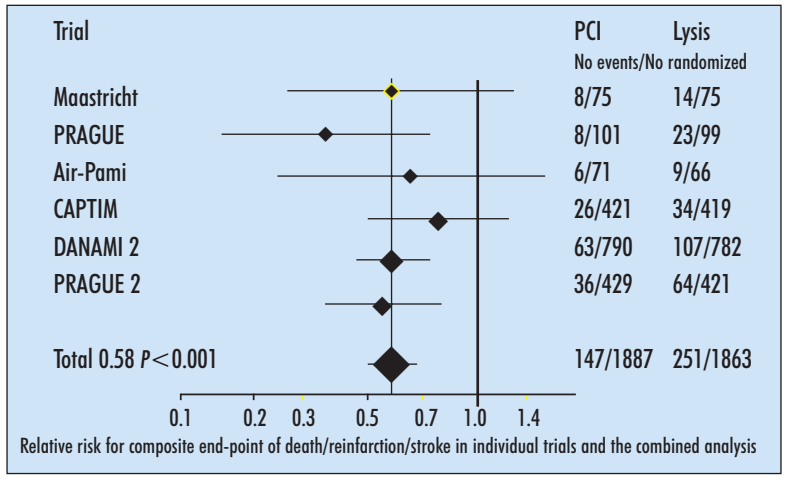
Figure 2. Meta-analysis of six trials of pre-hospital thrombolysis vs in-hospital thrombolysis. From Morrison et al (2000). Full details of trials analysed are accessible in Morrison et al (2000).

Primary percutaneous coronary intervention

Several meta-analyses and randomized clinical trials confirmed the superiority of primary percutaneous coronary intervention over fibrinolysis in acute myocardial infarction (Brodie et al, 2006). An early meta-analysis by Dalby et al (2003) (*Figure 3*) of seven trials showed a clear benefit for primary percutaneous coronary intervention.

An example of a primary percutaneous coronary intervention is shown in *Figure 4*. A totally occluded right coronary artery just distal to the margin has been reopened by angioplasty and stenting.

Figure 3. Meta-analysis of seven early trials comparing thrombolysis with primary percutaneous coronary intervention (PCI). There is a highly significant reduction in relative risk of the composite endpoint with primary PCI. See text for details. From Dalby et al (2003).



The Danish trial in Acute Myocardial Infarction-2 (DANAMI-2) (Andersen et al, 2003) analysed whether transfer of patients to a high volume centre within 3 hours of pain onset offered benefit over pharmacotherapy (intravenous alteplase given on admission). The primary end point at 30 days was significantly higher in the thrombolysis group *vs* primary percutaneous coronary intervention group (14.2% *vs* 8.5%; *P*=0.002) and the study showed that mortality increased significantly with symptom duration.

Data from the PRAGUE 2 trial, a randomized controlled study comparing long distance travel for percutaneous coronary intervention *vs* thrombolytic therapy in the nearest available hospital, suggested that provided the patient was treated within 3 hours of symptom onset the mortality with the two procedures was the same (Widimsky et al, 2003). With longer delays primary percutaneous coronary intervention was superior. The study was stopped prematurely because of a 2.5-times higher mortality in the fibrinolysis group in patients treated more than 3 hours after the onset of pain (15.3% thrombolysis *vs* 6% percutaneous coronary intervention).

A small French study, the Comparison of Primary Angioplasty and Pre-hospital Thrombolysis in the Acute Phase of Myocardial Infarction (CAPTIM), compared pre-hospital thrombolysis to transfer to interventional centres for primary percutaneous coronary intervention in patients presenting within 2 hours of symptom onset. (Steg et al, 2003). CAPTIM showed a lower 30-day mortality in the pre-hospital thrombolysis group (2.2% *vs* 5.7%; *P*=0.05), and suggested that thrombolysis might be even superior within the first 2 hours of pain onset. However, the results should be interpreted with caution as over two-thirds of the patients allocated to pre-hospital thrombolysis underwent percutaneous coronary intervention within 30 days.

A much quoted meta-analysis of 23 trials by Keeley et al (2003) comparing the two reperfusion methods in 7739 patients showed a definite benefit of primary percutaneous coronary intervention with a lower mortality, a lower incidence of recurrent ischaemia, reinfarction and stroke. Although this meta-analysis included many trials with small numbers it has become the gold standard meta-analysis proving the superiority of primary percutaneous coronary intervention over thrombolysis.

A strategy currently used in Europe is shown in *Figure 5*, demonstrating that almost all patients eventually have a percutaneous coronary intervention procedure.

Figure 4. a. Primary percutaneous coronary angioplasty of occluded right coronary artery. b. 2 hours from symptom onset.

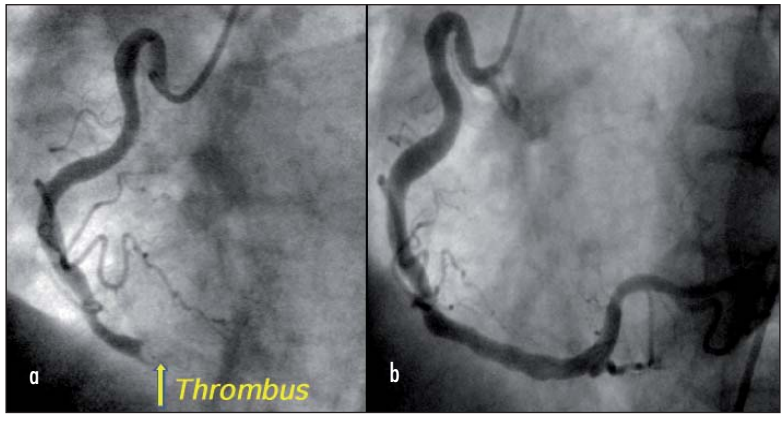
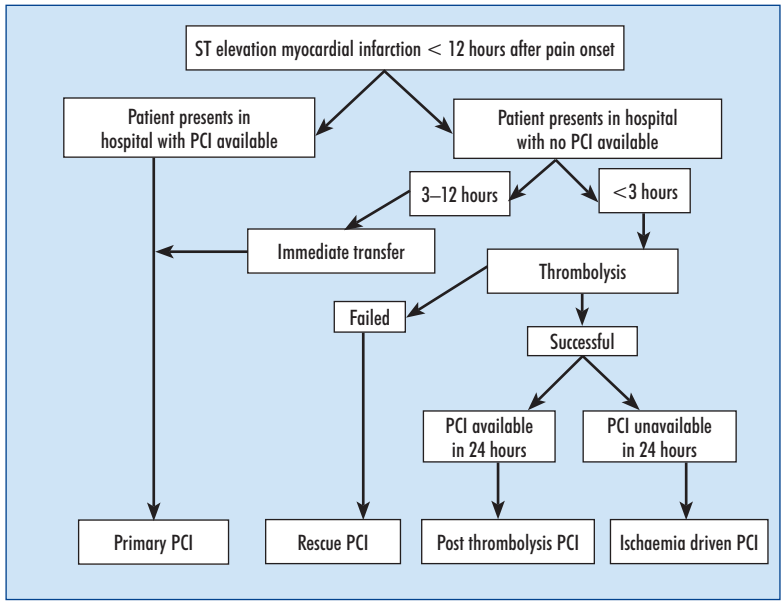


Figure 5. Algorithm for reperfusion therapy in acute myocardial infarction. From Silber et al (2005). PCI = percutaneous coronary intervention.



Time delay in primary percutaneous coronary intervention

Primary percutaneous coronary intervention-related delay is an important factor in selecting the optimal reperfusion strategy, but it is still not clear how long the initiation of reperfusion can be delayed in patients having a primary percutaneous coronary intervention.

Unfortunately neither PRAGUE-2 nor DANAMI-2 provided a clear answer as to how long the door-to-balloon time could be delayed to maintain the superiority of primary percutaneous coronary intervention over thrombolysis. Time from onset of pain to balloon inflation was initially thought to be less important than pain to thrombolysis time. This is not the case – delay in delivering a primary percutaneous coronary intervention procedure increases mortality. One study suggested that a percutaneous coronary intervention-related delay of >1 hour negates the advantage of the procedure. The best solution is for ambulance personnel to deliver the patient to the catheter laboratory rather than to accident and emergency or the coronary care unit where inevitable delays occur.

In the MINAP registry there is an inevitable percutaneous coronary intervention-related delay over pre-hospital thrombolysis (*Figure 6*) of 96 minutes. This delay is the sum of the transfer time from home to the admitting hospital, the time in the admitting hospital, the transfer time to the interventional centre, and the delay in the interventional centre catheter laboratory.

Delayed percutaneous coronary intervention after thrombolysis

In the past few years a number of studies have confirmed the relationship between pain onset to reperfusion time and mortality (Giugliano and Braunwald, 2003; Gersh and Antman, 2006). The outcomes from several meta-analyses have demonstrated that delayed percutaneous coronary intervention may have benefits over immediate percutaneous coronary intervention after thrombolytic therapy (Boersma, 2006; Di Pasquale et al, 2006).

In the GRACIA-2 randomized, controlled trial a total of 212 patients with ST elevation myocardial infarction (STEMI) were allocated to optimal primary angioplasty or facilitated intervention. Patients assigned to primary percutaneous coronary intervention underwent stenting of the infarct-related artery under the protection of abcximab within 3 hours of the onset of symptoms. By contrast, patients assigned to facilitated intervention received immediate thrombolysis with tenecteplase plus intravenous enoxaparin, followed by percutaneous coronary intervention performed within 12 hours of the onset of symptoms. This study showed that routine percutaneous coronary intervention performed within 3–12 hours of initial fibrinolysis, with the mean time to percutaneous coronary intervention 6 hours, was equivalent to primary stenting in terms of myocardial salvage. Moreover, a combination of immediate thrombolysis and delayed mechanical reperfusion of STEMI was safe. These findings may widen the time window for primary percutaneous coronary intervention (Fernandez-Avile et al, 2007).

Time to delay in primary percutaneous coronary intervention has been also reflected by the Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction (CARESS in AMI) trial which compared a strategy of early transfer (2.5 hours) of patients after thrombolysis for urgent percutaneous coronary intervention (facilitated percutaneous coronary intervention) *vs* a strategy of medical treatment at the admission hospital and transfer for rescue angioplasty only if there is no evidence of reperfusion (medical or rescue percutaneous coronary intervention). All patents were treated with half-dose reteplase and abciximab. However, primary outcome at 30 days showed that immediate transfer for percutaneous coronary intervention after the start of thrombolysis reduced death, reinfarction and refractory ischaemia in the facilitated percutaneous coronary intervention group compared to the group treated with thrombolysis (4.1% *vs* 11.1%; $P<0.001$), and the overall bleeding rates were significantly higher in the facilitated percutaneous coronary intervention group than in the medical/rescue group (12.2% *vs* 7.4%; $P<0.032$) (CARESS in AMI Study Investigators, 2007).

Hopefully, future randomized studies may provide further answers to questions about the optimal time window. Some data may come from the Strategic Reperfusion Early After Myocardial Infarction (STREAM) study which is planned to begin in early 2008. STREAM is a prospective randomized trial in which a tenecteplase bolus will be administered in the pre-hospital setting to patients presenting within 3 hours after symptom onset. Patients who cannot undergo percutaneous coronary intervention within 1 hour will be randomized to pre-hospital lysis or primary percutaneous coronary intervention. It is important that STREAM is not a trial of lytic-facilitated percutaneous coronary intervention, in which patients undergo a full dose of lytic followed by transfer for immediate percutaneous coronary intervention. In STREAM, only lytic-treated patients who do not achieve 50% ST resolution after lysis will undergo primary percutaneous intervention; the others will have angiography at 6–24 hours (STREAM Study Investigators, 2007).

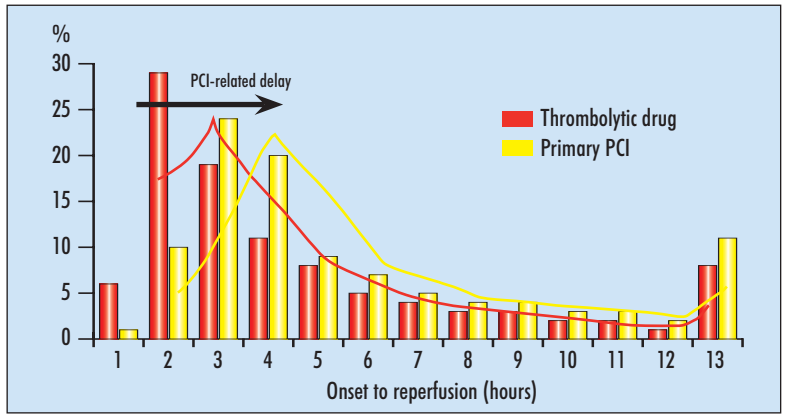


Figure 6. Time delay from symptom onset to thrombolysis or primary percutaneous coronary intervention (PCI). There is a PCI-related delay of 96 minutes. Data extracted from MINAP registry.

Facilitated percutaneous coronary intervention or pharmacoinvasive strategy?

The question is not whether primary percutaneous coronary intervention is better than immediate thrombolysis, but what reperfusion strategy is more efficient? Will the combination of both strategies be better than angioplasty alone in patients with acute myocardial infarction?

Theoretically a combination of pre-hospital lysis followed by primary percutaneous coronary intervention (facilitated percutaneous coronary intervention) should be superior to either intervention alone. Thrombolysis would offer the best choice for immediate myocardial salvage and angioplasty would subsequently deal with the stenosis preventing reocclusion and reinfarction.

However, the Assessment of the Safety and Efficacy of a New Treatment Strategy for Acute Myocardial Infarction (ASSENT-4) trial has shown this is not the case – immediate coronary intervention after the administration of full-dose tenecteplase was associated with higher rates of excess abrupt vessel closure, reinfarction and death *vs* primary percutaneous coronary intervention alone. Moreover, the additional thrombolytic carried an increased stroke and intracerebral bleeding risk, and an increase in reocclusion-related events by a transient early prothrombotic effect that may have increased the percutaneous coronary intervention risk. The trial was terminated prematurely as

the primary endpoint of mortality was higher in the facilitated group compared with percutaneous coronary intervention alone (6.0% *vs* 3.8%; *P*=0.04) at 30 days (ASSENT-4 PCI Investigators, 2006).

The same approach with a different treatment regimen was reviewed in the long-awaited Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events (FINESSE) study, which results were presented at the European Society of Cardiology Congress 2007 in Vienna. The largest trial of facilitated angioplasty to date was designed to compare whether the combination strategy of reduced-dose reteplase and abciximab would be better than abciximab alone or whether abciximab facilitation would be better than primary percutaneous coronary intervention with abciximab given in the catheter laboratory (FINESSE Investigators, 2007).

Data at 90 days from FINESSE suggest that neither facilitated percutaneous coronary intervention strategy tested had clinical benefit over primary percutaneous coronary intervention with in-lab abciximab. From a safety perspective, reteplase/abciximab facilitation and abciximab facilitation significantly increased bleeding compared to abciximab administration in the catheter lab. Primary percutaneous coronary intervention with in-lab abciximab has a better benefit/risk profile than the facilitated strategies in patients who can undergo percutaneous coronary intervention within 4 hours of first medical contact.

Despite the negative finding for facilitated percutaneous coronary intervention, the FINESSE study suggests that the accepted 90-minute time window (used as a limit to decide whether patients should be treated with thrombolysis or primary percutaneous coronary intervention) could be safely widened. Following the FINESSE trial more studies of possible benefits of new drug combinations in facilitated percutaneous coronary intervention as well as the optimal time frame for percutaneous coronary intervention after effective pharmacological reperfusion by thrombolysis are expected.

Table 2. Summary of choices of reperfusion therapy

Thrombolysis	Immediate (pre-hospital thrombolysis) or in-hospital	
Primary PCI	Direct transfer to catheter lab for primary coronary angioplasty	
Rescue PCI	Immediate thrombolysis followed by conventional care. Transfer for angioplasty if failure or reocclusion	
Facilitated PCI	A combination of pre-hospital thrombolysis followed by primary PCI	Lytic-facilitated PCI: Immediate full dose lytic followed by transfer for immediate PCI
		Combo-facilitated PCI; Immediate half dose lytic with glycoprotein IIb/IIIa followed by transfer for immediate PCI
		Pharmacoinvasive strategy: PCI delayed for a few hours after thrombolysis
Pre-hospital thrombolysis and elective PCI		Immediate thrombolysis followed by angiography in all patients within 24 hours followed by PCI if indicated

PCI = percutaneous coronary intervention

Recently published clinical trials, including FINESSE, suggest that the combination of pre-hospital thrombolysis followed by primary percutaneous coronary intervention (combination facilitated therapy) should no longer be called 'facilitated percutaneous coronary intervention', but 'pharmacoinvasive strategy' in which the angioplasty is delayed for a few hours after thrombolysis (*Table 2* gives a summary of reperfusion choices).

Current guidelines and future trends

The European Society of Cardiology recommends a pharmacoinvasive strategy for patients treated with fibrinolysis with or without evidence of myocardial ischaemia (Silber et al, 2005).

The American College of Cardiology and American Heart Association guidelines indicate that primary percutaneous coronary intervention is a preferred reperfusion strategy in STEMI provided it can be performed within 90 minutes from first medical contact by a skilled team of interventional cardiologists (operator experience >75 primary percutaneous coronary intervention cases per year; team experience >36 primary percutaneous coronary intervention cases per year). Medical contact-to-balloon or door-to-balloon time should be <90 minutes and door-to-balloon time <1 hour. Nevertheless, studies have shown that if the door-to-balloon time exceeds the optimal (<90 minutes) the benefit of percutaneous coronary intervention over lysis therapy is reduced. Therefore fibrinolysis is recommended when there is a delay in carrying out invasive treatment, i.e. where the door-to-balloon time is >1 hour and medical contact-to-balloon or door-to-balloon is >90 minutes (Anderson et al, 2007; *Table 3*).

The findings from the CARESS in AMI Study Investigators (2007) suggest that the percutaneous coronary intervention guidelines need to be changed and all patients with acute myocardial infarction should be referred for primary percutaneous coronary intervention.

Conclusions

Despite the publication of guidelines of the European and American scientific societies, treatment of patients with STEMI is still far from the optimal. Primary angioplasty is the gold standard of reperfusion for acute myocardial infarction and remains a better therapeutic option than fibrinolysis. One of the most important variables in coronary reperfusion is time; shortening the time to treatment should reduce mortality after acute myocardial infarction. Mortality from acute myocardial infarction remains high, with most deaths occurring before hospital admission. Despite standard pre- and in-hospital reperfusion strategies treatment delays in transferring patients from non-interventional to interventional centres remain prolonged. All the trials to date do not provide evidence that clinical outcomes are better with facilitated percutaneous coronary intervention. Therefore, facilitation with a high-dose thrombolytic, glycoprotein IIb/IIIa inhibitor or a combination therapy is not recommended yet and

should not be used routinely. The only recommended facilitation is abciximab given in the catheter laboratory at the time of percutaneous coronary intervention.

Current evidence and American guidelines do not support the practice of routine percutaneous coronary intervention following the administration of thrombolytics with successful reperfusion.

In the UK at present rural areas are best served by prehospital thrombolysis and urban ones by primary percutaneous coronary intervention. In many countries in Europe primary percutaneous coronary intervention has largely taken over from thrombolysis and there is no doubt that in the UK we shall see a gradual shift towards primary percutaneous coronary intervention as facilities and the necessary workforce expand to meet the need. **BJHM**

Conflict of interest: none.

Andersen HR, Nielsen TT, Vesterlund T et al (2003) Danish multicenter randomized study on fibrinolytic therapy versus acute coronary angioplasty in acute myocardial infarction: rationale and design of the DANish trial in Acute Myocardial Infarction-2 (DANAMI-2) *Am Heart J* **146**(2): 234–41

Anderson JL, Adams CD, Antman EM et al (2007) ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction. *J Am Coll Cardiol* **50**(7): e1–e157

Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) Investigators (2006) Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet* **367:** 569–78

Boersma E (2006) The Primary Coronary Angioplasty vs. Thrombolysis (PCAT)-2 Trialists' Collaborative Group. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. *Eur Heart J* **27:** 779–88

Boersma E, Maas A, Deckers JW et al (1996) Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* **348:** 771–5

Brodie B, Hansen Ch, Stuckey T (2006) Door-to-balloon time with primary percutaneous coronary intervention for acute myocardial infarction impacts late cardiac mortality in high-risk patients and patients presenting early after the onset of symptoms. *J Am Coll Cardiol* **47:** 289–95

CARESS in AMI Study Investigators (2007) Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction. Presented at the annual scientific sessions of the European Society of Cardiology, Vienna, 1–5 September

Dalby M, Bouzamondo A, Lechat P et al (2003) Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction. A meta-analysis. *Circulation* **108:** 1809–14

Di Pasquale P, Cannizzaro S, Parrinello G et al (2006) Is delayed facilitated percutaneous coronary intervention better than immediate in reperfused myocardial infarction? Six months follow up findings. *J Thromb Thrombolysis* **21:** 147–57

Fernandez-Avile F, Alonso J, Pena G et al (2007) Primary angioplasty vs. early routine post-fibrinolysis angioplasty for acute myocardial infarction with ST-segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. *Eur Heart J* **28:** 949–60

FINESSE Study Investigators (2007) Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events. Presented at the annual scientific sessions of the European Society of Cardiology, Vienna, 1–5 September

Fu Y, Goodman S, Chang WC et al (2001) Time to treatment influences the impact of ST-segment resolution on one-year prognosis: insights from the assessment of the safety and efficacy of a new thrombolytic (ASSENT-2) trial. *Circulation* **104:** 2653–9

Gersh B, Antman E (2006) Selection of the optimal reperfusion strategy for STEMI: does time matter? *Eur Heart J* **27**(7): 761–3

Giugliano R, Braunwald E (2003) Selecting the best reperfusion strategy in ST-elevation myocardial infarction: it's all a matter of time. *Circulation* **108:** 2828–30

GUSTO Angiographic Investigators (1993) 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* **329:** 1615–22

Keeley E, Boura J, Grines C (2003) Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* **361:** 13–20

MINAP Steering Group (2006) *How the NHS manages heart attacks.* Fifth Public Report 2006. Royal College of Physicians, London

Morrison LJ, Verbeek PR, McDonald AC et al (2000) Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. *JAMA* **283:** 2686–92

Rawles J (1994) Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region Early Anistreplase Trial (GREAT). *J Am Coll Cardiol* **23:** 1–5

Silber S, Albertsson P, Aviles FF et al (2005) Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. *Eur Heart J* **26:** 804–47

Steg PG, Bonnefoy E, Chabaud S et al (2003) Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation* **108:** 2851–6

STREAM Study Investigators (2007) STrategic Reperfusion Early After Myocardial Infarction. Presented at the annual scientific sessions of the American College of Cardiology, New Orleans: 24–28 March

Widimsky P, Budesinsky T, Vorac D et al (2003) Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction: final results of the randomized national multicentre trial - PRAGUE-2. *Eur Heart J* **24:** 94–104

Table 3. American College of Cardiology and American Heart Association guidelines for optimal reperfusion in acute myocardial infarction

Fibrinolysis recommended if:	3 hours from symptom onset and delay to PCI
	Invasive strategy not available
	Vascular access difficulties
	Delay to invasive strategy
	Prolonged transport (door-to-balloon) – (door-to-needle) >1 hour
	Contact-to-balloon or door-to-balloon >90 minutes
PCI recommended if*:	>3 hours from symptom onset
	Experienced cath lab available
	Contact-to-balloon or door-to-balloon <90 minutes
	(Door-to-balloon) – (door-to-needle) ≤1 hour
	High-risk patients (cardiogenic shock, Killip class ≥ 3)
	Contraindications to fibrinolysis
	Diagnosis of ST elevation myocardial infarction not clear

* Minimum requirement is a skilled interventional team: operator experience > 75 primary PCI cases per year, and team experience > 36 primary PCI cases per year. PCI = percutaneous coronary intervention. From Anderson et al (2007)

KEY POINTS

- Primary percutaneous coronary intervention is superior to pre-hospital thrombolysis in acute myocardial infarction.
- Time is crucial in both strategies.
- Failed thrombolysis must be followed by urgent angioplasty.
- Facilitated angioplasty (with preceding thrombolysis) is not recommended.