Management of the acute coronary syndromes

Con Aroney, Director of Coronary Care, Prince Charles Hospital, Brisbane

SYNOPSIS

Patients with acute coronary syndromes may be divided into those who have had a myocardial infarction with ST elevation on their ECG, and those without ST elevation. The latter group can be further classified as having a high, intermediate or low risk of death or having a myocardial infarction. These risks are stratified by newly determined clinical and ECG criteria, and specific serum markers of myocardial injury. There are protocols for the evaluation of chest pain. Structured protocols are used to assess intermediate risk patients in order to reduce the incidence of 'missed infarcts' and to facilitate early discharge where appropriate. Patients have a high risk if they have pain at rest, ST depression and elevated serum troponin. They are actively managed with combined medical and invasive therapy. Low molecular weight heparin and IIb/IIIa platelet receptor blockers have become an important part of management.

Index words: myocardial infarction, unstable angina, fibrinolytic therapy.

(Aust Prescr 2001;24:56–8)

Introduction

The acute coronary syndromes include unstable angina[1] and myocardial infarction. In patients with myocardial infarction the ST segment may or may not be elevated. Some patients without ST elevation do not develop Q waves although their serum markers demonstrate they have had an infarct.

These ECG changes, when combined with new serum markers of myocardial damage, can help in the assessment of patients with chest pain. This assessment suggests which patients will benefit from new drug treatments and revascularisation.

Aetiology

The patient's presentation is partly determined by the degree and duration of the reduction in coronary blood flow, the quality of collateral flow to the jeopardised myocardium and the nature of the thrombus which forms after an atherosclerotic plaque has ruptured. Patients with unstable angina or an infarction without ST elevation usually develop a white (platelet) non-occlusive thrombus. Approximately 80% of myocardial infarctions with ST elevation are associated with a red (fibrin with entrapped erythrocytes) occlusive thrombus.

The differences in treatment reflect these differences in pathophysiology:

- low molecular weight heparins (LMWH) and platelet glycoprotein IIb/IIIa inhibitors are effective for patients who present without ST elevation
- fibrinolytic therapy is useful for patients who have an infarct with ST elevation.

New serum markers

Cardiac enzymes, such as creatine kinase (CK), are often measured in patients with chest pain. These tests may not be specific for myocardial injury.

Cardiac troponins

Unlike the MB isoform of creatine kinase (CK-MB), the cardiac troponins are specific markers of myocardial injury. The presence of cardiac troponin I or T in the serum confirms myocardial damage. The serum concentration of cardiac troponin correlates with the subsequent risk of cardiac death and myocardial infarction, and is superior to CK-MB in predicting adverse events. CK-MB is now becoming an obsolete non-specific marker. Diagnosis and risk stratification are better achieved with the use of cardiac troponin I or T along with total CK.

Cardiac troponin should be remeasured 6–8 hours after chest pain presentation to exclude myocardial injury. Patients with elevated cardiac troponin but normal CK (or CK-MB) are a recently identified high risk group with an adverse prognosis and have been classified as having 'minor myocardial damage'.

Cardiac troponins are also elevated with other forms of cardiac injury. They are increased by myocarditis, severe cardiac failure and severe pulmonary embolism with right ventricular strain, and in patients with severe renal failure who have occult coronary disease.

The cardiac troponins can be used to 'tailor therapy' as they predict response to treatment with:

- LMWH in acute coronary syndromes without ST elevation[2]
- tirofiban in acute coronary syndromes without ST elevation[3]
- adjunctive use of abciximab with percutaneous coronary intervention.[4]

Management of ST elevation myocardial infarction

Patients with symptoms of less than 12 hours duration and ECG changes of ST elevation or left bundle branch block require emergency reperfusion. They should be given aspirin,

glyceryl trinitrate (for treating associated vasospasm), morphine and supplemental oxygen. Arrhythmias, acute heart failure or shock need specific management. Emergency department protocols for emergency reperfusion, with either percutaneous coronary intervention (PCI*) or fibrinolytic therapy, depend on the available facilities and personnel.

If PCI is available and can be performed by an experienced operator within one hour of presentation, it is often considered the treatment of choice. Immediate PCI has long-term advantages over fibrinolytic therapy.[5,6] Adjunctive therapy with abciximab should be given with PCI unless contraindications are present.

Where PCI is unavailable, fibrinolytic therapy is indicated for all patients without contraindications. Alteplase is preferred to streptokinase as it provides superior coronary patency and clinical benefits and a lower incidence of adverse effects. Newer fibrinolytic drugs (reteplase, tenecteplase) are convenient as they can be given as a bolus.

The most important complication of fibrinolytic therapy is bleeding, in particular intracranial haemorrhage. Uncontrolled hypertension (especially above 170/100) is a strong risk factor for intracranial haemorrhage. It is a contraindication for fibrinolytic drugs and should be controlled before fibrinolytic therapy. Patients with contraindications should be considered for immediate transfer to a unit equipped for PCI.

Management of patients without ST elevation

Compared to the management of patients who have a myocardial infarction with ST elevation, the management of patients with chest pain without ST elevation is less defined. It can be guided by risk stratification.

Risk stratification

The risk of the major cardiac events of death or myocardial infarction at six months is greater than 10% in high risk patients, 2–10% in intermediate risk patients and less than 2% in low risk patients.

High risk patients

These patients have any of the following:

- ongoing pain
- ST depression (greater than 0.5 mm) or deep T wave inversions in three or more leads
- elevated serum troponin
- recent (less than one year) history of infarction or revascularisation
- heart failure, shock or syncope.

Intermediate risk patients

These patients have:

- a history of prolonged, repetitive chest pain or pain at rest
- recent onset of angina (less than two weeks)
- a remote (greater than one year) history of infarction or revascularisation
- age over 65 years
- diabetes
- no high risk features.

Low risk patients

These patients have:

- a worsening anginal syndrome without prolonged, repetitive or resting chest discomfort
- normal ECG
- no detectable troponin
- no high or intermediate risk features.

(This group can be medically managed as outpatients, but should be referred for a cardiology assessment, preferably within two weeks.[1])

Rapid evaluation of intermediate risk patients

Patients who present with prolonged chest discomfort, but without new ECG changes or baseline elevation of serum troponin, are given aspirin. They are then recommended to undergo a rapid but intensive strategy of observation (for at least eight hours) and investigation. This includes cardiac monitoring, frequent ECGs (every three hours) or ST segment monitoring, repeat serum troponin at 6–8 hours, and, if patients remain pain-free with all tests negative, an exercise stress test before discharge.

Any positive results call for a reclassification into a high risk group and intensive treatment. LMWH is not recommended unless the patient is reclassified as high risk (for example, further pain, ECG changes or elevated troponin).

A rapid effective evaluation strategy for intermediate risk patients has the advantages of:

- reducing the incidence of 'missed infarcts'
- providing early identification (and treatment) of patients who develop high risk features during the observation period
- allowing prompt discharge of patients reclassified as low risk after the observation period.

Management of high risk patients

Patients with high risk features, but no ST elevation, are managed with aspirin and beta blockers. They are also given LMWH or intravenous tirofiban with unfractionated heparin. Patients with elevation of serum troponin have been shown to specifically benefit from treatment with LMWH or tirofiban.

A change from LMWH to tirofiban with unfractionated heparin is particularly indicated for patients with refractory ischaemia while on LMWH and for rural patients to facilitate their safe transfer to a tertiary hospital. Intravenous tirofiban should only be given along with unfractionated heparin (there is ongoing research to assess its administration with LMWH).

High risk patients benefit from a complementary aggressive medical and invasive strategy. Such a strategy[7] using initial

* Balloon angioplasty, often with coronary stent implantation

treatment with LMWH followed by early invasive therapy (with early angiography and PCI or bypass surgery) provides major benefits compared to an initial conservative strategy. There is a statistically significant reduction in:

- subsequent angina (22% vs. 39%)
- hospital readmission (31% vs. 49%)
- death or infarction (9.4% vs. 12.1%).

The benefit of PCI is enhanced by periprocedural treatment with IIb/IIIa blockers, particularly in patients with an elevated serum troponin.

Long-term management

Patients who have had a myocardial infarction or are in the high risk group should be referred to a cardiac rehabilitation program, with education, risk factor modification and regular exercise. Attending such a program leads to major improvements in functional health outcome, increased confidence, reduced depression and anxiety as well as a 20% reduction in death or infarction.

Long-term aspirin (or clopidogrel where aspirin is contraindicated) is recommended except possibly in patients with poorly-controlled hypertension. Beta blockers are indicated after myocardial infarction particularly in high risk patients with heart failure. ACE inhibitors are indicated, not only in patients with heart failure or left ventricular dysfunction but also in patients with other risk factors, especially diabetes and hypertension. In a large placebo-controlled study[8], patients with additional risk factors who were randomised to long-term ramipril had significant reductions in cardiac death, reinfarction and stroke. Long-term statin therapy is recommended after acute coronary syndromes if the patient's serum cholesterol is greater than 4 mmol/L.

Summary

Improved diagnosis and risk stratification of patients with acute coronary syndromes, using structured assessment protocols and specific serum markers (cardiac troponin), have led to the identification of those patients who benefit from aggressive medical and invasive treatments. This approach to management will provide a strong framework for future advances in therapy.

Dr Aroney is a member of the writing group for developing new guidelines for the management of unstable angina, for the National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand.

E-mail: conar@bigpond.net.au

REFERENCES

1. Unstable Angina Writing Group. Management of unstable angina guidelines – 2000. Med J Aust 2000;173 Suppl:S65-88.
2. Lindahl B, Venge P, Wallentin L. Troponin T identifies patients with unstable coronary artery disease who benefit from long-term antithrombotic protection. J Am Coll Cardiol 1997;29:43-8.
3. Heeschen C, Hamm CW, Goldmann B, Deu A, Langenbrink L, White HD. Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban. Lancet 1999;354:1757-62.
4. Hamm CW, Heeschen C, Goldmann B, Vahanian A, Adgey J, Miguel CM, et al. Benefit of abciximab in patients with refractory unstable angina in relation to serum troponin T levels. N Engl J Med 1999;340:1623-9.
5. Nunn CM, O'Neill WW, Rothbaum D, Stone GW, O'Keefe J, Overlie P, et al. Long-term outcome after primary angioplasty: report from the primary angioplasty in myocardial infarction (PAMI-1) trial. J Am Coll Cardiol 1999;33:640-6.
6. Zijlstra F, Hoorntje JCA, De Boer M-J, Reiffers S, Miedema K, Ottervanger JP, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1999;341:1413-9.
7. FRISC II Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999;354:708-15.
8. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients [published erratum appears in N Engl J Med 2000;342:748]. N Engl J Med 2000;342:145-53.

Self–test questions

The following statements are either true or false (answers on page 75)

1. The MB isoenzyme of creatine kinase is the most specific marker of cardiac damage.
2. Patients who present with prolonged chest pain and ST elevation should be treated with a glycoprotein IIb/IIIa inhibitor if percutaneous coronary intervention is not available.

Prescribing curriculum for senior medical students

The National Prescribing Service (NPS) is working with the 11 medical schools in Australia to develop a prescribing curriculum for senior medical students. The departments of pharmacology have agreed to develop their own modules on prescribing, following identification of interns' specific needs.

There was consensus as to the type of curriculum needed. It should use self-directed learning and be:

- modular
- problem-based
- adaptable to groups
- web interactive.

The prescribing curriculum will recognise the environments in which interns work and the common conditions they face.

The curriculum is now undergoing technical testing and is expected to be finalised by the end of 2001.

Postgraduate medical councils are interested in extending the prescribing curriculum to first- and second-year postgraduate students, and are currently working with the NPS on this.