The Management of ST-segment Elevation Myocardial Infarction

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Abstract

The definition and management of ST-segment elevation myocardial infarction (STEMI) has changed considerably over the past few years. This article has been written as an update to encompass the National Service Framework (NSF) for coronary heart disease (published in England in March 2000[1] and in Wales in July 2001[2]), the Scottish Intercollegiate Guidelines Network[3] and the recent Task Force Report by the European Society of Cardiology (January 2003).[4]

Key Words

Myocardial infarction, STEMI, Thrombolysis, Reperfusion

Key Points

1. Early reperfusion is the key to reducing mortality from acute ST elevation MI.
2. If not contraindicated, aspirin followed by intravenous thrombolytic therapy should be offered to all patients presenting within 12 hours of onset of STEMI.
3. Primary percutaneous coronary intervention may be associated with better outcome than thrombolysis, particularly if delivered within 90 minutes of arrival in hospital.
4. Unless contraindicated, all patients be prescribed aspirin, an ACE inhibitor, beta blocker and statin prior to leaving hospital.

Introduction

Acute STEMI is usually the end result of total occlusion of an epicardial coronary artery with platelet-rich thrombus, secondary to rupture of an atheromatous plaque with or without concomitant vasospasm. The 30 day mortality rate of those patients admitted to hospital with a diagnosis of acute MI (AMI) has reduced from 30-40 % in the 1960's to 5-7% in 2002.[5,6,7] When out of hospital deaths are included in the statistics the 30-day mortality rate remains virtually unchanged.[8-9] Importantly, of those patients reaching hospital the diagnosis of AMI is still missed in up to 25% of cases[10] and in these patients the 30 day mortality rate is ~72%. A correct diagnosis of acute STEMI with early administration of reperfusion therapy is therefore vital if lives are to be saved.

Diagnosis

The initial diagnosis of acute STEMI is usually based on the combination of symptoms consistent with cardiac ischaemia and ECG changes. The classical symptoms (usually severe chest pain lasting at least 20 minutes, not responding to nitroglycerine, often radiating to the lower jaw and left arm) may be absent in up to 25% of cases, especially elderly and diabetic patients, who may complain of fatigue, breathlessness or syncope.[12] ECG changes comprise persistent ST segment elevation >1mm in two contiguous limb leads, 2mm or more in two contiguous chest leads (including leads V7 and V8 for true posterior infarction) or left bundle branch block. Confirmation of the diagnosis usually requires measurement of biochemical markers of myocardial damage (creatinine kinase –MB fraction OR total creatinine phosphokinase > 2 times the upper limit of normal, OR positive troponin I or T assay).[11]

Management

Patients should be managed in an environment which allows for rapid, accurate diagnosis, continuous ECG monitoring, advanced resuscitation facilities and access to appropriate medication. Pain should be managed with opioid analgesia plus anti-emetics and oxygen. Intra-venous beta-blockade and nitrates may be helpful for symptom control in some cases.

Treatment comprises three principles:

1. Early reperfusion, in order to limit infarct size,
2. Secondary prevention, to provide conditions which favour endothelial integrity and plaque stabilisation
3. Risk stratification, enabling tailored treatment and targeting of resources

1. Reperfusion therapy

Reperfusion therapy should be offered to all patients unless contra-indicated. Two reperfusion modalities exist:

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a) ***Thrombolysis with fibrinolytic therapies*** i.e. streptokinase or tissue-type plasminogen activators (e.g. rtPA, reteplase, tenecteplase);
b) ***Mechanical disruption of thrombus*** i.e. percutaneous coronary interventional techniques (PCI).

Aspirin 300mg should be given to all patients to chew (buccal absorption), irrespective of timing of symptom onset unless true allergy, blood dyscrasia or active GI pathology exists, with 75 mg given daily thereafter.[15] Aspirin, a reversible cyclo-oxygenase inhibitor, acts synergistically with thrombolysis, achieving a 42% reduction in mortality when combined with streptokinase.[16] Clopidogrel, a thienopyridine, may be given if true aspirin allergy exists,[17] but no evidence exists for the routine combination of these two therapies.

a) Thrombolytic Drug Therapy

Unless contra-indicated (see table 1), all patients with STEMI (including those over 75 years of age[18]) presenting within 12 hours of onset of pain should be considered for intravenous fibrinolytic therapy. Within the first 6 hours, 30 deaths are prevented per 1000 patients treated compared to 20 deaths at 12 hours.[14] Beyond 12 hours there is no convincing evidence of an overall benefit unless the onset is stuttering and ECG criteria persist. The concept of the 'golden hour' is well recognised; each minute delay to thrombolysis within the first hour of symptom onset results in 11 days' reduced life to the patient.[13] The English NSF[1] for CHD established a target for April 2003 that 75% of eligible patients should receive thrombolysis with a "door to needle" time of less than 20 minutes. The Welsh NSF[2] set a similar target of a maximum of 20 minutes "door to needle" time, with the additional proviso that pre-hospital thrombolysis should be considered where local "call to door" times are likely to exceed 30 minutes.

Streptokinase (SK) is the most widely used thrombolytic drug, but administration should never be repeated due to reduced efficacy following antibody production. Tissue-type plasminogen activator (tPA) is more fibrin-specific than SK and the accelerated tPA regime (100 mg over 90 minutes) with concomitant IV heparin for 24-48 hours (with careful APTT adjustment) results in 10 fewer deaths per 1000 patients treated, compared to SK, at the expense of 2 additional cases of intracranial haemorrhage.[19] However, the greatest difference in outcome between tPA and SK is within the first 4 hours of symptom onset and the time to thrombolysis is more important than the actual thrombolytic administered.[19,20]

The newer thrombolytics, reteplase and tenecteplase, are derivatives of t-PA but with much longer half-lives, enabling bolus administration. Complication rate compared to tPA is similar for these agents.[21,22] Tenecteplase appears to demonstrate additional benefit in a subgroup of patients treated more than 4 hours after symptom onset, plus fewer non-cerebral bleeding complications.

In an attempt to improve patency levels following thrombolysis and to reduce re-occlusion, trials have been designed using Glycoprotein IIb/IIIa (GP IIb/IIIa) receptor antagonists in addition to aspirin, plus substitution of low molecular weight heparin (LMWH) for unfractionated heparin (UFH). Platelet aggregation is dependent upon cross-linking of fibrinogen strands between fibrinogen receptors (GP IIb/IIIa) on the platelet surface. LMWH possesses greater factor Xa specificity, hence more effective prevention of thrombin generation as compared to UFH, plus a longer half-life and greater bioavailability.

Although some studies have supported the use of reduced dose thrombolytic combined with a GP IIb / IIIa inhibitor or LMWH,[23,24,25] others have suggested a greater incidence of bleeding complications with such regimens.[6,7,26] In view of this, neither the routine use of LMWH nor reduced dose fibrinolytic with Gp IIb/IIIa receptor antagonists, can currently be recommended.

b) Primary percutaneous coronary intervention

Primary percutaneous coronary intervention (PCI) (angioplasty and/or stenting) without prior delivery of fibrinolysis is the recommended reperfusion strategy when it can be delivered within 90 minutes of contact with medical personnel.[4] Primary PCI has been demonstrated to result in greater patency rates, reduced re-occlusion and improved clinical outcome when compared with standard fibrinolytic drug regimens.[27,28] It is the recommended reperfusion strategy for patients in shock and is often feasible for patients in whom fibrinolysis is contraindicated.[4] However, it is recommended that only hospitals performing a high volume of PCI procedures should use primary PCI as a routine reperfusion strategy.[4]

Absolute
- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage and neoplasms
- Major trauma/surgery/head injury within the preceding 3 weeks
- Gastro-intestinal bleeding within the last month
- Known bleeding disorder
- Aortic dissection

Relative
- TIA in preceding 6 months
- Oral anticoagulant therapy
- Pregnancy or within 1 week post partum (*)
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mmHg despite treatment)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

* Increased risk of spontaneous coronary dissection as the cause of acute STEMI, therefore, consider primary coronary intervention rather than thrombolysis.

Table 1. Contraindications to thrombolysis.[4]

The additional deployment of stents reduces the need for target vessel revascularization but does not influence re-infarction or mortality.[29] Current data supports the use of abciximab in combination with low-dose UFH in primary PCI but its use as an adjunctive therapy in primary stenting is still debated.[29] PCI combined with fibrinolysis as a routine measure in all patients was assessed in a number of early trials in the late 1980's but resulted in an increased risk of complications and death. The ongoing PACT trial is assessing short-acting thrombolysis and immediate planned PCI; the results of this trial are awaited with interest.

The recent DANAMI-2 study,[30] assessing whether transfer to a tertiary centre for primary PCI is superior to in-hospital thrombolysis, demonstrated lower 30 day combined end-points of death, re-infarction and stroke in those receiving primary PCI but no difference in mortality. Transfer times of up to 3 hours were allowed from arrival at the referring hospital to arrival at the tertiary centre, although the median time between arrival at the referring hospital and the start of PCI was less than 2 hours.

2. Secondary prophylaxis

a) Antithrombotic therapies

All patients should be started on aspirin (or clopidogrel if aspirin contraindicated[17]), which should be continued lifelong. Routine anti-coagulation with warfarin cannot be recommended but may be indicated in patients unable to take anti-platelet agents or as an alternative in patients with extensive anterior akinesia, atrial fibrillation and left ventricular thrombus.[4]

b) ACE Inhibitors

All patients should be started on an ACE inhibitor within the first 24 hours, providing there are no contraindications.[31] Trials of ACE inhibitors have demonstrated reduced 30 day mortality (maximal over the

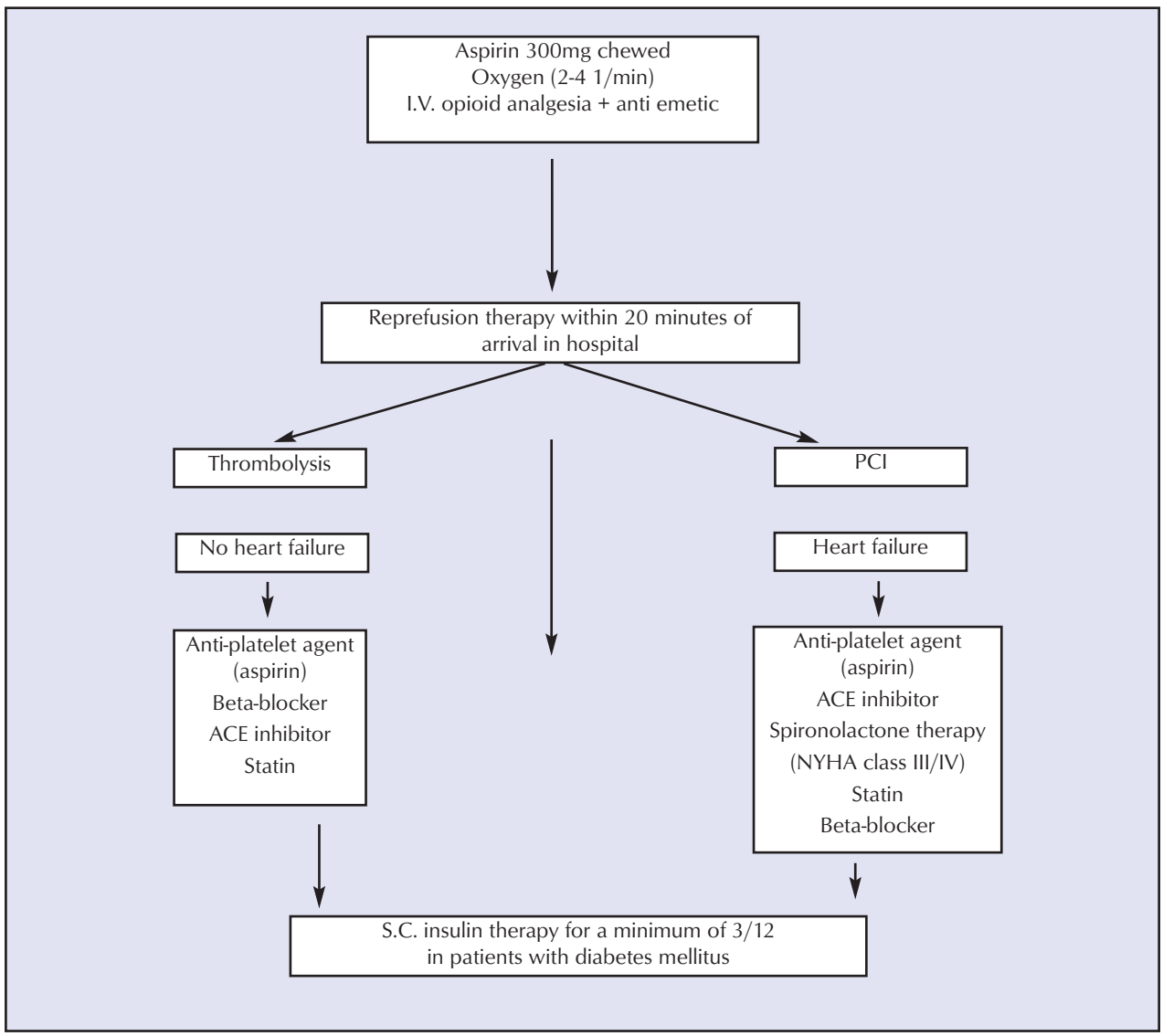

Table 2. Management of STEMI
Adapted from NICE guidelines (prophylaxis for patients who have experienced a myocardial infraction)[31]

first week)[32,33] in patients who have clinical and/or radiological evidence of heart failure or documented reduced (<40%) ejection fraction.[4] In addition, the recent EUROPA study[34] has demonstrated a 20% relative risk reduction in those patients with a history of myocardial infarction and no apparent heart failure prescribed the ACE inhibitor perindopril. Continuation of ACE inhibitors is recommended[31] providing there are no contra-indications; data from the HOPE trial suggested benefit is continued for at least 5 years, even in the absence of left ventricular dysfunction.[41]

c) Beta blockers

The routine use of intravenous beta-blocker therapy in all patients with acute STEMI cannot be recommended since the trials demonstrating benefit (6 lives saved per 1000 patients treated) were performed prior to the routine use of reperfusion therapies. Trials post thrombolysis have either failed to show benefit or are inconclusive due to low event rate.[35,36] In patients without a history of reversible bronchospasm, I.V. beta-blocker therapy is beneficial for treatment of persistent tachycardia, relative hypertension and for pain not responding to opioids.[4]

All patients (unless contra-indicated) should be commenced on long-term oral beta-blocker therapy[31] since several trials and meta-analyses have demonstrated a 20-25 % reduction in death and re-infarction post MI, the benefit being maintained irrespective of thrombolysis and/or ACE inhibitor therapy.[40]

d) Insulin

In patients with diabetes, a meta-analysis of the available data suggests that the routine use of a glucose-insulin-potassium infusion in the acute phase may favourably influence metabolism in ischaemic myocardium, conferring clinical benefit.[42] Intensive insulin therapy (4 daily insulin injections continuing for at least three months) initiated thereafter reduces mortality.[43,44]

e) Lipid lowering agents

Fasting cholesterol (LDL and HDL) and triglycerides should be measured within 24 hours of admission. Current NICE guidelines suggest that treatment with HMG CoA reductase inhibitor ("Statin") should be initiated if total cholesterol is > 4.8 mMol l^{-1} .[31] However there is an increasing consensus of opinion that the benefits of treatment with a Statin may extend to all patients irrespective of their cholesterol level. Addition of a Fibrate (eg Bezafibrate) should be considered if fasting triglyceride levels are high in the presence of low LDL and HDL cholesterol.

f) Non-drug therapies

Secondary prevention includes advice to stop smoking, a prescribed exercise programme plus a low fat Mediterranean-type diet.[39]

3. Risk stratification

Early revascularisation with PCI or coronary artery by-pass grafting (depending on lesion characteristics) has been shown to improve outcome in high risk patients.[37,38] Risk stratification by clinical assessment, exercise testing and echocardiography will help to identify such patients. Indicators of high risk include:

- Clinical evidence of on-going post-infarct angina
- Evidence of inducible ischaemia on exercise testing, stress echocardiography or myocardial perfusion scanning, particularly if >50% of the viable myocardium is affected
- Clinical evidence of heart failure or left ventricular ejection fraction <35%
- Significant arrhythmias

If I suffered an STEMI…

I would have chewed my 300mg aspirin whilst waiting for the ambulance to arrive, received oxygen and opioid analgesia and had my 12 lead ECG recorded in the ambulance. My ECG would be faxed to the admitting hospital and on arrival I would be admitted direct to CCU. Within 60 minutes of onset of pain I would either undergo primary PCI with stenting, adjuvant IV UFH and abciximab or, if no cardiac catheterisation facilities were available, I would wish to receive prompt thrombolytic therapy. I would receive low-dose aspirin, oral beta-blocker therapy, ACE inhibitor therapy and a statin and continue on these lifelong.

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