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PEER REVIEWED FEATURE

STEMI – a medical emergency

An overview of management

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ST-segment elevation myocardial infarction (STEMI) is a medical emergency and patients presenting with this in general practice should be given aspirin and glyceryl trinitrate and sent urgently to hospital by ambulance for reperfusion. GPs have a pivotal role in the postdischarge care of these patients.

Key points

- **ST-segment elevation (STEMI) is a medical emergency and almost entirely an ambulance- or hospital-managed condition as patients require immediate monitoring and emergency reperfusion treatment.**
- **Patients with possible STEMI presenting in general practice should be given aspirin and glyceryl trinitrate and referred urgently to hospital.**
- **Reperfusion treatment options are fibrinolysis and percutaneous coronary intervention.**
- **All patients with STEMI should receive antithrombotic and dual antiplatelet therapy unless contraindicated.**

ST-segment elevation myocardial infarction (STEMI) is a medical emergency where 'time is muscle' and 'minutes matter'. After the development of an occlusive thrombus upon rupture of an unstable coronary artery plaque (nonocclusive thrombi have been shown to occur and resolve often asymptomatically), myocyte necrosis is measurable after about 20 minutes, possibly earlier if high sensitivity troponin assays are used. However, it takes some hours for complete transmural myocardial necrosis to occur.

The recent Australian and New Zealand SNAPSHOT ACS study of patients admitted to hospital with suspected acute coronary syndrome has reported an in-hospital mortality of about 7% among unselected patients with STEMI.[1] This study showed that about 30% of these patients did not receive reperfusion therapy; although this percentage is similar to those in international unselected registries, it is too high a proportion. Furthermore, the majority of deaths still occur before patients reach a hospital, especially in those younger than 65 years.

STEMI is almost entirely an ambulance- or hospital-managed condition, except for the occasional patient who self-presents to a GP. Most states and territories in Australia have ambulances with paramedics who can perform ECGs 'in the field', including the transmission of these for expert remote ECG reading in some regions. This process allows for pre-hospital fibrinolysis if appropriate, and for the nearest hospital with suitable facilities to be pre-alerted to the arrival of a patient with STEMI, which can reduce the first medical contact-to-device time (formerly known as door-to-balloon, or D2B, time) for primary percutaneous coronary intervention (PCI).

If a patient with a possible STEMI presents to a GP, administering aspirin and glyceryl trinitrate (with documentation) and calling

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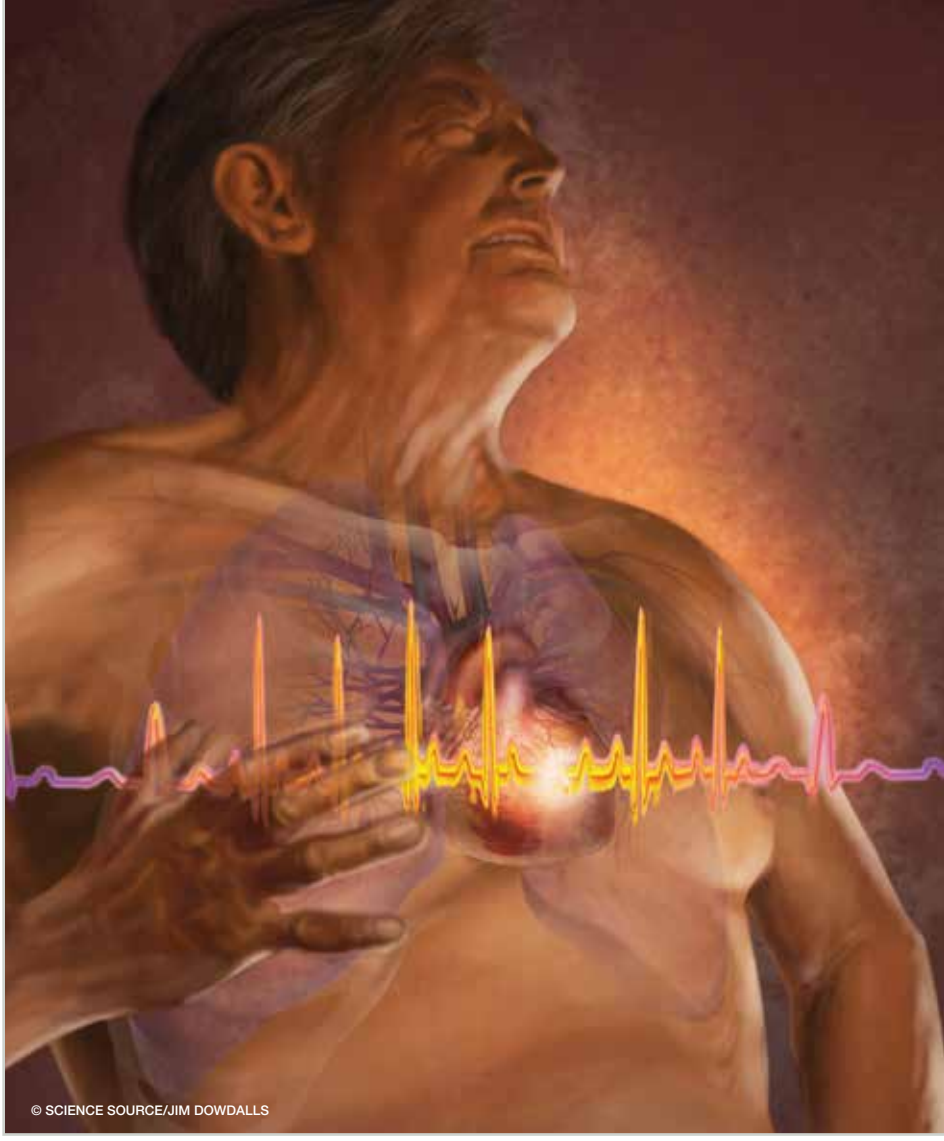
an ambulance is the preferred approach; if an ECG can be performed very rapidly (i.e. within 15 minutes) then one should be obtained. Patients with known coronary heart disease (CHD) and those at very high risk of CHD, such as patients with diabetes and multiple risk factors, should be advised to call an ambulance if they develop chest pain unresponsive to glyceryl trinitrate that lasts longer than 15 to 20 minutes, rather than present to their GP. In areas where ambulance call-out times are long, prompt performance of an ECG, with either computerised interpretation or an established system of transmission for expert remote reading, can markedly enhance emergency care.[2]

This article is intended to provide a 'through the looking glass' perspective on the hospital care of patients with STEMI. Apart from urgently referring to hospital the few patients with possible STEMI who present in general practice, GPs have a key role in the care of these patients after their discharge from hospital (Box). One-year age-standardised mortality rates for STEMI have been decreasing over the past 30 years, and GP involvement is pivotal in the maintenance and further reduction of these rates through their encouragement of the use of evidence-based secondary prevention therapies and support of smoking cessation efforts and attendance at cardiac rehabilitation, all of which improve outcomes. Articles focusing on non-STEMI and the secondary prevention of acute coronary syndrome will be published in future issues of *Medicine Today*.

EMERGENCY REPERFUSION THERAPIES

The management of patients with suspected myocardial ischaemia is guided by the patient's history and findings on the initial ECG(s).[3] The features of (persistent) ST-segment elevation of 1 mm or more in two contiguous, including posterior, leads (except in leads V1 to V3, where 2 mm or more of elevation is generally required) is an indication for emergency reperfusion therapy. Reperfusion therapy should be either pharmacological with fibrinolytic therapy (if within 30 minutes of first medical contact) or, preferably, mechanical with PCI if this is routinely available within 90 to 120 minutes of first clinical contact with an experienced interventional team.



Reperfusion therapy restores blood flow to viable myocardium. As 'time is muscle', minimisation of the time to reperfusion therapy minimises myocyte necrosis and infarct size, thus enhancing myocardial salvage.

Fibrinolysis or PCI?

Pharmacological reperfusion with intravenous fibrinolytic and antithrombotic agents has been shown unequivocally to reduce mortality in patients with STEMI, including those with presumed new onset left bundle branch block (LBBB), presenting within 12 hours of onset of symptoms.[4] Furthermore, meta-analyses have revealed lower mortality (and re-infarction) rates following mechanical reperfusion with primary PCI compared with in-hospital fibrinolytic therapy,[5] although data so far suggest administration of pre-hospital fibrinolysis achieves similar outcomes to transport for primary PCI, particularly when delays occur. Indeed, studies with major patient recruitment from France, where doctors are part of ambulance teams, have shown potential advantages

THE ROLE OF THE GP IN CARING FOR PATIENTS WITH STEMI

Patient presents in general practice with possible STEMI

- Administer aspirin and glyceryl trinitrate
- Refer patient as an emergency to hospital (by ambulance)
- Obtain an ECG if it can be performed within 15 minutes

Patient discharged from hospital after treatment for STEMI

- Encourage and facilitate secondary prevention therapies: antiplatelet therapies, statins, β-blockers, ACE inhibitors/angiotensin receptor antagonists, aldosterone antagonists (in those with heart failure or impaired left ventricular function)
- Support smoking cessation
- Support cardiac rehabilitation attendance

in administration of pre-hospital fibrinolysis compared with transfer for primary PCI, especially in those presenting early (within two hours of symptom onset).[6-8]

Early angiography is now guideline-recommended for STEMI patients without contraindications.[3] In Australia, some 85 to 90% of patients with STEMI undergo angiography at some time during their initial hospitalisation, and about 65% undergo PCI.[9] Although immediate transfer of all fibrinolytic-treated patients for angiography would require considerable resources, including increased after-hours ambulance services and cardiac catheterisation laboratory staffing, those patients who have not achieved 50% ST-segment recovery at 60 to 90 minutes after fibrinolytic therapy or who have cardiogenic shock have been shown to benefit from emergency revascularisation.[3] As these patients have a life-threatening medical emergency somewhat analogous to major trauma or critical intracranial events, emergency angiography is recommended, and rescue PCI if indicated. Time delays for rescue PCI in the SNAPSHOT ACS study were unacceptable by international standards and those patients who fail to achieve pharmacological reperfusion should receive enhanced prioritisation for transfer to a PCI centre.

Technical considerations in PCI for STEMI patients

The use of radial arterial access at the time of primary PCI has been reported to be associated with improved survival compared with femoral artery access in registries and small randomised trials.[10,11] Confirmation of these results is awaited in the coming months, when results of a large randomised controlled trial (RCT) are due to be reported. Aspiration thrombectomy – 'sucking out the clot' – is also conceptually appealing but the improved survival compared with primary PCI alone that was found in a small RCT has not been confirmed in a recently completed much larger RCT.[12]

The choice of stent to be used in most patients undergoing primary or rescue PCI for STEMI may be influenced by the ability of the patient to appreciate the need to comply with the prolonged dual antiplatelet therapy that is recommended after insertion of a drug-eluting stent.

Drug-eluting stents have lower rates of target vessel revascularisation than bare metal stents, and the current second-generation drug-eluting stents seem to have overcome issues of stent thrombosis that occurred with previous drug-eluting stents. However, in patients with large (diameter) infarct-related arteries in particular, if there is uncertainty about compliance with prolonged dual antiplatelet therapy for a variety of reasons including the need for noncardiac surgery, the use of a bare metal stent should be considered as the rate of target vessel revascularisation has recently been reported as only about 3% in these patients.[13]

The use of bioabsorbable scaffolds is conceptually appealing in patients with STEMI, but evaluation in large RCTs of their efficacy compared with the latest drug-eluting stents is awaited.

Antithrombin therapies

All patients with STEMI should receive thrombin inhibitor therapies unless there are major contraindications (Table).

For those undergoing primary PCI, the lower bleeding rates with the direct thrombin inhibitor bivalirudin compared with unfractionated intravenous heparin and a glycoprotein IIb/IIIa antagonist appear to more than compensate for a higher acute stent thrombosis rate associated with using this antithrombin agent. Indeed, the unexpected one-year mortality benefit reported with bivalirudin use has increased at late follow up in the HORIZONS-AMI trial; this RCT had not been powered to detect a mortality reduction.[14] The low molecular weight heparin enoxaparin has been used as an antithrombin agent, and compared with heparin in a small trial but not in large studies.

Enoxaparin used as an adjunct to fibrinolytic therapy in patients with STEMI (given as a 30 mg bolus intravenously, followed by twice daily 1 mg/kg subcutaneous injections, with dosage reduction for those aged over 75 years or with renal dysfunction) has been shown to be superior to intravenous unfractionated heparin.[15] This enoxaparin regimen has been compared with primary PCI in RCTs of pre-hospital fibrinolytic therapy.

For ease of administration by intravenous bolus, the preferred fibrinolytic agents are tenecteplase and reteplase (given as a double bolus). Fibrinolytics should be given as full doses; the strategy of half-dose fibrinolytics and routine immediate PCI after transfer requires validation in RCTs.

With respect to oral anticoagulants, in an earlier era warfarin was shown to enhance survival in patients with STEMI but it has not been routinely used except for patients with atrial fibrillation. More recently, the use of 'low dose' rivaroxaban (2.5 mg twice daily) has shown improved clinical outcomes in patients with STEMI, most of whom were on dual antiplatelet therapy,

TABLE. COMMONLY USED DRUGS IN STEMI*

Drug class	Drugs	Action	Comments
Direct thrombin inhibitor	Bivalirudin	Anticoagulant	May be used for patients undergoing primary PCI or with streptokinase
Heparin: Low molecular weight Unfractionated	 Enoxaparin Heparin	Anticoagulant	May be used for patients undergoing fibrinolysis (all agents)
Plasminogen activators	Reteplase, tenecteplase	Fibrinolytic	Commonly used for fibrinolysis
COX inhibitor	Aspirin	Antiplatelet	Used for all STEMI patients
ADP/P2Y12 inhibitors: Thienopyridines ADP receptor antagonist	 Clopidogrel, prasugrel Ticagrelor	Antiplatelet	Although all agents are used in both primary PCI and fibrinolytic-treated patients, only clopidogrel has been studied as 'up front' rather than 'switching' therapy in fibrinolytic-treated patients
Glycoprotein IIb/IIIa antagonists	Abciximab, tirofiban, eptifibatide	Antiplatelet	Used in selected patients undergoing PCI

ABBREVIATIONS: ADP = adenosine diphosphate; COX = cyclo-oxygenase; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.
* All drugs are injected except aspirin and clopidogrel.

although its use for this indication is not approved in Australia.[16]

Antiplatelet therapies

All patients with STEMI should receive dual antiplatelet therapy, unless contraindicated (Table).

Aspirin (a cyclo-oxygenase inhibitor) reduces mortality in all categories of myocardial infarction, and 300 mg should be administered at first medical contact.

In fibrinolytic-treated patients, the only P2Y12 inhibitor studied in an RCT is the irreversible inhibitor clopidogrel (a thienopyridine) at a loading dose of 300 mg.[17] In patients undergoing primary PCI, both the thienopyridine prasugrel (an irreversible inhibitor) and the adenosine diphosphate antagonist ticagrelor (a reversible inhibitor) have been shown to be superior to clopidogrel,[18,19] but have not been compared head to head. Because prasugrel was studied in patients with known coronary anatomy prior to PCI and there are restrictions in its use in those with low body weight (below 60 kg), the elderly (over 75 years of age) and those with prior cerebrovascular events, the use of ticagrelor in a broad spectrum of patients with ACS, including those with STEMI, seems to be considered favourably in Australia.

Unresolved pharmacological issues

Intravenous glycoprotein IIb/IIIa antagonists, particularly abciximab, were advocated for more than a decade as adjunctive antiplatelet agents in the primary PCI setting. However, bleeding rates are lower in patients with STEMI treated with bivalirudin than in those given unfractionated heparin and (generally) a glycoprotein IIb/IIIa inhibitor (mainly abciximab and tirofiban), and there are similar rates of ischaemic events.[14]

With bivalirudin there remains an increased risk of early stent thrombosis, which is associated with a fivefold increased mortality risk. However, the mortality risk for major bleeding also is higher, emphasising the importance of bleeding as both an adverse clinical outcome and as a trial endpoint. To address this problem, the recent PHOENIX trial tested the conceptually attractive approach of an infusion of the reversible P2Y12 inhibitor cangrelor (not TGA approved), with the result that cangrelor was shown to improve early clinical outcomes in PCI.[20] The STEMI cohort comprised fewer than 2000 patients and whether this is seen as sufficient numbers to change practice in patients with STEMI undergoing primary PCI is currently unclear.

The choice of pharmacological strategy to be used in fibrinolytic-treated patients referred for emergency angiography and, if anatomically suitable, for rescue PCI, requires clarification. Some clinicians at referral centres, concerned about transfer delays and anxious to provide some treatment, prefer to initiate glycoprotein IIb/IIIa antagonist therapies, usually tirofiban. Other clinicians are concerned about the bleeding risks associated with the use of glycoprotein IIb/IIIa antagonists in patients who have received full doses of fibrinolytic therapies, aspirin, thienopyridines and unfractionated or low molecular weight heparin.

Prior to and during primary PCI, platelet inhibition following loading with clopidogrel 300 mg (the most frequently used dose in HORIZONS-AMI) is likely to be

suboptimal as clopidogrel is a prodrug requiring metabolism for its activation. However, newer thienopyridines, which are either prodrugs that are activated more rapidly than clopidogrel (prasugrel and ticagrelor) or the active drug (cangrelor), have not been studied in fibrinolytic-treated patients (and thus the setting of rescue PCI).

Whether bivalirudin has a better (bleeding) safety profile in the setting of rescue PCI than unfractionated or low molecular weight heparin, with or without a glycoprotein IIb/IIIa antagonist, while maintaining efficacy, requires clarification.

SECONDARY PREVENTION THERAPIES

Statins should be commenced in the first 24 hours after a STEMI. Some data suggest that acute administration of high doses of statins (equivalent to 80 mg or more of atorvastatin) prior to primary PCI improves cardiac and renal outcomes. This strategy is to be the subject of further trials to assess emergency amelioration of a thromboatherosclerotic unstable coronary artery plaque.

Lipid modifying therapies, β-blockers, ACE inhibitors (or angiotensin receptor antagonists), aldosterone antagonists (in STEMI patients with congestive heart failure and/or ejection fraction below 40%), smoking cessation and cardiac rehabilitation have all been associated with improved post-STEMI outcomes and should be used.

GPs have a key role in encouraging and facilitating evidence-based secondary prevention for patients post-STEMI and in supporting smoking cessation efforts and encouraging attendance for cardiac rehabilitation.

FOLLOW UP

Patients treated for STEMI should generally have specialist reassessment at two to six weeks after the acute event to confirm compliance and functional status, including assessment of inducible ischaemia especially in those who did not have complete revascularisation in hospital. Those with inducible ischaemia should be considered for further revascularisation.

Left ventricular function should be assessed by noninvasive cardiac imaging, and patients with poor function (ejection fraction below 40%) at six weeks post-STEMI should be considered as candidates for implantable cardiac defibrillators, which reduce late mortality.

SUMMARY

STEMI is a medical emergency as myocyte necrosis starts after about 20 minutes. Furthermore, avoidance of sudden death out of hospital by obtaining emergency (ambulance) monitoring is a crucial goal. Based on data from a recent Australia and New Zealand study of patients admitted to hospital with suspected acute coronary syndrome, the rate of use of any reperfusion strategy is unacceptably low, reflecting a substantial treatment gap. Enhanced identification of reperfusion eligibility, if necessary by expert ECG interpretation (directly or remotely) is indicated to improve the use of fibrinolytics in rural and remote areas. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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