Myocardial infarction
improving patient outcomes

Early recognition of myocardial infarction – by both patient and doctor – is an essential part of the chain of survival. This article outlines a management framework for ST elevation and non-ST elevation myocardial infarction.

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The chain of survival

Myocardial infarction is the single largest cause of death in Australia. The chain of survival includes early recognition and response to symptoms by patients, ambulance transport, and appropriate medical and invasive management, including prompt application of reperfusion therapy.

Patient presentation

For myocardial infarction, patient delay is the weakest link in the chain of survival. Large registries have shown that about 30% of patients never receive reperfusion therapy – usually because they present too late. Previous public awareness campaigns in Australia have been uniformly unsuccessful in reducing this delay, but a directed campaign in which local doctors educate patients about appropriate responses to chest discomfort may be helpful. A patient handout is provided on page 36 of this article that might be discussed with all adult patients – particularly those with risk factors or known disease. Patients should also be encouraged to discuss the contents of the handout with their partners.

Diagnosis and management

Failure to recognise patients with myocardial infarction – by either local or hospital doctors – is the second weakest link in the chain of survival. Symptoms may be unheralded or preceded by unstable angina. Very often the symptoms are atypical, particularly in the elderly and in patients with diabetes. In addition, ECGs are normal in about 50% of patients presenting with myocardial infarction or unstable angina (one or more episodes of chest discomfort), particularly those with circumflex coronary artery occlusions. In such patients, myocardial infarction is only diagnosed after repeated ECGs and the later finding of an elevated cardiac troponin level. Unstable angina may only be confirmed after assessment with stress testing or coronary angiography.

IN SUMMARY

- **The greatest opportunity to improve outcomes after myocardial infarction lies in reducing patient delay. Early recognition of symptoms by patients allows for emergency assistance.**
- **Many patients with myocardial infarction or unstable angina present to their local doctor rather than a hospital. All adults should be educated that the appropriate response to chest discomfort lasting more than 10 minutes is to call an ambulance.**
- **All undiagnosed chest discomfort in adults over 30 years of age should be treated as possible coronary disease until proven otherwise.**
- **Treatment for STEMI (ST elevation myocardial infarction) includes aspirin and emergency reperfusion therapy with either angioplasty or fibrinolytic therapy.**
- **NSTEMI (non-ST elevation myocardial infarction) carries a worse long term prognosis than STEMI. Treatment includes early antiplatelet and antithrombotic therapy followed by angiography, preferably within 24 or 48 hours.**

MedicineToday **PATIENT HANDOUT**

What are the symptoms of heart attack? A guide for all adults

Heart attack is the single largest cause of death in Australia. The most common symptom is chest pain but this does not always occur – other symptoms include discomfort or tightness in the chest, arms, neck or jaw that lasts for 10 minutes or more, and breathlessness.

Do's

- If the discomfort lasts for 10 minutes or more then assume that you may be having a heart attack. Call an ambulance.
- Take one aspirin tablet (chewed or swallowed) while you are waiting for the ambulance. Everyone should have aspirin in the house.
- If you have a history of angina or previous heart attack and have glyceryl trinitrate tablets (Anginine or Lycinate) or spray (Nitrolingual Pumpspray), use this under the tongue when the discomfort begins. Continue to use either the tablets or spray every 5 minutes if the discomfort persists while you are waiting for the ambulance.
- If you live in a remote or rural area, it may be appropriate to have a relative or friend drive you to meet the ambulance. This should be discussed with the rural ambulance or Royal Flying Doctor Service.

Don't's

- Don't assume that the discomfort is caused by indigestion. You may be right, or you may be making a fatal mistake instead. It's not worth the risk.
- Don't waste time by calling your local doctor. He or she will only advise you to call an ambulance.
- Never wait until the next morning or 'the next available appointment' before seeking help. Your heart can be permanently damaged in the meantime and may even stop beating. Don't take the chance – call an ambulance immediately.
- Don't be embarrassed if the pain turns out to be indigestion or due to another cause. Hospital doctors know that it is vitally important to rule out a heart attack and they will not be concerned if the problem turns out to be something else.
- Don't drive yourself or get someone to drive you to hospital. It is much safer to call an ambulance.

This patient handout was prepared by Dr Con Aroney.

It is recommended that, unless another diagnosis is clear, all patients with recent chest discomfort lasting longer than 10 minutes be transported to hospital by ambulance for further investigations. Wrongly labelling chest discomfort of unknown cause as gastro-oesophageal may lead to patients ignoring subsequent myocardial infarction and even to their death. All undiagnosed chest discomfort in adults over 30 years of age should be treated as possible coronary disease until proven otherwise.

Hospital doctors are now trained to observe patients with undiagnosed chest pain for at least eight hours with monitoring and multiple investigations. About 16% of patients who are pain free at admission with normal baseline ECGs and troponin levels (intermediate risk patients) will later be reclassified as patients with high risk coronary syndromes requiring angiography. Chest pain assessment units have been shown to reduce the possibility of discharging a 'missed infarct' and facilitate early recognition and treatment. They also provide monitoring and prompt defibrillation for ventricular fibrillation.

A management framework

Myocardial infarction is caused by acute thrombosis and/or spasm of a fissured or ulcerated atheromatous coronary plaque. STEMI (ST elevation myocardial infarction) is associated with 'red thrombus' (fibrin and entrapped red blood cells) causing occlusive mural thrombus. NSTEMI (non-ST elevation myocardial infarction) is associated with 'white thrombus' (platelet thrombus) causing subocclusive or transitorily occlusive mural thrombus, distal microembolisation and small or moderate troponin elevations.

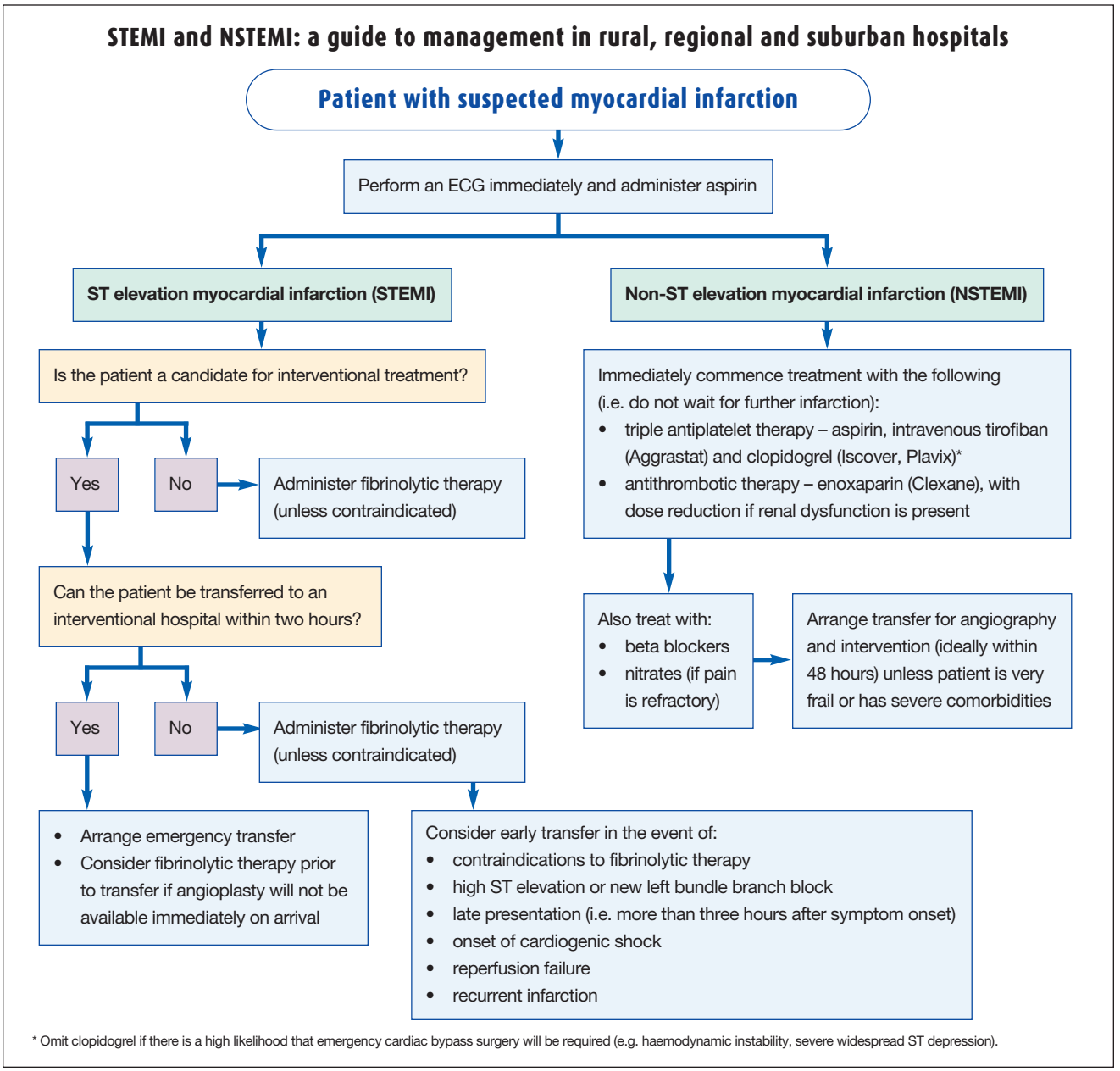
Use of cardiac troponin measurements has greatly increased ability to diagnose 'small' infarcts and prompted a joint American–European committee to re-evaluate this diagnostic criterion in patients presenting with an acute coronary syndrome (i.e. unstable angina, STEMI or NSTEMI) to a cutoff level corresponding to the 99th percentile of a reference population. The diagnosis of NSTEMI is differentiated from unstable angina by a significant elevation in cardiac troponin.

A new definition of myocardial infarction applicable to local practice is currently being considered by the Australian Heart Foundation and the Cardiac Society of Australia and New Zealand. However, the subdivision into STEMI and NSTEMI is already accepted, and provides a clear framework for different management strategies. Older terms like coronary occlusion are no longer used in cardiology units because many myocardial infarcts – particularly NSTEMI – are caused by platelet microembolisation and not by occlusive thrombus.

Treatment of STEMI and NSTEMI is discussed below, and a flowchart for management in rural, regional or suburban hospitals is shown on page 37.

STEMI: minimise delay, maximise patency

STEMI is a medical emergency, and a good outcome requires minimising the delay to treatment and applying reperfusion

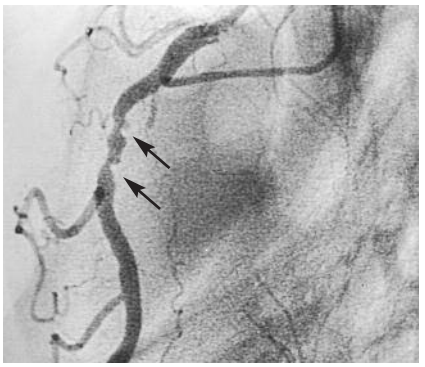


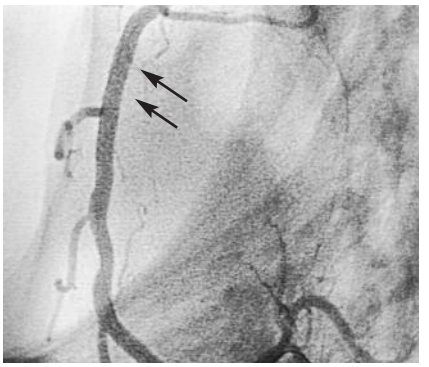
therapy to maximise epicardial coronary flow and myocardial tissue perfusion. Treatment includes aspirin and either emergency angioplasty or fibrinolytic therapy; an ECG is the sole investigation required before reperfusion treatment is initiated. Patients who have ST elevation, new left bundle branch block or acute posterior wall infarction should be treated similarly.

Angioplasty or fibrinolytic therapy?

A meta-analysis of 23 randomised trials has shown angioplasty to be superior to fibrinolytic therapy in reducing short term mortality (7% *v.* 9%, p<0.0002), nonfatal reinfarction (3% *v.* 7%, p<0.0001) and stroke (1% *v.* 2%, p<0.0004). Fibrinolytic therapy is most useful when administered early (within three hours) and is much less efficacious later – stent angioplasty is then markedly superior. Fibrinolytic therapy should be used when angioplasty is not readily available.

In three European studies, improved outcomes were obtained by transferring patients for angioplasty from regional centres to a hospital with interventional facilities up to two hours away compared with administration of fibrinolytic therapy locally. However, initial fibrinolytic





Figures 1a and b. Coronary angiography of a patient with inferior NSTEMI. a (left). A severe ulcerated plaque (arrows) in the mid-portion of the right coronary artery. b (right). After angioplasty and implantation of a stent the appearance of the lumen is smooth (arrows).

therapy and immediate transfer ('drip and ship') may maximise the chances of early reperfusion – this form of facilitated angioplasty may dilute the effects of delay and promote anterograde flow prior to arrival in the catheter lab. In the PAMI study, the degree of coronary flow on arrival in the lab and mortality were strongly correlated: the six-month mortality for patients with normal flow, partial flow or no flow was 0.5, 2.8 and 4.4%, respectively (p=0.009). The four-year results of the Prague study showed that survival was 66% in those receiving a fibrinolytic alone, 74% in those transferred for angioplasty without a fibrinolytic, and 82% in those receiving a fibrinolytic before transfer for angioplasty (p<0.05).

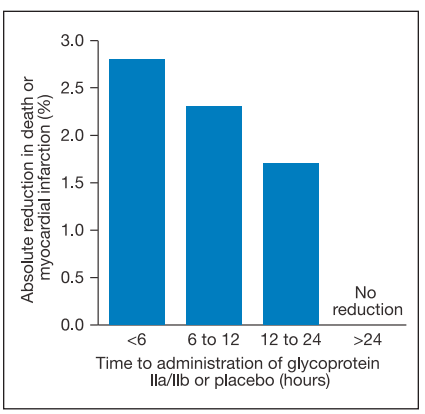


Figure 2. Reduction in death or nonfatal myocardial infarction at 30 days in patients treated with eptifibatide, a glycoprotein IIb/IIIa receptor inhibitor, early after symptom onset. There was no reduction in adverse events if the time to administration was more than 24 hours (Reference: Bhatt DL, Topol EJ. JAMA 2000; 284: 1549-1558).

Patients with a contraindication to fibrinolytic therapy benefit from early interventional therapy, with unadjusted hospital mortality reduced by 63.7% (from 30.6 to 11.1%); such patients should be considered for emergency transfer if they have not presented at an invasive facility. Patients with myocardial infarction who are developing cardiogenic shock derive a long term prognostic advantage from early revascularisation.

New developments

Techniques to prevent downstream microembolisation and improve myocardial tissue perfusion after angiography are being assessed in clinical trials of drugs (adenosine, glucose–insulin–potassium infusions) and mechanical methods (thrombectomy, distal protection, hypothermia, hyperoxygenation). Preliminary results from a STEMI trial of the X-sizer thrombectomy device before stent angioplasty showed an improvement in ST segment resolution and a reduction in slow flow and distal embolisation. Results from the COOL-MI study, which evaluated hypothermia before angioplasty in STEMI patients, showed no reduction in infarct size.

In the recent ESTEEM study, treatment with the oral direct thrombin inhibitor ximelagatran after STEMI and NSTEMI showed a 24% reduction in adverse cardiac events. However, this agent is not yet available in Australia.

Table. Long term drug therapy after myocardial infarction

- Aspirin
- Beta blockers
- ACE inhibitors
- Statins
- Clopidogrel, for 12 months after NSTEMI (CURE study) or stent implantation (CREDO study)

NSTEMI: early aggressive medical and invasive therapy

NSTEMI is a medical emergency and actually carries a worse long term prognosis than STEMI. Failure to provide early aggressive treatment may result in severe recurrent transmural infarction or death.

NSTEMI is treated with emergency antiplatelet and antithrombotic therapy followed by angiography, preferably within 24 or 48 hours (Figures 1a and b). Ideally, all NSTEMI cases should receive triple antiplatelet therapy with aspirin, intravenous tirofiban (Aggrastat) and clopidogrel (Iscover, Plavix) and low molecular weight heparin (enoxaparin [Clexane]) as soon as possible. Early intravenous tirofiban has been shown to reduce adverse cardiac events by about 70% in NSTEMI (troponin positive patients) if given early, but the benefits of glycoprotein IIb/IIIa receptor antagonists may be lost completely if administration is delayed for 24 hours or until a second event occurs (see Figure 2). Early oral clopidogrel reduces adverse cardiac events by 20% in acute coronary syndromes, including NSTEMI, and enhances the

long term benefits of coronary stenting, particularly if continued for at least nine to 12 months. Clopidogrel should be avoided if there seems to be a high likelihood that emergency bypass surgery will be required (for example, patients with haemodynamic compromise or very severe widespread ST depression). Indirect comparisons suggest that enoxaparin may be superior to other low molecular weight heparins, possibly because of greater specificity for factor Xa.

Patients with diabetes and NSTEMI are a very high risk group and have a particularly high sudden death rate. The benefits of intravenous tirofiban or invasive therapy are amplified in this group. Optimal glycaemic control, particularly with a switch to insulin therapy for at least three months, has been shown to reduce the one-year mortality in diabetic patients with myocardial infarction.

After myocardial infarction

Unless contraindications are present, both STEMI and NSTEMI patients should be treated long term with aspirin, beta blockers, ACE inhibitors and statins, which have been shown to reduce adverse cardiac events following infarction (Table). In those with heart failure or significant left ventricular dysfunction, ACE antagonists have been shown to reduce mortality to a similar extent as ACE inhibitors (the VALIANT study). In addition, clopidogrel should be used for 12 months for patients with NSTEMI or have had a stent implanted. ACE inhibitors had formerly been shown to reduce adverse cardiac events by about 20% in high risk vascular patients (HOPE study), but have now shown a similar benefit in all patients with coronary disease (EUROPA study). After myocardial infarction, patients with a significant impairment in left ventricular function (ejection fraction less than 30%) have a 31% reduction in mortality (from 19.8 to 14.2%, $p<0.02$) when treated with an implantable cardiac defibrillator.

Patients with myocardial infarction should also be advised to stop smoking, eat a Mediterranean diet high in fish oils, and exercise regularly. If possible, each patient should also be referred to a cardiac rehabilitation program; such programs have been shown to improve functional health outcomes and reduce recurrent adverse cardiac events. Depression is an independent risk factor for adverse cardiac events after myocardial infarction – sertraline (Zoloft), a selective serotonin reuptake inhibitor, can be safely used to treat depressed patients with myocardial infarction or unstable angina.

Conclusion

The largest gain in the chain of survival of myocardial infarction is early patient recognition of the symptoms allowing for emergency assistance. All patients should be treated with early aspirin, with NSTEMI patients also receiving upstream intravenous tirofiban, oral clopidogrel and low molecular weight heparin. Coronary

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Myocardial infarction: key management strategies

Chest pain

- Discuss the appropriate response to chest pain with all your adult patients. (A patient handout is provided on page 36 of this article.)
- Do not mislabel new onset chest discomfort in an adult patient as 'indigestion' – assume it is cardiac in origin unless proven otherwise.
- Remember that a normal ECG or troponin measurement does not exclude an acute coronary syndrome.
- Refer patients with prolonged or repeated chest, arm or neck discomfort to hospital by ambulance.

STEMI (ST elevation myocardial infarction)

- Maximise efforts to provide early patency of the occluded artery.
- Consider early percutaneous intervention wherever possible.
- Fibrinolytic therapy should be considered if percutaneous intervention is impossible or would be delayed by more than two hours.

NSTEMI (non-ST elevation myocardial infarction)

- Remember that the six-month mortality rate for NSTEMI is greater than that for STEMI. Aggressive management is required.
- Commence triple antiplatelet therapy (aspirin, tirofiban [Aggrastat], clopidogrel [Iscover, Plavix]) and low molecular weight heparin (enoxaparin [Clexane]) early. Do not wait for recurrent infarction.
- Plan early transfer for invasive management.

Patients after myocardial infarction

- Unless contraindications are present, use aspirin, beta blockers, ACE inhibitors and statins.
- Refer patients to a cardiac rehabilitation program.
- Assess patients for depression two to four weeks after myocardial infarction. Consider treatment with sertraline (Zoloft).

angiography and revascularisation is the preferred management of all myocardial infarctions, with emergency intervention (<2 hours) in STEMI and semi-urgent intervention (<48 hours) in NSTEMI. Long term medical management, dietary modification, risk factor control, exercise and cardiac rehabilitation have been shown to reduce recurrent adverse events.

A summary of management strategies discussed in this article is provided in the aide-mémoire box above. MT

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