1: N Engl J Med. 1994 Mar 10;330(10):670-4.

Comment in:

- N Engl J Med. 1994 Jul 28;331(4):277.
- N Engl J Med. 1994 Mar 10;330(10):707-9.

Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I.

Adams JE 3rd, Sicard GA, Allen BT, Bridwell KH, Lenke LG, Davila-Roman VG, Bodor GS, Ladenson JH, Jaffe AS.

Cardiovascular Division, Washington University School of Medicine, St. Louis.

BACKGROUND. Perioperative myocardial infarction is the most common cause of morbidity and mortality in patients who have had noncardiac surgery, but its diagnosis can be difficult. The present study was designed to determine whether the measurement of serum levels of cardiac troponin I, a highly sensitive and specific marker for cardiac injury, would help establish the diagnosis of myocardial infarction. METHODS. We obtained preoperative measurements of MB creatine kinase, total creatine kinase, and cardiac troponin I, in addition to base-line electrocardiograms and two-dimensional echocardiograms, in 96 patients undergoing vascular surgery and 12 undergoing spinal surgery. Blood samples were obtained every 6 hours for at least the first 36 hours after surgery, and electrocardiograms were obtained daily; a second echocardiogram was obtained approximately three days after surgery. The appearance of a new abnormality in segmental-wall motion on the postoperative echocardiogram (that is, an abnormality that had not been seen on the preoperative echocardiogram) was considered to be indicative of perioperative infarction. RESULTS. Eight patients who underwent vascular surgery had new abnormalities in segmental-wall motion and received a diagnosis of perioperative infarction. All eight had elevations of cardiac troponin I, and six had elevations of MB creatine kinase. Of the 100 patients without

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perioperative infarction detected by echocardiography, 19 had elevations of MB creatine kinase, and 1 had a slight elevation of cardiac troponin I. CONCLUSIONS. The measurement of cardiac troponin I is a sensitive and specific method for the diagnosis of perioperative myocardial infarction. It avoids the high incidence of false diagnoses associated with the use of MB creatine kinase as a diagnostic marker.

PMID: 8054012 [PubMed - indexed for MEDLINE]

1: Ital Heart J. 2002 Sep;3(9):543-57.

The new definition of myocardial infarction: analysis of the ESC/ACC Consensus Document and reflections on its applic to the Italian Health System.

Galvani M, Panteghini M, Ottani F, Cappelletti P, Chiarella F, Chia Crea F, Dolci A, Golino P, Greco C, Nicolosi GL, Plebani M, Tubaro Zaninotto M; Intersocietary Study Group "Markers of Myocardial Damage".

Divisione di Cardiologia Ospedale G.B. Morgagni Piazza Solieri, 1 4710
galvanim@tin.it

The recent document of the ESC/ACC Committee for the redefinition of myocardial infarction (MI) has introduced the measurement of cardiac tr the biochemical standard for the diagnosis of MI. This change has been m driven by the demonstration that any amount of myocardial damage, as d by cardiac troponins, implies a worse long-term outcome of the patient. T results of several studies consistently show that there is a continuous rela between the degree of troponin elevation and the patient's prognosis. The definition has important consequences on the diagnostic and therapeutic approaches to patients with acute coronary syndromes; in fact, patients w increased troponins, i.e. patients with MI, necessitate more aggressive tre than those without troponin elevations, i.e. patients with unstable angina. application of the new definition is expected to increase the number of ca MI by about 30% and to decrease mortality. We believe that several aspe new definition need to be discussed before the new criteria for MI are use clinical practice in Italy. The most relevant issues are the following: 1) th definition of troponin elevation should meet the analytical performance o available assays, the diagnostic cutoff of which is frequently too imprecis propose that troponin elevations be defined as values exceeding the conc corresponding to a total analytical imprecision of 10%. We disclose such concentration for the currently available assays and suggest its use in clin practice to mitigate the possibility of false-positive values; 2) the number samples required for the diagnosis should be sufficient for the assessment changes in concentration over time. When only one sample is available, c the temporal pattern of the changes in marker concentration is not consist the time elapsed from the onset of symptoms, we suggest that objective e that myocardial ischemia is the likely cause of myocardial damage shoul obtained; 3) the diagnosis of MI after a percutaneous coronary interventi represents a unique situation. In contrast with myocardial damage occurri during spontaneous ischemia, available data do not support the concept th troponin elevation is associated with an adverse prognosis. In the absence

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conclusive studies, we suggest that the diagnosis of MI after a percutanec coronary intervention be based on conventional criteria. Finally, we prop summary with the aim of overcoming some of the more controversial asp the ESC/ACC redefinition of MI: Criteria for acute, evolving or recent M one of the following criteria satisfies the diagnosis for an acute, evolving MI: 1) elevation of biochemical markers of myocardial necrosis (preferat troponin) with at least one of the following: a) ischemic symptoms; b) development of pathologic Q waves on the ECG; c) ECG changes indicat ischemia (ST segment elevation or depression); d) coronary artery interve (e.g., coronary angioplasty). Marker elevations should be accompanied b objective evidence that myocardial ischemia is the likely cause of myocar damage when: a) only one blood sample is available; b) marker changes c are not consistent with the onset of symptoms; 2) pathologic findings of a MI. Criteria for established MI. Anyone of the following criteria satisfies diagnosis for established MI: 1) development of new pathologic Q waves ECGs. The patient may or may not remember previous symptoms. Bioch markers of myocardial necrosis may have normalized, depending on the l time that has passed since the infarct developed; 2) pathologic findings of or healing MI.

PMID: 12407856 [PubMed - indexed for MEDLINE]

QUEST Volume 7, Number 1, February 2000

Simply Stated . . .
The Creatine Kinase Test

Almost everyone with a neuromuscular disorder has had, or will have, a creatine kinase test. But what exactly is creatine kinase (CK), and why are its levels measured in neuromuscular diseases?

CK, also known as phosphocreatine kinase, or CPK, is a type of protein called an enzyme. It catalyzes, or "encourages," a biochemical reaction to occur. The normal function of CK in our cells is to add a phosphate group to creatine, turning it into the high-energy molecule phosphocreatine. Phosphocreatine is burned as a quick source of energy by our cells.

However, the normal function of CK isn't as relevant, in this case, as what happens to CK when muscle is damaged. During the process of muscle degeneration, muscle cells break open and their contents find their way into the bloodstream. Because most of the CK in the body normally exists in muscle, a rise in the amount of CK in the blood indicates that muscle damage has occurred, or is occurring.

To measure CK levels, a blood sample is taken and separated into fractions that contain cells and a fraction that doesn't — the serum. The amount of CK in the serum is reported in units (U) of enzyme activity per liter (L) of serum. In a healthy adult, the serum CK level varies with a number of factors (gender, race and activity), but normal range is 22 to 198 U/L (units per liter).

Higher amounts of serum CK can indicate muscle damage due to chronic disease or acute muscle injury. For this reason, if you're scheduled to have blood drawn for a CK test to diagnose a potential muscle disorder, you should limit your exercise to normal activities before the test.

CK tests are used to evaluate neuromuscular diseases in five basic ways:

1. To confirm a suspected muscle problem before other symptoms occur
2. To determine whether symptoms of muscle weakness are caused by a muscle or a nerve problem
3. To differentiate between some types of disorders such as dystrophies versus congenital myopathies

4. To detect "carriers" of neuromuscular disorders, particularly in Duchenne muscular dystrophy. A carrier has a genetic defect, but doesn't get the full-blown disease. A carrier's child may have the full disease.

5. To follow the course of a disease that fluctuates (primarily the inflammatory myopathies), or to document episodes of acute muscle injury, as might occur in some metabolic myopathies.

Because elevated CK levels indicate muscle damage, many parents wonder why their children with Duchenne muscular dystrophy (DMD) had higher CK levels when they were younger and had more muscle function. This seeming paradox occurs because muscle degeneration is more rapid at the earlier stages and, possibly, because there's more muscle bulk available to release CK into the circulation at this time.

CK levels can be slightly elevated (500 U/L) in nerve disorders like Charcot-Marie-Tooth disease, amyotrophic lateral sclerosis or spinal muscular atrophy, or grossly elevated (3,000 to 3,500 U/L) in DMD or inflammatory myopathies.

During episodes of acute muscle breakdown (rhabdomyolysis), CK levels can temporarily go off the scale, topping out at 50,000 to 200,000 U/L. At the same time, some neuromuscular disorders, such as the congenital myopathies (nemaline, central core disease and others) and myasthenia gravis, may not trigger any elevation of CK levels. CK levels don't always reflect the level of functional impact on the individual. ❑

"Simply Stated" is a new Quest column designed to explain some terms and basic facts about neuromuscular disease. In each issue, "Simply Stated" will present essential information about a different topic.

Serum Cardiac Marker

Cardiac Marker

I. **Indications**
   A. Myocardial Infarction Evaluation

II. **Best protocol for identifying AMI when EKG normal**
   A. Protocol
      1. Obtain Troponin at 0 hours, 8 hours and 16 hours
         a. Primary cardiac marker: Specific for cardiac event
         b. Not useful for monitoring event extension
            i. Levels stay elevated for 14 days
      2. Obtain CK-MB at 0 hours, 8 hours, and 16 hours
         a. Primary purpose: Follow cardiac event extension
         b. Decreases more rapidly than Troponin after event

III. **Test Sensitivity of combined protocol** Test Sensitivity: >98% at 8 hours
IV. Test Specificity: 80 to 95% at 8 hours
V. References
   1. *Jernberg (2000) Am J Cardiol 86:1367-71*

- **Troponin**

A. Rises: 3-6 hours
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C. Duration: 14 days
D. Subunits
   1. Troponin T
   2. Troponin I (>1.0 suggests Acute MI)

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   1. CK-MB Fraction (duration for 2-3 days)
   2. CK-MB over 5% of total CPK suggests Myocardial

0356

- **Myoglobin**

  A. Advantage: First cardiac marker to increase
  B. Disadvantage: Poor Specificity (only helps if negative)
  C. Rises: 1-2 hours
  D. Peaks: 4-6 hours
  E. Duration: 1-2 days

- **Glutamic oxaloacetic transaminase (AST, SGOT)**

  A. Peaks: 24-36 hours
  B. Duration: 5 days

- **Lactic Dehydrogenase (LDH)**

  A. Peaks: 24-48 hours
  B. Duration: 14 days

- **White Blood Cell Count**

  A. Predicts adverse events in Unstable Angina
  B. Morbidity and mortality increase with increased WBCs
     1. WBC Count >10,000: High risk of adverse event
     2. WBC Count >15,000: Very high risk of adverse event
  C. References
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troponin T and troponin I (cardiac enzymes)

Cardiac Troponins

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    - 84% sensitivity for myocardial infarction 8 hours after onset of 81% specificity (1)
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    as a result of causes other than MI e.g. myocarditis, coronary artery s
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    of cardiac troponin(s)
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Reference:

- Ebell MH et al (2000). A systematic review of troponin T and I for diagnosing
  myocardial infarction. J Fam Pract, 49, 550-6.
- Rev Esp Cardiol 2002 Feb;55(2):100-106 [Is Troponin I Useful for Predicting
  Risk for Unstable Angina Patients in a Community Hospital? Results of a Pros
  Bodi V V, Sanchis J, Llacer A, Graells ML, Llorca L, Chorro FJ, Insa LD, Navai
  E, Cortes FJ, Ponce De Leon JC, Valls A
- British Heart Foundation (Factfile 08/2003). What are cardiac troponins?

Links:

- **cardiac enzymes**
- **troponin C**
- **myocardial infarction**
- **cardiac troponin biomarkers**

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0346

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  - failure to show a rise in cTnT or cTnI does not exclude the diagnosis of ischaemic heart disease
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  - reference ranges may vary between laboratories and are dependent on methods of

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Links:

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troponin T and troponin I (cardiac enzymes)

Troponin

- rises after 3-6 hours
- tests for troponin T and I are insensitive within 6 hours of symptoms (1); a negative troponin test result can effectively rule out myocardial infarction is drawn >= 8 hours after symptom onset (1)
- peaks at about 20 hours
- may remained raised for 14 days

Troponin T

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- advantages
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  - levels may help to stratify risk afterward
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  - increased in unstable angina
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- advantages
  - more specific than Troponin T
  - is not increased in chronic renal failure
- interpretation

0342

- level >1.2 suggests myocardial infarction
- negative values predict low likelihood of coronary event - obtain two negative troponin values 4 hours apart

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tro·po·nin Pronunciation Key (trō′pə-nĭn, trŏp′ə-)
n.

A calcium-regulated protein in muscle tissue occurring in three subunits with tropomyosin.

[tropo(myosin) + -in.]

Source: *The American Heritage® Dictionary of the English Language, Fourth Edition*

tro·po·nin (trō′pə-nĭn, trŏp′ə-)
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Source: *The American Heritage® Stedman's Medical Dictionary*

Main Entry: **tro·po·nin**

Pronunciation: 'trOp-&-n&n, 'träp-, -"nin
Function: *noun*
: a protein of muscle that together with tropomyosin forms a regulatory protein complex controlling the interaction of actin and myosin and that when combined with calcium ions permits muscular contraction

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Unstable Angina Guideline Update - Figures & Tables

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Figure 16 . ORs of selected characteristics, treatment, outcome, and discha medications in elderly patients (aged more than 75 years) vs younger patie unstable angina and non–ST-segment elevation MI in the TIMI III registry. T
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ADDENDUM JULY 2002

People with diabetes comprise about 7.6% of the Australian population over 25 years' and the incidence is increasing. About 75% of those with diabetes will die from coronary heart disease.

20-25% of patients in registries and clinical studies of acute coronary syndromes are diabetics and subgroup data from these trials, though mostly not stratified for diabetes, has consistently demonstrated that diabetics are a high risk group who may have a specific response to medical and revascularisation therapies. People with diabetes also have a higher incidence of silent or atypical presentation with infarction or ischaemia and a higher rate of sudden death than those without diabetes.

In a recent meta-analysis[2], diabetics presenting with non-ST elevation acute coronary syndromes had a 30 day mortality rate of 6.2% compared with 3.0% for non-diabetics ($p<0.0001$). Similarly, in TACTICS[3], diabetic patients had a significantly higher cardiac event rate at 6 months than non-diabetics (23.8% v. 15.2%, $p<0.001$). This increased risk is similar to that observed in patients with elevated troponin or ST deviation.

Diabetics in TACTICS[3], who had an early invasive strategy had a reduction in the primary end-point (death, infarction or rehospitalised ACS at 6 months) by 27% with a reduction from 27.7 % (conservative) to 20.1% (invasive) with 95% confidence intervals for the odds ratio not crossing unity. In non-diabetics a 13% reduction from 16.4% (conservative) to 14.2% (invasive) showed a trend towards benefit, although this was non-significant. In the meta-analysis[2] of diabetic patients with non-ST elevation acute coronary syndromes:

- the use of intravenous glycoprotein IIb/IIIa receptor inhibitors reduced 30 day mortality from 6.2% to 4.6% (OR 0.74, $p=0.007$).
- the use of intravenous glycoprotein IIb/IIIa receptor inhibitors in patients undergoing percutaneous coronary intervention reduced 30 day mortality from 4.0% to 1.2% (OR 0.30, $p=0.002$).

In the DIGAMI study[4], diabetic patients with myocardial infarction treated with an insulin/glucose infusion for 24 hours and multidose subcutaneous insulin for three or more months had a mortality reduction at one year compared with patients randomised to receive conventional therapy (18.6% vs. 26.1%, $p=0.027$). The reduction in 1 year mortality was particularly reduced in patients with a low cardiovascular risk profile and no prior use of insulin (8.6% vs. 18.0%, $p=0.02$).

Recommendations

In patients with unstable angina, diabetes has emerged as an independent risk factor for adverse cardiac events (E1) and should be regarded as a high risk feature.

Patients with diabetes with unstable angina benefit from a combination of aggressive medical and invasive management. Concomitant IIb/IIIa receptor blockade is particularly advised in diabetic patients undergoing percutaneous coronary intervention (E1).

Tight glucose control with insulin for three or more months should be considered in patients with diabetes with acute coronary syndromes (E2).

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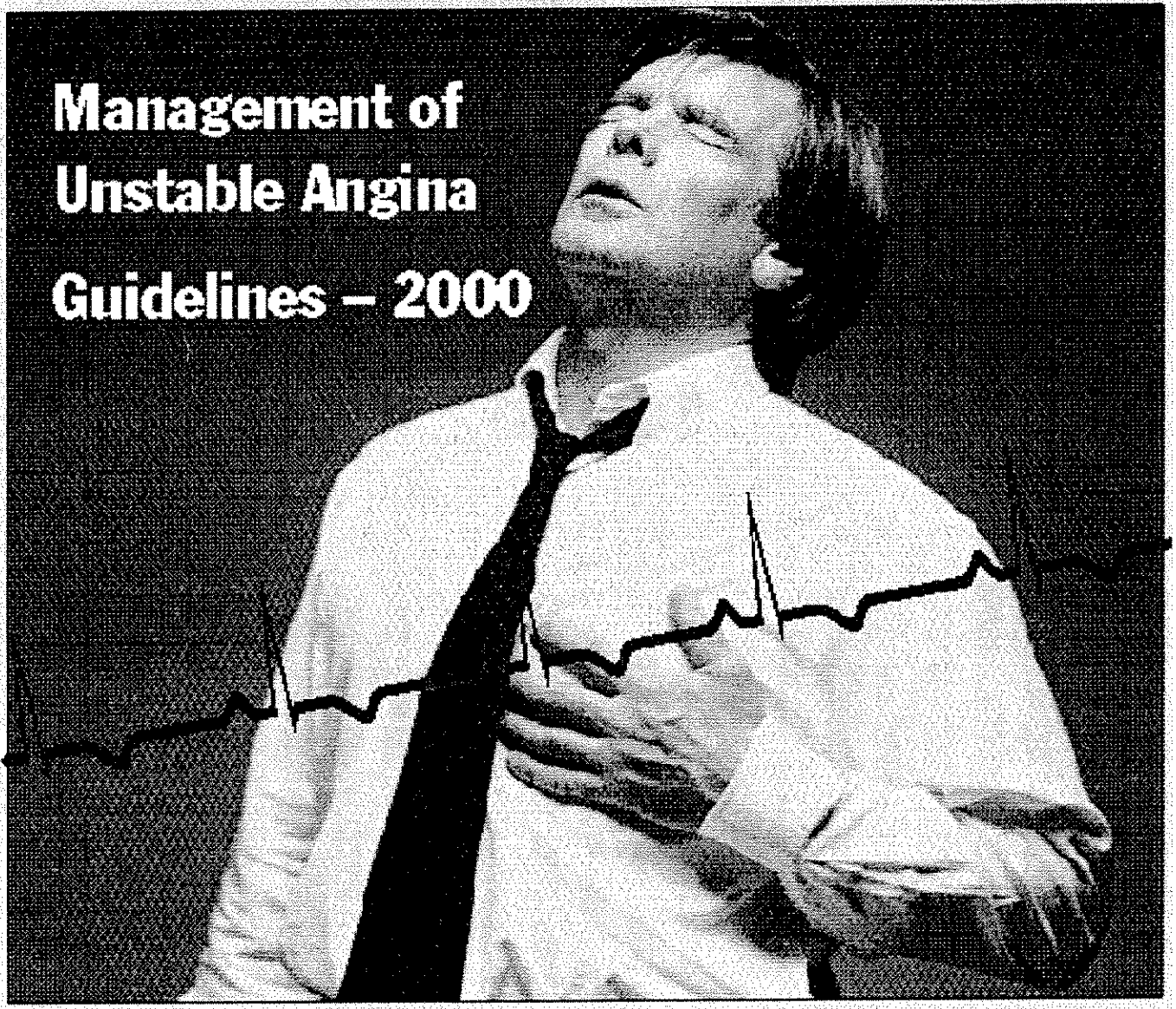

Management of Unstable Angina Guidelines – 2000

The National Heart Foundation of Australia

The Cardiac Society of Australia and New Zealand

Heart Foundation

Management of Unstable Angina

Guidelines – 2000

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Management of Unstable Angina Guidelines – 2000

THE PURPOSE OF THESE GUIDELINES is to incorporate contemporary information on the diagnosis and management of unstable angina into a set of recommendations that defines the boundaries of the highest-quality care in July 2000. The guidelines are directed at caring for patients presenting with the acute coronary syndrome without electrocardiographic ST-segment elevation, and therefore include patients with unstable angina and non-Q-wave myocardial infarction. The emphasis in the guidelines is on developments that have arisen since the previous National Health and Medical Research Council (NHMRC) Australian guidelines, *Diagnosis and management of unstable angina*, published in 1996. The current guidelines are an entirely local synthesis of more recent evidence.

The guidelines provide a general framework for appropriate practice, to be followed subject only to the medical practitioner's judgement in each individual case. They are directed primarily at doctors in a hospital environment (emergency physicians, rural doctors, and cardiologists) who manage patients with unstable angina, but also contain information relevant to general practitioners. The guidelines are designed to provide information to assist decision-making and are based on the best information available up to July 2000. It should be understood that the context in which clinical trials are performed and the local environment in which practice is undertaken must always be considered when assessing the evidence base for guidelines and, at times, their local implementation.

The guidelines were developed on a foundation of evidence-based criteria, using a consensus approach. They are the outcome of a workshop of representatives of key expert groups and stakeholders held in November 1999, followed by written submissions and further meetings of writing group members during January–July 2000.

Level-of-evidence codes

Evidence in the guidelines is graded according to the level-of-evidence classifications endorsed by the National Health and Medical Research Council (NHMRC) in 1995.

These are:

E1 Level I: Evidence obtained from a systematic review of all relevant randomised controlled trials.

E2 Level II: Evidence obtained from at least one properly designed randomised controlled trial.

E3 Level III: Evidence obtained from all well-designed controlled trials without randomisation, well-designed cohort or case–control analytic studies, preferably from more than one centre or research group, or from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence;

E4 Level IV: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

The 1995 evidence classifications allow the inclusion of opinions of respected authorities (E4). In the 1999 NHMRC guidelines level of evidence E4 has been removed. This makes it difficult to categorise the evidence for unstable angina, some of which is still empiric and not based on clinical trial evidence. Hence the writing group has used the 1995 NHMRC levels of evidence.

Contents

Summary of recommendations

Prehospital care

- Patients with a history of rest or prolonged chest discomfort (longer than 10 minutes, not relieved by sublingual nitrates), recurrent chest discomfort, or discomfort associated with syncope or heart failure are considered a medical emergency and should be transferred by ambulance to a hospital for urgent assessment.

Acute hospital assessment and triage

- The following investigations should be carried out for patients presenting with rest or prolonged chest or arm discomfort:
  - Baseline tests: electrocardiography (ECG), serum cardiac troponin (I or T) level (or serum CK-MB level if troponin testing is not available), full blood count, serum creatinine and electrolyte levels, serum CK levels, serum lipid levels (within 24 hours of onset of acute coronary syndrome), blood glucose level and chest x-ray.
  - The ECG is the sole test required to select patients for emergency reperfusion (thrombolytic therapy or direct PCI).
  - Continuous ECG monitoring of heart rhythm (ST segment monitoring is desirable, if available) and serial ECGs should be performed in patients with high and intermediate risk features.
  - Ongoing chest discomfort requires frequent follow-up 12-lead ECGs (15 minutes apart if continuous ST segment monitoring is unavailable) to rapidly diagnose eligibility for a reperfusion strategy.
  - A repeat serum troponin assay (unless already positive) should be performed at least six hours after presentation.
  - In patients with myocardial infarction, serial measurements of total CK should be performed for 48 hours, so that if reinfarction is suspected later total CK can be remeasured to confirm a second event. (A specific marker, such as CK-MB, is not required for the diagnosis of reinfarction, and troponin is not useful for diagnosing early reinfarction, as it remains elevated for 7–10 days.)
- All patients presenting with chest discomfort should have an ECG completed within five minutes of arrival at a medical facility and be assessed by the most appropriately qualified available person.
- Patients with chest discomfort should be evaluated with a careful history and physical examination completed within 10 minutes of arrival at a medical facility.
- High and intermediate risk patients should be admitted for continuous ECG monitoring, intensive medical therapy and observation by appropriately qualified nursing and medical staff.
- Recurrent chest discomfort (including in patients observed in a general ward environment) requires urgent reassessment, including immediate ECG, by the most appropriately qualified person.
- Patients whose ECG shows ST segment elevation or left bundle branch block should be immediately considered for reperfusion therapy.

Management

Low risk patients

- Low risk patients with a history of a moderate increase in angina frequency or severity, or angina onset more than two weeks before presentation, can be referred for cardiac assessment within two weeks.

Intermediate risk patients

- Intermediate risk patients who develop further ischaemia (pain or dynamic ST deviation) or positive serum markers are reclassified as high risk.
- Intermediate risk patients need not be treated with low molecular weight heparin unless reclassified into a high-risk group.
- Intermediate risk patients who have no further pain, have a normal ECG for the period of observation, have normal serum markers at baseline and six hours after presentation and a normal stress test may be reclassified as being at low risk.
- Patients with documented coronary artery disease without high-risk features are usually managed by increasing anti-anginal therapy, followed by a period of observation for clinical stability. Investigation will depend on the clinical context.
- Patients with symptoms strongly suggestive of myocardial ischaemia, but normal ECGs and serum markers, may be considered for either further provocative testing (stress radionuclide or stress echocardiography) and outpatient cardiac follow-up or coronary angiography in selected patients.

continued over

High risk pa tients

Intensive medical management

- In addition to aspirin, either LMW heparin or intravenous tirofiban with unfractionated heparin is recommended in high risk patients, and in geographically isolated patients requiring transfer to a tertiary facility, or patients not suitable for an invasive approach (very elderly, severe comorbidities).
- Intravenous tirofiban and unfractionated heparin are particularly recommended where LMW heparin fails and in high-risk patients for whom an invasive strategy is planned.

Early invasive approach

- With the exception of patients of advanced age or with severe or multiple comorbidities, an early invasive approach should be considered in patients with the following high-risk features:
  - pain or ischaemia refractory to medical therapy;
  - electrocardiographic changes (ST-segment depression or T-wave inversion in multiple leads);
  - positive serum markers (troponin I or T);
  - associated heart failure or haemodynamic instability;
  - high-risk features on early exercise testing; or
  - recent myocardial infarction or revascularisation.

  In rural centres and units that lack invasive facilities, these markers may be used to determine which patients may benefit from transfer for an invasive approach.
- The complementary use of aggressive medical and invasive approaches should be considered in all patients with high-risk features.

Long term management

- Statin therapy should be considered in all patients following unstable angina or non-ST elevation myocardial infarction if serum cholesterol level is greater than 4 mmol/L.
- Angiotensin-converting enzyme (ACE) inhibitors should be considered, particularly if hypertension or diabetes is present.
- All patients with a diagnosis of unstable angina or myocardial infarction should be referred to, and participate in, an appropriate cardiac rehabilitation and prevention program.

1. Background

A non-structured approach to the diagnosis of chest pain leads to a rate of missed myocardial infarction of 1% to 5%,[1,2] and the unnecessary hospital admission of more than 50% of patients.[3] The sequelae of non-Q-wave myocardial infarctions include recurrent angina with the need for re-admission to hospital (and possibly revascularisation if not already undertaken) in 40%–50% of patients,[4] reinfarction in 9.8%[5] of patients at six months, and mortality of 11.1% at one year.[5] The aims of management should reflect these issues; that is, to:

- reduce the incidence of death and myocardial infarction;
- reduce the incidence of recurrent angina and readmission to hospital and improve long term functional health outcomes; and
- provide the most useful and cost-effective diagnostic and management strategies, which may be readily adapted to local conditions.

2. New terminology

New terminology for acute coronary syndromes is emerging to:

- more accurately describe these at the time of presentation; and
- describe a newly identified group of patients with an adverse prognosis who have elevated serum cardiac troponin levels without elevation of total serum creatine kinase levels.

Rather than making a retrospective diagnosis of Q or non-Q myocardial infarction at the time of the patient's discharge from hospital, the description of infarction in terms of the presence or absence of significant ST elevation at presentation is now considered more appropriate. This classification also reflects differences in pathophysiology between ST elevation and non-ST elevation infarction. It also reflects management, which is determined by the presence or absence of ST elevation and not by the presence of Q waves. Thus, the new terminology (Box 1) to more accurately describe the acute coronary syndromes at the time of presentation is *ST elevation myocardial infarction* (STEMI) and *non-ST elevation myocardial infarction* (non-STEMI), rather than Q or non-Q myocardial infarction.

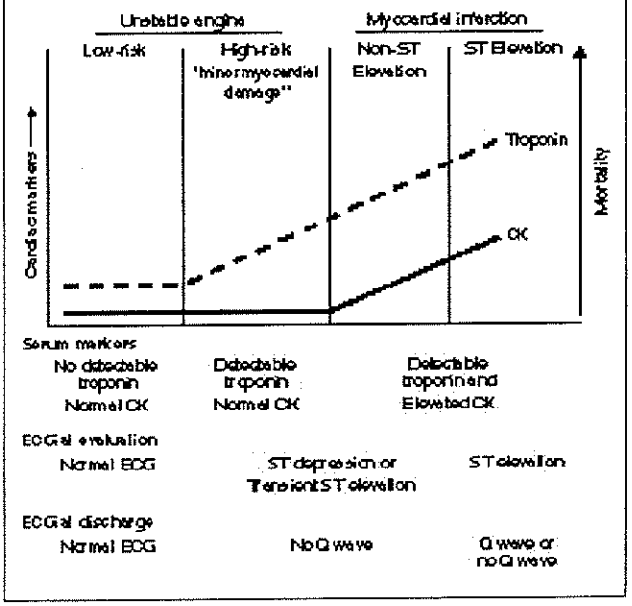
The differentiation between the diagnosis of unstable angina and non-STEMI has become clouded, with the subgroup of patients with elevated serum cardiac troponin levels without elevated serum creatine kinase (CK) or CK-MB levels being labelled as having *minor myocardial damage.*[1] These patients with "minor myocardial damage" who have an adverse cardiac prognosis[2] are a newly identified subgroup of patients with an acute coronary syndrome. The diagnoses of unstable angina, minor myocardial damage and non-STEMI may therefore be considered a continuum, with prognosis closely correlated with troponin level (Box 1). This entire diagnostic continuum will be considered in these guidelines. Patients presenting with persistent STEMI will not be considered, as, although they may "evolve" into non-Q wave myocardial infarctions, their pathophysiology and management are very different.[3]

3. Pathophysiology

Unstable angina is a syndrome that incorporates rest angina, new onset or crescendo effort angina, post-infarct angina, or angina early after percutaneous coronary intervention (PCI) or bypass surgery. The pathophysiology of acute coronary syndromes has been described in detail elsewhere.[6] Essentially, the established coronary plaque contains extracellular and intracellular lipid (the latter within foam cells), collagen and other connective tissue matrix proteins synthesised by smooth muscle cells, and inflammatory cells including macrophages derived from monocytes, T lymphocytes and mast cells. Foam cells in the plaque produce large numbers of cytokines and inflammatory mediators, including proteolytic enzymes, such as metalloproteinases. This inflammation is in response to modification (probably oxidation) of low-density lipoproteins in the subendothelial (intimal) space and to local monocyte adhesion and migration. Ongoing inflammation may, in part, be mediated by platelet interaction with leukocytes, and identified by inflammatory markers such as C-reactive protein, which is a predictor of poor long term outcome.

The extracellular lipid core in the plaque is encapsulated by a collagen cap, which can be infiltrated by macrophages. Intracoronary ultrasound has demonstrated that atheromatous plaques, which are vulnerable to plaque rupture and the development of acute coronary syndromes, are more likely to be eccentric, with a shallow, lipid-rich echolucent zone.[7] In unstable angina and non-ST or ST elevation myocardial

1: New terminology for coronary syndromes



infarction, there is a reduction in coronary perfusion due to plaque rupture or erosion and associated platelet aggregation, leading to varying degrees of coronary thrombosis and vasospasm and distal platelet microembolisation. Whether the patient develops unstable angina or non-ST or ST elevation myocardial infarction is determined by the degree and duration of reduction in coronary flow, the quality of collateral flow to the jeopardised myocardium, and the nature of the thrombus forming at the site of plaque rupture.

Patients with unstable angina or non-ST elevation infarction usually develop white (platelet) thrombi, whereas 80% of ST elevation infarctions are associated with red (fibrin with entrapped erythrocytes) thrombi.[8] These differences in pathophysiology are reflected by the effectiveness of platelet glycoprotein IIb/IIIa receptor antagonists in unstable angina and non-ST elevation infarction compared with the utility of fibrinolytic therapy for ST elevation infarction.

4. Serum markers

Cardiac troponins

The cardiac troponins have changed ideas regarding the pathophysiology of unstable angina, improved diagnostic accuracy, enhanced risk stratification and identified patients who respond to specific therapies.

The cardiac troponins are sensitive and specific markers of myocardial cell injury, with demonstrated value for prediction of cardiac events and outcomes in the short and longer term. It has been shown that 6%–8% of cardiac troponin T (cTnT)[9,10] and 3%–8% of cardiac troponin I (cTnI)[10,11] is present in the cytosol of the cardiac myocyte, with the rest being structurally bound to the contractile elements. Unlike CK-MB, cTnI and cTnT are specific for myocardial injury or necrosis, and, with usual current techniques, any circulating level of cTnI or cTnT is considered as abnormal. It is controversial whether cytosolic troponin is released with reversible myocardial ischaemia, but accepted that with myocyte necrosis the structurally bound troponins are released.

Prognostic value

Any circulating level of cardiac troponin (greater than 0.1 μg/L) is associated with greater mortality at 30 days than in patients with no detectable level (11.8% v. 3.9%; $P < 0.001$).[12] In one study, after a five-month follow-up of patients presenting with unstable angina, the risks of cardiac death and myocardial infarction for cTnT levels < 0.06μg/L, 0.06–0.18 μg/L, and > 0.18 μg/L were 4.4%, 11.4% and 14.1%, respectively.[13] A further study has shown a strong correlation between baseline cTnI level and mortality alone at 42 days in patients admitted with unstable angina (<0.4 μg/L, 1%; 1–2 μg/L, 3.4%; 5–9 μg/L, 6%).[14]

On multivariate analysis, electrocardiography (ECG) is the strongest predictor of 30-day mortality ($\chi^2 = 11.5$), followed by cTnT ($\chi^2 = 9.2$). CK-MB appears to add no prognostic information after correction for ECG and cTnT findings.[12] Long term risk of death or myocardial infarction in patients without ST elevation is also predicted by an elevated cTnT level (41.9% v. 23.1% at three years).[15]

There is additional prognostic value in measuring a 6–8 hour troponin level, particularly if the baseline level is normal. In the GUSTO IIa study, 30-day mortality was 10% with a positive baseline cTnT, 5% with a late positive level, and zero in patients with both normal baseline and normal late troponin levels.[16]

Risk stratification

The importance of negative troponin assays in identifying low-risk individuals was shown in a study of 773 consecutive patients presenting with acute chest pain and no new ST segment changes on ECG.[17] Patients with normal troponin levels at baseline and at least six hours later were discharged from the emergency department, and their 30-day event rates for death or myocardial infarction were 1.1% for cTnT and 0.3% for cTnI. This suggests that a policy of early discharge of such patients without elevated troponin levels is relatively safe. Bedside assays of both cTnT[18,19] and cTnI,[20] which provide point-of-care testing, may allow for earlier discharge and reduce hospital stay.

Late troponin level is predictive of left ventricular function. In one study, a cTnT level of 2.8 μg/L measured 12–48 hours following admission was predictive of a left ventricular ejection fraction of 40% or less, with a sensitivity of 100% and a specificity of 93%.[21] If initial troponin levels are negative, the assay should be repeated after 6–8 hours. Following myocardial infarction, troponin levels remain elevated for at least a week and CK levels may be used to diagnose (re)infarction in this period.

The combination of troponin level and exercise testing is

2: Five-month risk of cardiac death or myocardial infarction (MI) in relation to exercise test response and maximal cardiac troponin T levels during the first 24 hours

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also useful in the categorisation of risk. The risk of death or infarction at five months was 1% in patients with cTnT < 0.06 μg/L and with a negative exercise stress test, compared with 34% in patients with cTnT > 0.2 μg/L and a "high risk" stress test (Box 2).[22,23]

Cardiac troponins can also predict response to therapy. Patients with positive troponin levels will benefit from treatment with dalteparin,[24] tirofiban,[25] and from abciximab if they undergo PCI.[26]

Diagnostic utility

Around a third of patients with a positive troponin level but normal CK and CK-MB levels will develop an adverse outcome.[27] It has been suggested that, with the advent of the troponins as the preferred markers of myocardial injury, CK-MB level should be regarded as an obsolete assay.[28] As it is not cost-effective to measure both cardiac troponin and CK-MB, and because of the superior prognostic value of the troponins, many cardiac units have abandoned the use of CK-MB assays.

The International Federation of Clinical Chemistry has suggested the use of two cut-off levels for the optimum use of serum troponin: a low abnormal level to confirm minimal myocardial damage, and a higher level to make a definitive diagnosis of myocardial infarction.[29] The levels, specific assay, and time from presentation or symptom onset for the specimen to be discriminative have not yet been decided.

Of the cardiac troponins, only cTnI is never detected in skeletal muscle, either at any point in fetal development or in any pathologic state.[30-32] Troponin levels are sometimes elevated in patients with renal failure[25,26,30] and it was originally thought this may reflect a false positive result. However, a newer assay of cTnT has demonstrated that these elevated levels in renal failure do not represent a false positive finding,[33] but represent subclinical myocardial injury and predict an adverse cardiac prognosis.[34,35] As troponin levels indicate myocardial injury of any cause, they have been documented to be elevated in patients with myocarditis,[36] including heart transplant rejection[20] and the acute phase of Kawasaki disease.[37] An elevated cTnT level predicted an adverse outcome in patients with severe cardiac failure in the absence of acute ischaemia,[28] with a one-year mortality of 40%, compared with 10% in those without an elevated cTnT level. This may represent a subgroup of patients with ongoing myocyte loss. Elevation of cardiac troponin levels is also documented in acute pulmonary embolism, possibly caused by severe acute right ventricular ischaemia.[20,38,39]

C-reactive protein

Instability of coronary plaques is associated with macrophage accumulation,[40] inflammation, and an increase in acute phase proteins such as high sensitivity C-reactive protein and serum amyloid A.[41] Both baseline[42-47] and discharge[48] elevated high sensitivity C-reactive protein levels are independent predictors of subsequent events and, in the future, may also be used in risk stratification. However, a high sensitivity commercial assay required to detect minimal elevations of C-reactive protein has only recently been released. Although it is the subject of intense clinical research, there is insufficient evidence to recommend it for risk stratification at this stage.

5. Initial evaluation

Initial assessment is based on the clinical history, physical examination, and 12-lead ECG. The two objectives are to define the likelihood of significant coronary heart disease and to determine the risk of adverse short term outcomes.

Defining the likelihood of significant coronary heart disease

Patients with myocardial ischaemia or infarction can present with chest pain or pressure, syncope, palpitations, dyspnoea, or sudden death. Many patients deny a history of pain, but instead complain of pressure, tightness, or constriction, or place a fist over the central chest. The discomfort may radiate to the neck or one or both arms. Prolonged pain or discomfort occurring at rest or after physical exertion is mostly characteristic of unstable angina or myocardial infarction. The severity of this discomfort is not strongly correlated with the degree of ischaemia, with about a quarter of myocardial infarcts being painless.[49]

There are several features of pain which are characteristic of a non-ischaemic aetiology;[50] however, atypical presentations, such as dyspnoea, diaphoresis, interscapular or pleuritic pain, and nausea and vomiting, may occur, particularly in the elderly or people with diabetes.[49,51] Sharp or pleuritic pain has been described in 5%–19%[52,53] of patients with myocardial infarction and in 17% of patients with unstable angina.[52] About 15% of patients with myocardial infarction have tenderness on chest wall palpation.[53] Patients presenting with atypical symptoms often have a delayed diagnosis and treatment and an increased mortality

Summary: serum markers for coronary syndromes

- Cardiac troponin T or I are considered serum markers of choice in acute coronary syndromes.
- The presence in the serum of cardiac troponin T or I indicates myocardial damage.
- The level of cardiac troponin correlates with early risk of cardiac death and myocardial infarction.
- Baseline measurements of cardiac troponin level should be repeated after 6–8 hours, particularly if the baseline level is normal.
- Cardiac troponins predict response to therapy with low molecular weight heparin, tirofiban, or the adjunctive use of abciximab with percutaneous coronary intervention.
- Current assays of cardiac troponin T and I offer about equivalent information; the choice of assay and appropriate cut-off of abnormality is dependent on local expertise and laboratory facilities.
- At this stage, there is insufficient evidence to recommend C-reactive protein for risk stratification.

3: Risk stratification of unstable angina

High risk features
- Prolonged (> 10 min) ongoing chest pain/discomfort.
- ST elevation or depression (≥ 0.5 mm) or deep T wave inversion in three or more leads.
- Elevated serum markers of myocardial injury (especially cardiac troponin I or T).
- Associated syncope.
- Associated heart failure, mitral regurgitation or gallop rhythm.
- Associated haemodynamic instability (systolic blood pressure < 90 mmHg, cool peripheries, diaphoresis).

Intermediate risk features
- Prolonged but resolved chest pain/discomfort.
- Nocturnal pain.
- New onset grade III or IV chest pain* in the previous two weeks.
- Age >65 years.
- History of myocardial infarction or revascularisation.
- Electrocardiography (ECG) normal or pathologic Q waves.
- No significant (< 0.5 mm) ST deviation, or minor T wave inversion in less than three leads.

Low risk features
- Increased angina frequency or severity.
- Angina provoked at a lower threshold.
- New onset angina more than two weeks before presentation.
- Normal ECG and negative serum troponin.
- No high or intermediate risk features.

* Grade III: Marked limitation of ordinary physical activity. Grade IV: Inability to carry out any physical activity without discomfort. Grading of angina by the Canadian Cardiovascular Society. Campeau L. Grading of angina pectoris. *Circulation* 1976; 54: 522-523.

(50%) compared with patients presenting with typical symptoms (18%).[54]

Age is very important in determining diagnosis. The high prevalence of coronary disease in older people in Western societies means that the presence (or otherwise) of cardiac risk factors adds little to the accuracy of the diagnosis in middle-aged or elderly patients with a history suggestive of unstable angina. Coronary disease will account for more than 50% of cases of all chest pain presentations in patients aged over 40 years,[55] and only 7% in patients younger than 35 years.[56] In contrast, in these younger patients, cardiac risk factors (particularly smoking and family history),[57] as well as a history of physical stress before pain onset, increase the likelihood of unstable angina or myocardial infarction.

4: Simplified risk-assessment algorithm

	Six-month risk of death or myocardial infarction		
	Low risk (<2%)	Intermediate risk (2%–10%)	High risk (>10%)
Any pain	+	+	+
Rest, repetitive or prolonged pain	–	+	+
ECG changes or elevated troponin level	–	–	+

Defining the risk of adverse short term outcomes

Patients with unstable angina can be classified into high-, intermediate- and low-risk groups (Box 3). Physical examination is normal in most patients with unstable angina, but evidence of heart failure, mitral regurgitation or an extra heart sound are considered very high risk features. A simplified risk algorithm that could be used in emergency departments is shown in Box 4.

6. Accelerated chest pain assessment of intermediate risk patients

Almost two-thirds of patients with chest pain presenting to emergency departments are admitted, many to coronary care units, with only about 15% proven to have myocardial infarction.[3] Of the third of patients discharged from the emergency department, 1%–5% have a myocardial infarction,[1,2] and these "missed" infarcts carry a high mortality — up to 16% in one study.[2] One approach to this problem has been the development of an accelerated chest pain assessment strategy for intermediate-risk unstable angina patients.

Depending on the hospital, the chest pain assessment service might be located in the coronary care unit, emergency department, or a monitored bed in a country hospital. Irrespective of the location, patients with chest pain should be observed by staff who are specifically trained in coronary care practice, and should undergo accelerated diagnostic evaluation and risk stratification. Patient care is facilitated by integration of care between the emergency medical services, emergency medicine department, coronary care unit and cardiac diagnostic laboratories. Accurate assessment can be improved by the use of structured admission and continuing evaluation forms.

During the evaluation process, intermediate risk patients should be observed with frequent ECG and, often, continuous ST segment monitoring for six or more hours. After this period, serum troponin level is assayed and, if this is negative, an exercise stress test should be performed.[58] Following this period of observation and assessment, the patients are reclassified as high or low risk.

Reclassification of intermediate risk patients after a period of observation

Intermediate risk patients without ECG changes, further ischaemia, or a positive serum troponin level need not be treated with heparin,[24] but may be given aspirin during a period of observation, and other medical therapy may be commenced or upgraded if there is previous evidence of coronary artery disease.

The presence of dynamic ST depression is an independent marker of high risk, and carries a worse prognosis than T wave inversion (7% v. 2% death in GUSTO IIa).[59] ST

depression of 0.5 mm has the same prognostic significance as 1 mm of depression.[60,61] However, some investigators consider that dynamic T inversion in five or more leads suggests a high degree of risk.[62] In the TIMI IIIB study, rest pain occurring in the first 48 hours following admission was associated with a significantly increased incidence of adverse cardiac events at both six weeks and one year.[63] In GUSTO-IIb, recurrent ischaemia occurred in 35% of patients without ST elevation and nearly tripled the number of late adverse cardiac events.[5] Thus, patients who have recurrent pain or dynamic ECG changes during the period of observation should be immediately reclassified as high-risk.

After at least six hours of observation,[58] serum troponin level should be assayed, with a positive level also leading to a reclassification as high risk.[17] Finally, in patients with no further ischaemia and a negative troponin assay, an exercise stress test[64,65] or other provocative study should be performed. The combination of cardiac troponin level and exercise stress test is particularly useful in risk stratification (Box 2).

Patients reclassified as low risk and discharged should be instructed to return to the emergency department if symptoms recur. They may also benefit from early follow-up by their local doctor or cardiologist.

Advantages of a structured chest pain assessment service

A structured period of observation and investigation is likely to reduce the number of patients discharged with a "missed infarct". There are also clear opportunities to more rapidly identify and apply a reperfusion strategy to patients who develop ST elevation after being admitted to hospital, and to enhance the treatment of those who develop other high risk features. Effective and rapid risk stratification should also reduce length of stay of low risk patients. A structured chest pain assessment service has demonstrated a reduction in missed myocardial infarctions (from 4.5% to 0.4%) while also reducing total hospital admissions (from 57% to 47%) and costs.[66,67] Units employing this strategy have already been established in a number of Australian centres.

This strategy has the advantages of:

- allowing the rapid diagnosis of patients who develop high risk features during the observation period, facilitating rapid, specific therapy of these patients;
- avoiding the discharge of patients with "missed" infarcts; and
- promoting the prompt discharge of patients reclassified as being at low risk after the observation period.

7. Evidence for medical therapies

Aspirin and dipyridamole

Aspirin irreversibly inhibits cyclooxygenase, preventing platelet synthesis of thromboxane A_2, a potent vasoconstrictor and stimulator of platelet aggregation. Part of the benefit of aspirin could relate to its anti-inflammatory properties, which could reduce plaque rupture and its sequelae, as, in the Physicians' Health Study, benefits of aspirin were shown, particularly in those with higher serum levels of C-reactive protein, an inflammatory marker.[68]

The use of aspirin in acute coronary syndromes has been clearly established,[69-71] and it reduces the rate of death or myocardial infarction by about 50%.[72] Despite clear evidence of benefit in all patient subgroups with acute coronary syndromes, aspirin is frequently underutilised. In the GUARANTEE registry of unstable angina patients, only 82% of patients received aspirin.[73] Aspirin should be given to all patients unless there is intolerance.

In patients with unstable angina, dipyridamole does not confer benefit when added to aspirin.[74,75]

Ticlopidine and clopidogrel

Ticlopidine, an ADP-receptor antagonist, is useful where there is intolerance to aspirin,[76] but is associated with severe side effects, including neutropenia and thrombotic thrombocytopenic purpura.

Clopidogrel, another ADP-receptor antagonist, may be a safer alternative in patients who are unable to tolerate aspirin, and is currently being assessed in patients with unstable angina (CURE trial). Unlike ticlopidine, clopidogrel is not associated with neutropenia. It also produces less gastrointestinal bleeding than aspirin. Clopidogrel is more effective than aspirin in preventing vascular events in patients with recent stroke, myocardial infarction or symptomatic peripheral vascular disease.[77] At 1.9 years' follow-up, there was an 8.7% reduction with clopidogrel compared with aspirin, with the incidence of ischaemic stroke, myocardial infarction or vascular death corresponding to an extra five events prevented per 1000 patients treated with clopidogrel for one year. However, clopidogrel has not been assessed in acute coronary syndromes and its increased cost precludes general use when aspirin has proven efficacy in cardiovascular disease.

Nitroglycerine and nicorandil

Nitroglycerine has systemic and coronary effects. The systemic effects include venous pooling, which reduces left ventricular preload and end-diastolic pressure, as well as having a more modest effect on reducing afterload. The coronary effects include vasodilatation of normal and atherosclerotic coronary arteries, an increase in coronary artery collateral flow, redistribution of flow from subepicardial to subendocardial regions, and antiplatelet activity.

There are no large randomised trials of intravenous nitroglycerine in unstable angina, although several small studies have demonstrated symptomatic relief with open label nitroglycerine.[78-80] The combination of intravenous or transdermal nitroglycerine and N-acetylcysteine has been shown to be superior to nitroglycerine alone, but is associated with increased side effects.[81,82]

Nicorandil is a newly available agent with nitrate and potassium channel opening activity, with effects in reducing both preload and afterload as well as causing coronary

vasodilatation.[83] There is preliminary evidence that, unlike intravenous nitroglycerine, nicorandil may not lead to tolerance after 24 hours of administration.[84] In a study of 188 patients with unstable angina, the addition of nicorandil to medical therapy reduced the incidence of recurrent myocardial ischaemia and ventricular and supraventricular arrhythmias.[85]

β-Blockers

The primary benefits of β blockade in unstable angina are owing to its effects on β_1 receptors, resulting in decreased cardiac work and myocardial oxygen demand.

Randomised studies[86-88] have shown no definite reduction in mortality, but a meta-analysis[89] has shown a 13% reduction in progression to myocardial infarction. Patients with significant AV block (first degree heart block with PR interval > 0.24 seconds, 2nd or 3rd degree heart block), bradycardia < 60 bpm, hypotension (systolic blood pressure < 90 mmHg), a history of asthma, or uncontrolled heart failure should not be given β-blockers until these conditions have resolved. Intravenous administration of β-blockers may be particularly useful in patients with uncontrolled ischaemia and hypertension, and when used in conjunction with nitrates.

Calcium channel blockers

Calcium channel blockers may exert a beneficial effect in unstable angina by promoting coronary vasodilatation, reducing heart rate (verapamil and diltiazem) and reducing cardiac work and myocardial oxygen demand.

There are a number of small trials of calcium channel blockers demonstrating relief of symptoms or ischaemia in patients with unstable angina.[90-92] The largest study (HINT)[88] tested nifedipine, metoprolol, and the combination of both. Nifedipine increased the risk of myocardial infarction and recurrent angina relative to placebo by 16%, metoprolol reduced it by 24%, and the combination reduced it by 20%. It is not recommended that dihydropyridine calcium channel blockers be used without the concomitant use of β-blockers. If a calcium channel blocker alone is considered (eg, in patients with obstructive airways disease), then one which reduces heart rate (verapamil or diltiazem) is recommended.

Perhexiline

Perhexiline is believed to reduce myocardial ischaemia by causing a shift from fatty acid to glucose metabolism.[93]

Addition of perhexiline to standard medical therapy improves anginal symptoms and exercise tolerance in patients with severe refractory angina.[94] There is preliminary evidence that perhexiline is useful in the treatment of unstable angina.[95]

Unfractionated heparin

Heparin binds with antithrombin, enhancing its ability to inactivate factor Xa and thrombin.

The evidence for benefit of unfractionated heparin for the treatment of unstable angina is weak, particularly when compared with the proven benefits of low molecular weight heparins. A meta-analysis of six randomised short-term trials has assessed the value of the addition of unfractionated heparin to aspirin for the treatment of unstable angina in 1353 patients.[96] There was a trend towards reduced death and myocardial infarction (risk ratio, 0.67; 95% CI, 0.44–1.02; $P = 0.06$) in the patients receiving heparin. However, only four studies reported results to 12 weeks, when much of the trend in benefit was attenuated (risk ratio, 0.82; 95% CI, 0.56–1.20; $P = 0.76$).

Although it has not been definitively established that the combination of heparin and aspirin is superior to either aspirin or heparin alone, guidelines usually recommend their combined use in patients with unstable angina or non-STEMI who are considered to be at higher risk. Rebound ischaemia on cessation of treatment may occur, particularly in patients not taking aspirin. The target activated partial thromboplastin time (aPTT) is recommended to be in the range of 45–60 seconds on the basis of TIMI IIIB.[97] Control may be facilitated by the use of bedside monitoring and dosing titrated to patient weight.

A number of factors may contribute to limited efficacy of unfractionated heparin. These include the need for antithrombin for its action, and reduced effectiveness of the heparin–antithrombin complex in the presence of fibrin monomers. The release of platelet factor 4 in response to heparin may also contribute to reactivating acute ischaemia. Other limitations of unfractionated heparin are the need for continuous infusions and difficulty in achieving target aPTTs because of wide variation in antithrombotic response. Heparin-induced thrombocytopenia syndrome occurs in about 1%–3% of patients.[96]

Low molecular weight heparins

Low molecular weight (LMW) heparins are derived from unfractionated heparin by depolymerisation. They have a number of practical advantages, including greater activity against factor Xa than thrombin, and greater bioavailability than unfractionated heparin because of less binding to plasma proteins and endothelial cells. This leads to a more predictable antithrombotic dose–response relationship without the need for factor Xa monitoring, which is not recommended. The long half-life of about four hours after subcutaneous injection allows twice-daily subcutaneous injection.

Trials do not show a lower incidence of bleeding compared with unfractionated heparin; indeed, there may be an increase in minor (cutaneous) bleeding. However, LMW heparins have distinct advantages in that they do not require aPTT monitoring, they have a reduced rate of heparin-induced thrombocytopenia,[98] and intravenous site infections are avoided. Because of the long half-life of LMW heparins and difficulties in achieving rapid reversal of effect, unfractionated heparin is often preferred in patients in whom early or immediate intervention is planned. However, administration of protamine sulfate results in about 60% reversal of

the antifactor Xa effects of LMW heparins, and may result in decreased bleeding.[99,100]

The only clinical trial of LMW heparin (dalteparin) compared with placebo in patients taking aspirin (FRISC)[101] showed a benefit in death and myocardial infarction (1.8% v. 4.8%) at six days, which persisted at 40 days. For inclusion in that study, patients were required to have an unstable coronary syndrome and transient or persistent ECG changes (ST depression of 1 mm or more, or T wave inversion of 1 mm in two adjacent leads). A positive cTnT level ($\geq 0.1\,\mu g/L$) differentiated between patients who responded to dalteparin (48% less death or MI at 40 days) and those who did not.[24]

Several major clinical studies of LMW heparins have examined their efficacy compared with intravenous unfractionated heparin. Both the FRIC study (dalteparin)[102] and the FRAXIS study (nadroparin)[103] demonstrated equivalence but no advantage of LMW heparins over unfractionated heparin. Two studies of enoxaparin (ESSENCE[104] and TIMI 11B)[105] demonstrated superiority over unfractionated heparin, with reduction in the composite endpoint of death, infarction, recurrent angina, or revascularisation. A prospectively planned meta-analysis[106] of the two trials of enoxaparin (ESSENCE and TIMI 11B) demonstrated superiority, with a 20% reduction in the combination of death and myocardial infarction when compared with unfractionated heparin ($P = 0.05$) at 8, 14 and 43 days. Benefit has been confirmed to persist at one year.[107] Economic analyses of data from ESSENCE show cost savings at both 30 days[108] and one year[109] in patients treated with enoxaparin.

The LMW heparins differ in their ratio of anti-Xa to anti-IIa activity, with enoxaparin having relatively greater anti-Xa activity (3.5:1) than dalteparin (2.5:1).[110] The LMW heparins also vary in their pharmacological effects,[111,112] including their rates of clearance, the amount of non-specific binding, as well as duration of effect and effects on Von Willebrand factor. In the absence of direct comparisons in clinical trials, the relative effectiveness of the different LMW heparins is uncertain. Current evidence, however, demonstrates the clinical benefit of enoxaparin[106] over unfractionated heparin; this is not proven with dalteparin or nadroparin.

It was hoped that the LMW heparins might be particularly effective for prolonged therapy in low-dependency areas or in outpatients. However, this has not been substantiated, with a three-month study of twice-daily dalteparin compared with placebo (FRISC II) showing a reduction in the composite endpoint of death and myocardial infarction at one month, which was not sustained at six-month follow-up.[113] Another study (TIMI 11B) of prolonged enoxaparin for 35 days after initial stabilisation demonstrated persistence of the early benefit at 43 days (without convergence of the event curves), but was associated with an increased risk of major bleeding.[105]

Direct antithrombins

Hirudin, hirulog, inogatran and argatroban are selective antithrombin agents that have been subject to clinical trial but are not available for clinical use in Australia. They differ from heparin in that they do not require interaction with an intermediate enzyme; instead, they bind directly to the catalytic site of thrombin. Their proposed benefits over heparin include the ability to inactivate clot-bound thrombin, and reduction in thrombin-induced platelet activation, factor V and factor VIII activation, and endothelin release. The direct antithrombins are not inhibited by platelet factor 4, remain active in platelet-rich environments, and are not associated with thrombocytopenia.

Despite these "laboratory" advantages, large-scale trials of direct antithrombins have been disappointing. Only a small, incremental benefit has been shown over standard unfractionated heparin in large-scale studies. A meta-analysis[114] of the hirudin trials from the OASIS pilot, OASIS-2 and GUSTO-IIb studies of non-ST elevation acute coronary syndrome patients demonstrated a trend to benefit (risk ratio, 0.90; $P = 0.06$). Compared with heparin, hirudin was associated with a higher rate of bleeding requiring transfusion. Similarly, a study of inogatran[115] showed no improvement in ischaemic end-points, despite a clear dose-related improvement in activated partial thromboplastin time.

Early benefit at seven days[114,116] may be attenuated by 30 days because of rebound activation of the coagulation system after termination of treatment.[115,117] Owing to low event rates in these large trials, it has been difficult to demonstrate significant differences in outcomes, and apparent gains appear to be small. In addition, these agents are associated with an increase in major bleeding and are more expensive than heparin. These agents are not available for clinical use in Australia.

Thrombolytic therapy

In the TIMI IIIB study,[118] 1473 patients with unstable angina or non-Q myocardial infarction were randomised to receive tissue-type plasminogen activator (tPA) or placebo, in addition to unfractionated heparin and aspirin. It was found that tPA did not lead to an improvement in clinical endpoints, but was associated with an increase in fatal and non-fatal myocardial infarction at six weeks and one year (7.5% v. 4.9%; $P = 0.04$). Cerebral haemorrhage occurred in four patients with tPA but not in control patients ($P = 0.06$).

Warfarin

Two randomised trials of combined aspirin and warfarin compared with aspirin alone have been reported.[119,120] The ATACS trial[119] randomised 214 patients to 162.5 mg aspirin alone or aspirin plus heparin for 3–4 days followed by warfarin with a target INR of 2–3. There was no significant difference in the combined endpoint of ischaemic events at 12 weeks (28% v. 19%; $P = 0.09$) and an excess of major and minor bleeds in the warfarin group. In phase I of the OASIS pilot study,[120] 309 patients were randomised to aspirin or aspirin and warfarin (low intensity anticoagulation with target INR of 1.5) after three days of intravenous heparin or hirudin. Of patients in the warfarin group, 6.5% experienced a primary ischaemic end-point (cardiovascular

death, new myocardial infarction, or refractory angina) at six months, compared with 3.9% in the aspirin group ($P=0.31$). Phase II of this study employed moderate intensity warfarin (target INR, 2–2.5). Of patients in the warfarin group, 5.1% experienced a primary ischaemic end-point, compared with 12.1% of patients in the aspirin group ($P=0.08$). There was an excess of minor bleeds in the warfarin group in both phases of the study.

Glycoprotein IIb/IIIa receptor antagonists

Platelets are central to coronary thrombosis. Their aggregation may be stimulated by a variety of substances, but the common final mechanism is activation of the glycoprotein IIb/IIIa receptor, the platelet membrane receptor for fibrinogen.

The first glycoprotein IIb/IIIa receptor antagonist to reach clinical practice was abciximab, a murine monoclonal Fab antibody fragment. Subsequently, both peptide (eptifibatide) and non-peptide (tirofiban, lamifiban, sibrafiban, xemilofiban and orbofiban) small molecules have been assessed in clinical trials. Abciximab has been mainly studied with PCI, and these agents have not been compared directly. However, results of trials with the agents support their place as a major advance in medical therapy for patients with unstable angina.

In the PRISM-PLUS study,[121] the combination of aspirin, heparin and tirofiban (compared with aspirin and heparin alone) reduced the composite end-point of death, non-fatal infarction and refractory ischaemia at seven days (12.9% v. 17.9%; $P=0.004$), 30 days (18.5% v. 22.3%; $P=0.03$) and six months (27.7% v. 32.1%; $P=0.02$). Death and non-fatal infarction were reduced at seven days (4.9% v. 8.3%; $P=0.006$) and 30 days (8.7% v. 11.9%; $P=0.03$), but not at six months (12.3% v. 15.3%; $P=0.06$). Similarly, the combination of aspirin, heparin and eptifibatide[122] reduced the combination of death and myocardial infarction from 15.7% to 14.2% ($P=0.042$) at 30 days compared with heparin and aspirin alone. Low-dose lamifiban, heparin and aspirin (compared with heparin and aspirin alone) led to a reduction in death or myocardial infarction at six months (12.6% v. 17.9%; $P=0.025$).[123]

In the PRISM study, 13% of patients who were cTnI-positive had a cardiac event (death, myocardial infarction) at 30 days, compared with 4.9% in cTnI-negative patients ($P<0.0001$).[25] At 30 days, among cTnI-positive patients, tirofiban had lowered the risk of death (adjusted hazard ratio, 0.25; 95% CI, 0.09–0.68; $P=0.004$) and myocardial infarction (adjusted hazard ratio, 0.37; 95% CI, 0.16–0.84; $P=0.01$). This benefit was seen in medically managed patients (adjusted hazard ratio, 0.30; 95% CI, 0.10–0.84; $P=0.004$) and those undergoing revascularisation (adjusted hazard ratio, 0.37; 0.15–0.93; $P=0.02$) after 48 hours' infusion treatment. However, no treatment effect was seen for cTnT-negative patients. Similar benefits were seen for cTnT-positive patients.

The benefits of the glycoprotein IIb/IIIa receptor antagonists tirofiban[121,124] eptifibatide[122] and lamifiban[123] have been consistent in patients with acute coronary syndromes, with early decrease in death, myocardial infarction and refractory ischaemia, but there was some attenuation of benefit at six months. Tirofiban is currently available in Australia for the treatment of unstable angina or non-STEMI, and abciximab is available for adjunctive therapy with PCI. The combination of glycoprotein IIb/IIIa receptor antagonists together with LMW heparins has not yet been studied in large clinical trials, although this is being actively assessed. A small study of tirofiban in combination with enoxaparin demonstrated more consistent inhibition of platelet aggregation than when combined with unfractionated heparin.[125] There are no head-to-head studies of glycoprotein IIb/IIIa receptor antagonists compared with LMW heparins.

Some glycoprotein IIb/IIIa receptor antagonists may have other clinically important effects on long term inflammation and hyperplasia. Abciximab binds the leukocyte Mac-1 receptor,[126,127] which may have long term benefits in reducing inflammation. It also blocks the vitronectin receptor,[128,129] which is an integrin involved in tissue hyperplasia.

Although oral glycoprotein IIb/IIIa receptor antagonists

Summary: evidence for medical therapy in unstable angina

- Aspirin reduces progression to myocardial infarction and cardiac mortality by about 50% (E1).
- Dipyridamole does not confer any additional reduction in coronary events when added to aspirin (E1).
- Clopidogrel may be a useful alternative when there is intolerance to aspirin (E4).
- Intravenous nitroglycerine can achieve symptomatic relief (E3).
- β-Blockers reduce progression to myocardial infarction (E1).
- Calcium channel blockers that increase heart rate should not be used without concomitant β-blockers (E2).
- When used alone, only calcium channel blockers that reduce heart rate should be used (E2).
- Unfractionated heparin, when used with aspirin, only marginally reduces death and myocardial infarction compared with placebo (E1).
- Dalteparin reduces death and myocardial infarction when compared with placebo (E2).
- Enoxaparin is superior to unfractionated heparin in reducing death and myocardial infarction (E1), whereas dalteparin and nadroparin are not (E2).
- Prolonged use of low molecular weight heparins shows no additional benefit over short term use (E1).
- Direct antithrombins appear to have a marginal advantage over heparin and have the risk of increased bleeding (E1).
- Intravenous thrombolytic therapy is ineffective and may be harmful (E2).
- Warfarin has minimal benefits over aspirin (E2).
- Glycoprotein IIb/IIIa receptor antagonists in combination with aspirin and unfractionated heparin reduce death and myocardial infarction in the first months after treatment, but with attenuation of effect at six months (E1).
- The benefits of glycoprotein IIb/IIIa receptor antagonists are additive to the use of revascularisation (E1).

could provide prolonged receptor inhibition and thus have potential value in prevention of chronic recurrent ischaemia, they have thus far been disappointing.

Antibiotics

There is serological evidence that *Chlamydia pneumoniae* is associated with atherosclerosis.[130] Furthermore, *C. pneumoniae* has been shown to localise in coronary plaque and to promote LDL-cholesterol oxidation.

A report of the use of roxithromycin in patients with unstable angina demonstrated a reduction in ischaemic events at 30 days,[131] with continued benefit apparent at six months.[132] However, more data are required on the role of antibiotics.

8. Evidence for early angiography and revascularisation

Direct randomised comparisons of invasive versus conservative strategies

The recent large FRISC II study[4] (Box 5) has attracted considerable attention. It examined an early invasive strategy in 2457 patients with unstable angina who had ECG changes or positive serum markers. Patients first received dalteparin for at least two days before a randomised comparison of an early invasive strategy employing early PCI (stenting in 61%–70%) or bypass surgery, which significantly reduced death and myocardial infarction (the primary end-point) by 22% (from 12.1% to 9.4%) ($P = 0.03$) at six months, compared with a conservative strategy in which revascularisation was driven by recurrent or ongoing ischaemia. The event curves continued to diverge at six months after randomisation. In addition, there was a strong trend to reduction (by 35%) in total mortality alone (from 2.9% to 1.9%; $P = 0.10$). Total mortality was significantly reduced in men but not women treated with the invasive strategy. Myocardial infarction alone was significantly reduced (from 10.1% to 7.8%) ($P < 0.05$) at six months. At six months, there were highly significant reductions in angina (22% v. 39%; $P < 0.001$), class III–IV angina (3% v. 8%; $P < 0.001$), requirement for long-acting nitrates (17% v. 38%; $P < 0.001$) and hospital readmission rates (31% v. 49%; $P < 0.001$) in the invasive compared with the non-invasive group (Box 5).

PCI was performed at a median of four days (10th and 90th percentiles being at 2 and 7 days, respectively) and coronary bypass surgery at a median of seven days (10th and 90th percentiles being at 5 and 13 days, respectively). It is possible, but not proven, that this complementary medical therapy with an average of four days of "early plaque passivation" (with LMW heparin and aspirin) before angiography and intervention may have been synergistic in leading to an improved outcome. The benefits of an immediate invasive strategy without at least two days of medical therapy are unknown.

The TIMI IIIB[118] and VANQWISH[133] studies, two earlier and smaller studies (1473 and 920 patients, respectively) that included the use of balloon angioplasty before the widespread availability of intracoronary stents, did not demonstrate an overall reduction in death or infarction from an early invasive approach. Whereas there was a large difference in intervention rates between invasive and conservative groups in the FRISC II study (71% v. 9% at 10 days, and 77% v. 37% at six months), there was only a small difference in intervention rates between invasive and conservative groups in both the TIMI IIIB (61% v. 49% at six weeks)[118] and VANQWISH (44% v. 33%)[133] studies. Thus, these studies have been criticised because of the similar intervention rates of their "invasive" and conservative arms. VANQWISH has also been heavily criticised because 78% of adverse events in the early "invasive" group occurred in patients who had not undergone an intervention. However, like the FRISC II study, the TIMI IIIB study showed that an invasive strategy reduced readmission to hospital by 45% at six weeks, and reduced death and myocardial infarction by 47% in the subgroup of patients aged 65 years and over.[118]

Coronary artery bypass surgery is considered appropriate in patients in whom angiography has demonstrated left main coronary artery disease or triple vessel disease with left ventricular dysfunction. Registry data show operative mortality is increased when patients undergo surgery while they are still unstable; thus, where possible, the timing of coronary artery bypass surgery may be delayed until symptoms are controlled. The third major criticism of the VANQWISH study[133] is that patients treated with early coronary artery bypass surgery had a very high (12%) mortality. Even though patients in the VANQWISH study having early PCI had no early mortality, the high surgical complication rate led to an overall worse outcome in the invasive group. However, this early risk with bypass surgery has not been verified in other studies (1.2% in FRISC II).[4] Even though recurrent angina and readmission to hospital are the most common adverse events occurring after an initial presentation with unstable angina, these events were not assessed in the VANQWISH

5: The FRISC II Study:[4] status at six months

	Invasive	Conservative	Risk ratio (95% CI)	P
Number	1222	1235		
Intervention				
PCI	43%	18%		
CABG	34%	19%		
Outcome				
Death or myocardial infarction	9%	12%	0.78 (0.62–0.98)	0.031
Any angina	22%	39%	0.56 (0.50–0.64)	< 0.001
CCS class 3/4 angina	3%	7%	0.38 (0.25–0.56)	< 0.001
Any readmission	31%	49%	0.62 (0.60–0.69)	< 0.001

PCI = percutaneous cardiac intervention. CABG = coronary artery bypass grafting. CCS = Canadian Cardiovascular Society.

study; however, they were significantly reduced in the invasive arms of both the TIMI IIIB and FRISC II studies.

Aggressive medical management used with an invasive strategy

Contemporary clinical trials of medical therapy for unstable angina usually incorporate a high rate of coronary angiography and revascularisation. In the PRISM-PLUS study[121] of intravenous heparin with tirofiban versus heparin, coronary angiography was encouraged at 2–4 days after randomisation, leading to a 90% rate of early angiography. Consequently, there was a 54% rate of early revascularisation overall (31% angioplasty and 23% bypass surgery). Although there was no randomisation between invasive and medical strategies, the reduction in the composite endpoint with heparin and tirofiban was only significant in patients undergoing angioplasty (risk ratio, 0.55; 95% CI, 0.32–0.94) and not in patients treated medically (risk ratio, 0.87; 95% CI, 0.60–1.25). This suggests that the major benefit of this aggressive medical management accrues when it is used as a complement to an early invasive strategy.

An angiographic assessment of patients treated with heparin and tirofiban in the PRISM-PLUS study demonstrated persistent thrombus in 45% of patients.[134] Persistent thrombus was associated with an increase in both death (risk ratio, 2.4; 95% CI, 1.3–4.3) and myocardial infarction (risk ratio, 2.0; 95% CI, 1.3–3.1) at 30 days. This problem illustrates the need for possible complementary mechanical revascularisation, as well as a need for continued research to develop more effective medical regimens.

PCI and adjunctive medical therapy

Platelets play a central role in complications after PCI or stenting. Use of the glycoprotein IIb/IIIa platelet receptor antagonist abciximab improves outcomes in patients undergoing PCI and stenting, particularly in patients with unstable angina or myocardial infarction.[135-139] Troponin level can predict which patients will benefit from abciximab therapy, with a risk ratio of myocardial infarction at six months of 0.23 (95% CI, 0.12–0.49; $P<0.001$) for troponin-positive patients receiving abciximab compared with placebo.[26] Improved outcomes are maintained for three years following treatment.[140]

After stent implantation, treatment with the combination of aspirin and clopidogrel[141,142] for 2–4 weeks provides excellent protection against thrombotic complications.

Invasive therapy in post-infarction angina

Although a trial assessing an invasive versus conservative strategy in patients with post-infarction angina has not been carried out, invasive therapy has been evaluated in a group of post-infarction patients with exercise-induced myocardial ischaemia.[143] In this study (DANAMI), there was a reduction in readmission for unstable angina at one year (17.9% v. 29.5%; $P<0.001$), stable angina (21% v. 43%; $P<0.001$) and reinfarction (5.6% v. 10.5%; $P<0.004$) in patients being treated invasively.

Summary: evidence for early invasive strategies

In high-risk patients, an early invasive strategy employing angiography and percutaneous coronary intervention (PCI) or bypass surgery:

- reduces anginal symptoms and need for nitrates by 50% (E1);
- reduces subsequent hospitalisation by 45%–50% (E1);
- reduces subsequent death or myocardial infarction by 22% (E2);
- provides definitive early diagnosis and prognostic stratification;
- provides for an early clear therapeutic plan;
- reduces hospital length-of-stay overall, and especially promotes early discharge and return to normal activities of patients with low-risk coronary anatomy;
- defines patients without obstructive coronary disease where other diagnoses should be considered (60% of these will have gastrointestinal disease, especially gastro-oesophageal reflux).

The benefit from PCI is enhanced by peri-procedural heparin/tirofiban (E2), or by concomitant administration of abciximab (E1).

Patients with minor coronary disease or "normal" coronary arteriograms

In TIMI IIIA, 14% of patients enrolled with a diagnosis of unstable angina did not have a coronary obstructive lesion of 60% or greater.[144] Of this group, half had no detectable disease and a third had "slow-flow" (TIMI flow grade 1 or 2). Prognosis was much better than in patients with severe obstructive lesions. Lipid-lowering therapy has been shown to reduce cardiac events, at least in part, by the stabilisation of minor or moderate coronary lesions.[145] Clearly, patients with even minor coronary artery lesions should be managed with aggressive risk factor modification.

In patients with "normal" coronary arteries, other pathology should be considered. Oesophageal disease, especially reflux oesophagitis, has been reported in up to 36% of patients presenting with chest pain,[146] and should be considered when myocardial ischaemia has been excluded.

9. Management strategies

Prehospital care

Patients experiencing chest discomfort for more than 10 minutes, chest discomfort at rest, or chest discomfort associated with syncope or heart failure, should call an ambulance and be transferred to hospital. Because of the time-critical nature and increased potential for cardiac arrest in these patients, ambulance services should respond as a medical emergency. All ambulances responding to patients with chest pain should be equipped with a defibrillator. When a patient experiencing chest discomfort calls his or her GP, an ambulance should also be called immediately and the patient instructed to take aspirin if available. In rural and remote centres, it may be more expedient for the patient to

be taken by private transport to the nearest healthcare facility. Local doctors in these centres should discuss an appropriate "action plan" with their patients to deal with these emergencies.

The prehospital management by ambulance services for patients with chest pain of presumed cardiac origin should include rest and reassurance, oxygen, monitoring vital signs and cardiac rhythm, aspirin, nitrates, and analgesia.

High and intermediate risk patients should be transferred to a hospital; low risk patients may be treated medically and referred for non-urgent cardiac assessment (Box 6). However, depending on the expertise and assessment by the medical practitioner or other healthcare professional who first evaluates the patient in the community environment, many patients will need to be assessed in a hospital, irrespective of this classification. The imperatives in management are to prevent out-of-hospital cardiac arrest and to avoid a delay in application of a reperfusion strategy for patients with acute STEMI (Box 6). A definitive positive diagnosis should not be sought at the expense of a delay in transfer. Nor should the possibility of non-cardiac pain prevent urgent triage when high-risk features are present.

Acute hospital assessment and triage

Patients who are admitted to the emergency department with chest pain or discomfort should be treated as emergencies and should be regarded as qualifying for the Australasian College for Emergency Medicine triage category 2. An ECG should be completed within five minutes of arrival and reviewed immediately by a medical officer, and a careful history and physical examination completed within 10 minutes of arrival.

A normal ECG is found initially in up to 50% of patients with acute coronary syndromes and can not be used to exclude the diagnosis.[147-149] In one study, patients who were diagnosed with definite or probable unstable angina on clinical history alone had myocardial ischaemia proven in 95%, and, in patients with a normal ECG, myocardial ischaemia was still confirmed in 89%.[147] ST segment elevation is a marker of jeopardised myocardium and signifies a medical emergency. Patients with ST segment elevation (without response to sublingual nitrates) or left bundle branch block should be considered for an emergency reperfusion strategy (thrombolytic therapy or PCI) (E1). Where available, previously recorded ECGs should be used for comparison.

Always consider other diagnoses such as pulmonary embolism (especially in patients with associated syncope and precordial ST depression), aortic dissection, and pericarditis, possibly with tamponade and pneumothorax. Consider also secondary causes of angina, including arrhythmias, anaemia, hyperthyroidism, aortic stenosis and hypertrophic cardiomyopathy. In some patients, critical aortic stenosis may be associated with only a soft systolic murmur.

Management of patients initially assessed as being at low risk

Patients who can be definitely classified as low risk can be managed in an outpatient setting. These patients should be referred for semi-urgent cardiology assessment, preferably within two weeks. However, if there is uncertainty regarding the risk category, patients should be immediately transferred to an acute care setting.

Aspirin should be administered to all patients with unstable angina (its use reduces the risk of further events by 50%) (E1). If there is a contraindication to aspirin, clopidogrel should be considered. Patients should also be provided with buccal nitroglycerine (E4) and instructed in its use. β-Blockers should also be commenced, unless contraindicated (E1). If β-blockers are contraindicated, and if there is no evidence of heart failure or heart block, a heart-rate-slowing calcium channel blocker (diltiazem or verapamil) may be used (E2).

Education about angina and myocardial infarction should be provided, and patients instructed to contact the ambulance service directly in the event of discomfort not relieved by nitroglycerine and lasting longer than 10 minutes. These patients are at low risk of short-term infarction, but are at increased risk of further cardiovascular events in the medium to long term. Consequently, reversible risk factors (eg, cholesterol level, hypertension, diabetes) need to be actively managed.

Management of intermediate risk patients

Intermediate risk patients require observation for at least 6–8 hours (E2). During or after this period, they may be reclassified into low or high risk categories, on the basis of the development of further pain, ST depression of 0.5 mm or more (12 lead ECG or continuous ST segment monitoring), evolution of T wave inversion in multiple leads, positive serum markers (especially troponin) obtained at least six hours after presentation, and the results of exercise stress testing (Box 2). Comparisons with earlier ECGs should be performed where these are available, and significant changes indicate a high-risk classification.

Management of high risk patients

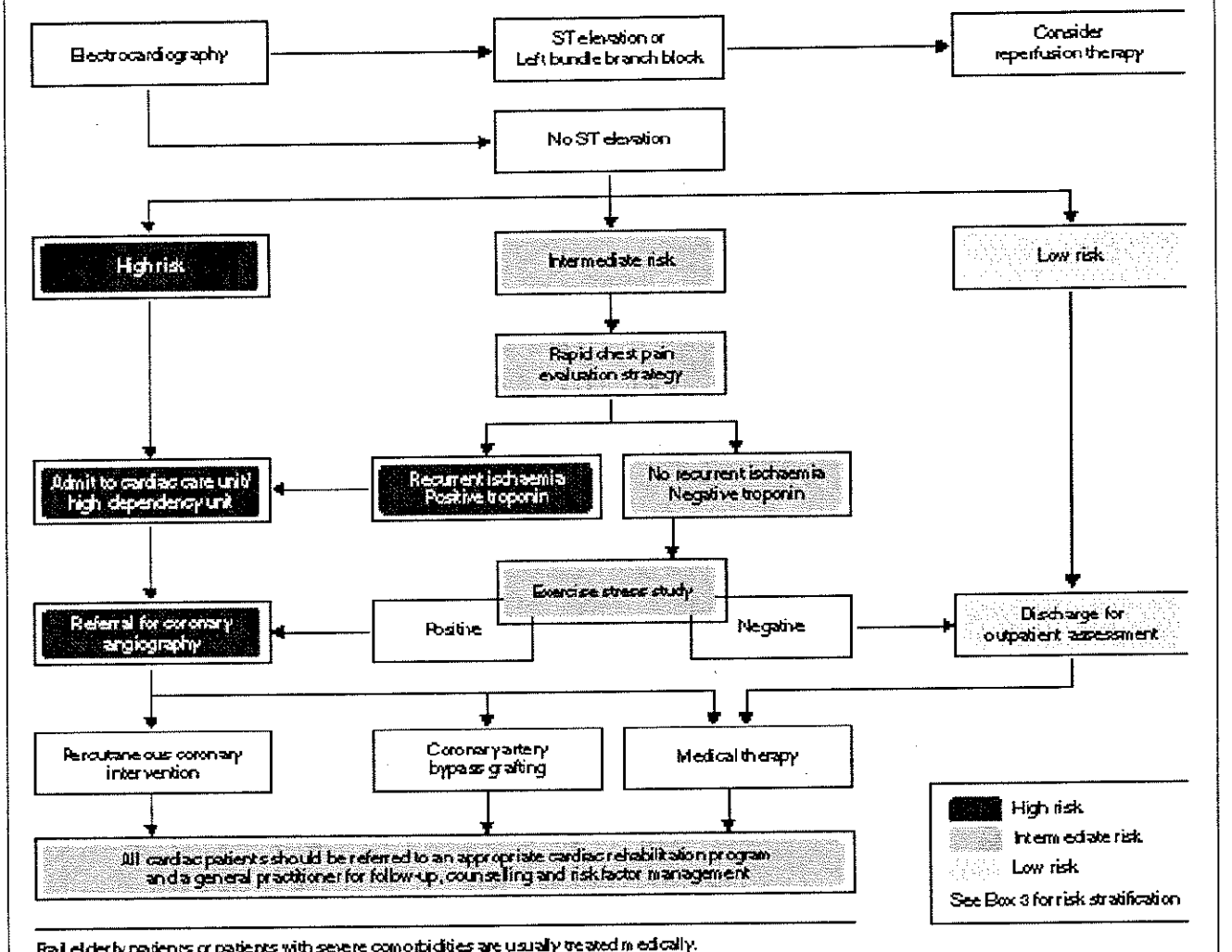
Intensive medical management

Patients with prolonged or rest angina should be treated with sublingual nitroglycerine, aspirin and supplemental oxygen. Ongoing pain should be treated with intravenous nitroglycerine and intravenous or oral β-blockers titrated to heart rate and blood pressure (E3).

Patients with any high-risk features, especially ST depression (0.5 mm or more) or elevated serum troponin levels, should be treated with LMW heparin[24] (E1) or tirofiban and heparin[121] (E1). Patients in cardiogenic shock should be considered for intravenous dopamine, and a very early invasive strategy, including intra-aortic balloon counterpulsation (E2).[150,151] This strategy should also be considered for patients with severe widespread ST depression (which suggests critical left main or three vessel coronary artery disease) and ongoing evidence of ischaemia despite maximal medical therapy. In these patients, intravenous heparin and tirofiban is suggested before emergency coronary angiography (E3).

In addition to treatment with aspirin and β-blockers,

6: Recommended management of a patient presenting with chest pain or discomfort



Frail elderly patients or patients with severe comorbidities are usually treated medically.

patients who develop an elevated serum cardiac troponin level should be treated with LMW heparin for at least 3–4 days (E1). Refractory angina may be defined as the recurrence of ischaemia after the commencement of optimal treatment with aspirin, LMW heparin and β-blockers. Refractory angina, particularly dynamic ECG changes (ST depression or transient ST elevation), is considered an indication for a change to intravenous tirofiban with heparin (E1). In these patients, referral for invasive investigations is also recommended, usually after a period of stabilisation on medical therapy, if possible.

Tirofiban and heparin are particularly beneficial in patients for whom an invasive strategy is planned (E2), and may be useful in facilitating the safe transfer of high-risk isolated and rural patients for invasive management. They may also be beneficial in patients who are unsuitable or unwilling to undergo invasive therapy.

Patients who develop acute STEMI while taking intravenous heparin and tirofiban should be considered for either direct PCI or half-dose thrombolytic therapy with alteplase, reteplase or TNK, but not streptokinase (E4).

Amlodipine or long-acting nifedipine may be added to β-blockers,[152] and nitrate therapy increased to maximally tolerated doses. Oral nicorandil added to standard therapy has been shown to reduce transient myocardial ischaemia and tachyarrhythmias.[85] Perhexilene should also be considered. Nocturnal pain can often be controlled by switching oral or cutaneous long-acting nitrates from a morning to an evening dosing schedule.

Early invasive approach

It was hoped that intensive medical therapy of unstable angina with antiplatelet and antithrombin therapy might "passivate" the coronary plaque. However, results have been disappointing, with a 6–9-month failure rate of about 12%

of death or myocardial infarction and 40% of ischaemia-driven revascularisation.[4] Therefore, it appears to be appropriate to consider an early strategy of direct intervention in patients with high-risk features. However, the complementary use of aggressive medical and invasive approaches should be considered in all patients with high-risk features (ongoing ischaemia and positive serum markers). Early coronary angiography and revascularisation with either PCI or coronary artery bypass surgery is associated with significant and sustained reductions in death, infarction, recurrent angina and readmission to hospital.[4] These benefits are most apparent in patients with high-risk features.

PCI and adjunctive medical therapy

Patients undergoing PCI or stenting should be considered for concomitant administration of intravenous glycoprotein IIb/IIIa receptor antagonist therapy (E1). From a practical point of view, patients already taking intravenous tirofiban before PCI may be continued on this treatment for a further 12–24 hours (E2), whereas patients undergoing PCI without having received tirofiban should be considered for intravenous abciximab. Patients undergoing stent implantation are also treated with additional oral antiplatelet therapy: clopidogrel for 2–4 weeks[141,142] and aspirin long term (E2). In most cases, patients having PCI even after having unstable angina can return to light activities in a few days and full activities at one month.

Long term management after control of myocardial ischaemia

All patients with unstable angina, particularly those with documented coronary disease (even minor lesions)[145] should be considered for treatment with lipid-lowering therapy if the total cholesterol level is 4 mmol/L or more. In the 4S, CARE and LIPID studies, lipid lowering with simvastatin and pravastatin improved outcomes in patients following myocardial infarction[153-155] (E1). The LIPID study included patients with previous unstable angina (3–36 months previously). Benefits of pravastatin were the same as in patients following myocardial infarction. The LIPID study also included patients with average cholesterol levels in the range of 4.0–7.0 mmol/L, following an eight-week run-in period during which dietary advice was given. Statins also improve endothelial function in diseased coronary arteries, but their role in the early (within three months) treatment of unstable angina is unproven and is currently being evaluated in several studies.

In a recent large study,[156] patients older than 55 years with evidence of vascular disease or diabetes plus one other cardiac risk factor were randomised to 10 mg of the angiotensin-converting enzyme (ACE) inhibitor ramipril or to placebo for a mean of five years. Ramipril reduced cardiac death (6.1% v. 8.1%; relative risk, 0.74; $P<0.001$), myocardial infarction (9.9% v. 12.3%; relative risk, 0.80; $P<0.001$), stroke (3.4% v. 4.9%; relative risk, 0.68; $P<0.001$), death from any cause (10.4% v. 12.2%; relative risk, 0.84; $P=0.005$), and revascularisation procedures (16.3% v. 18.8%; relative risk, 0.85; $P<0.001$). These benefits are being assessed in two further trials, but, at present, ACE inhibitors should be considered in patients with vascular disease and diabetics, particularly if hypertension is present.

Obesity and diabetes should be controlled, smoking should be proscribed, and, once ischaemia is controlled, a regular exercise program should be instituted. All patients with a diagnosis of unstable angina or myocardial infarction should be referred to, and participate in, an appropriate cardiac rehabilitation and prevention program.[157] Meta-analyses have shown that coordinated cardiac rehabilitation programs improve functional health outcomes, reduce recurrent coronary events, and may result in reduced early mortality.[158,159]

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Consultation Cover Sheet
20.9.04

File Note

040036

Consumer: Mrs [redacted] (DEC'D) Provider: [redacted] Assessment Extension

Encryption Key:
Date Composed: 31/08/2004 11:47 AM Composed By: Karen Harbus/HRC

Body Text:

Given in confidence: 5519 8211. I called Dr [redacted] (Cardiology Registrar) as he had given earlier indep. advice in relation to this matter. He said he could recall the case quite well. I advised him that I had written to P again to request who made the misdiagnosis and how, and had received a response which named the doctor and explained that he worked in both the public and private sectors and that the private sector used a "portable card reader method" to measure cardiac troponins whereas the public hospital used a Roche Elecsys 1010 analyser. The adviser commented that both methods give a "normal/abnormal" reading so this should not really have been an issue for the doctor and said that the results have "a reference range beside them". He stated that it was possible that the doctor was used to looking at "one set of numbers" and this may be how the error occurred. I outlined the contents of the further letter from P and he said he did not think it would be "productive" to look further into the matter. He stated that P had admitted to systems errors and said they were making changes as a result of this i.e. the private sector had purchased a tropinin machine which matched theirs. He said that P acknowledged they had deviated from the state-wide guidelines. I advised him that C wanted to see the doctor de-registered and he commented that P could not "defend the issue" and the man may be able to seek compensation through the legal system. I advised him that the man did not want compensation and he commented that he could understand that C "wanted justice done". The adviser said that maybe C could go back to the District and say he wasn't happy with their explanations and changes. Thanked him for his assistance.

Health Rights Commission

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FACSIMILE COVER SHEET

TO: Dr Paul Garrahy

ADDRESS:

PHONE: 3240 2381

FAX: **3240 7630**

FROM: Karen Harbus

PHONE: 3234 0258

TOTAL NUMBER OF PAGES (including this sheet): 4

DATE: 08/09/04 **TIME:** 11.15 a.m.

COMMENTS:

Private & Confidential

Dear Dr Garrahy

Thank you for your thoughtful and considered comments in relation to this matter. Please find enclosed a File Note which I hope accurately reflects our discussion. Please do not hesitate to call me with any changes you may wish to make.

Kind regards

Karen Harbus

IF YOU DO NOT RECEIVE ALL PAGES, PLEASE ADVISE IMMEDIATELY! 0407

Given in Confidence. Do not release name of adviser. Dr Garrahy returned my call. I advised him that I was seeking his informal independent advice about a complaint where a 68 y.o. woman who had a history of heart problems, began to suffer ongoing chest pain and was taken by ambulance to a public hospital in a rural area in Queensland in the early hours of 01/12/03. I informed the adviser that the woman was diagnosed with "*unstable angina*" and given aspirin, lipitor and lasix in addition to her regular medication regime. I explained that a blood test was taken, results "*checked*" and the hospital began to make arrangements to transfer her to a pre-arranged stress (sestamibi) test booked for 9.30 a.m. on 02/12/03 at a private nuclear medicine unit. I informed the adviser that in its response to the HRC, the provider acknowledged that the woman had raised troponin levels which indicated she had suffered a recent heart event, was misdiagnosed with "*unstable angina*" and discharged whereas they said they should have diagnosed her with "*acute coronary syndrome*" and kept her in for observation. I informed the adviser that the woman died in the early hours of 03/12/03 from 1.(a) cardiac arrest; (b) myocardial infarction; and (c) ischaemic heart disease. I explained that the widower believed that if his wife had been diagnosed and treated appropriately, she would have been given appropriate medication and still be alive. I also informed the adviser that the man was concerned that a nurse at the public hospital had not acted in a timely manner in transferring her to the stress test appointment at the private facility as he believed that as the provider had misdiagnosed the woman, the stress test would have correctly diagnosed her and he "*could have flown her down to Brisbane in a private plane for an urgent operation*". I explained to the adviser that the man wanted the doctor and the nurse sacked/de-registered.

The adviser agreed with previous independent advice obtained that (a) the stress test was contraindicated and (b) it would only have confirmed what the hospital should have already known and he further said that, in any event, given the time frame of the woman's death, by the time the stress test had been performed, diagnosis made and arrangements made to transport the woman to a larger public hospital for surgery, it would have been "*too late*", as she died in the early hours of 03/12/03. I explained to the adviser that after its initial response, the HRC wrote back to the provider to ask who had made the misdiagnosis and how. I read him excerpts from the provider's subsequent letter as follows:

[The doctor, FRACP, general physician, internal medicine] was the attending specialist medical practitioner to [the woman] during her last admission to hospital. The doctor is a Visiting Medical Officer in General Medicine, who also practices in the private sector. He acknowledges that he didn't appreciate the significance of [the woman's] raised troponin result due to different measurement systems being used in the public and private health sectors in [the area] leading to potential discrepancy between troponin values for the same patient. This discrepancy contributed to the doctor attaching limited significance to such values at the public hospital.

The doctor was using a private sector pathology laboratory which measured cardiac troponins using a portable card reader method. Negative values are recorded as less than 0.05 mg/L and positive values are recorded as greater than 0.1 mg/L. There is a grey or uncertain zone between these two readings. The value is also operator dependent. At the public hospital, troponins are measured using a Roche Elecsys 1010 analyser, which is internally validated daily and externally checked under the Royal College of Pathologists Australasia Quality Program every two weeks. Negative values are recorded as less than

0.03 mg/L while positive values are equal to or greater than 0.03 mg/L. This level is standard across all Queensland Health pathology laboratories with the result electronically recorded and distributed. The public sector method is more sensitive than the private sector method.

The doctor's confusion led to a strong support of the private sector method and belief that the public sector method was inaccurate and possibly inferior. Consequently the doctor also utilised measurement of creatinine kinase (CK) in patients with acute coronary syndrome as happened in [the woman's] case. The doctor asserts that he attempted to reduce his concern through inquiries with the [larger area] based management of the public hospital's pathology laboratory, but didn't obtain a satisfactory response. After [the woman's] death, he again made inquiries and was provided with the above information. At this time he realised his mistaken belief in the private sector's methodology for troponin measurement. Since this time, he has undertaken further study, attended a cardiology conference and sought ongoing advice from his cardiology peers. He states that he understands the significance of troponin values, particularly in risk stratification of patients with coronary artery disease. It should be noted that the private pathology provider in [the area] has recently installed the same troponin analyser as installed in the public hospital in order to improve sensitivity of testing, reduce unnecessary duplication and avoid discrepancy in values.

The adviser stated that in his opinion a good question would be: "*Was it an error to have diagnosed the woman with unstable angina?*". He said no and explained that the term "*acute coronary syndrome*" was a very broad umbrella term to cover lots of coronary conditions and as the hospital stated "*the woman was stable throughout her admission*", the hospital was not incorrect to have diagnosed her with unstable angina. He explained that the health care system had been dealing with subtle changes of differing nomenclature for a few years now. He stated that the error made by the hospital was to discharge her too soon. He stated that the blood tests certainly flagged that she was at a higher risk of suffering from a heart related problem and this had indeed occurred. The adviser stated, "*So the error was not so much in the diagnosis as in failing to recognise that her troponin levels mandated that she receive more intensive therapy rather than be discharged*". The adviser noted that the hospital had undertaken procedural changes and that the man was given a sincere apology.

In relation to the outcome that the man was seeking, the adviser stated that he "*absolutely disagreed*" with this as, firstly, the hospital was not in a major metropolitan area, and by sacking a doctor who had made an error, one would be depriving that locality of a specialist doctor. He said he noted from the provider's response that the doctor had undertaken further study, attended a cardiology conference and liaised with cardiology peers and was sorry for what had happened. He explained that secondly, another important issue that had to be taken into account was that some laboratories track troponin 'T' and some laboratories track troponin 'I' and the testing methodology for testing the normal range for each of these is different. He said that by way of example, a doctor may look at a reading of 0.04 mg/L in reference to what he recognised as normal but this would depend on which type of troponin the doctor was testing for (i.e. T or I types). He said that in his experience private laboratories tested for the I type whereas public hospitals tended to track for the T type.

In summing up, the independent adviser stated that an honest mistake had been made and as it appeared to be a "*one off*", he did not see the error as being an issue of a breach of professional standards but rather one of misadventure. He stated that he could understand the

man's grief and anger but "*to deprive a community of a specialist who was willing to work in both the private and public arenas*" was not the answer. He said that about 85% of doctors preferred to work in the private sector.

Thanked him and agreed to fax him a copy of the File Note for clarification.

Management of non-ST elevation chest pain/discomfort

ECG Non-ST elevation

Within 10 minutes of arrival:
Brief history
Examination
ECG

Risk stratify

High risk features
Prolonged (>10 mins) chest pain/discomfort
ST elevation or depression (≥ 0.5 mm) or deep T wave inversion in 3 or more leads
Elevated serum markers (troponin I or T)
Associated syncope
Associated heart failure, mitral regurgitation or gallop rhythm
Associated haemodynamic instability
Diabetes

Intermediate risk features
Prolonged but resolved chest pain/discomfort
Nocturnal pain
New onset class III* or IV* chest pain in the past 2 weeks
Age > 65 yrs
History of MI or revascularisation
ECG normal or pathologic Q waves
No significant (< 0.5 mm) ST deviation or minor T wave inversion in less than 3 leads

Low risk features
Increased angina frequency or severity
Angina provoked at a lower threshold
New onset angina > 2 weeks before presentation
Normal ECG and negative troponin
No high or intermediate risk features

Admit to Coronary Care or other High Dependency Unit

Recurrent ischaemia
Elevated troponin

No recurrent ischaemia
Troponin not elevated

Refer for angiography

Positive

Stress test:
Exercise
Echocardiography
Thallium scintigraphy

Negative

Medical therapy

Discharge for outpatient assessment

PCI or CABG

All cardiac patients should be referred to cardiac rehabilitation and a general practitioner for follow-up, counselling and secondary prevention management

*Grade III: Marked limitation of ordinary physical activity
Grade IV: Inability to carry out physical activity without discomfort.
Grade of angina by Canadian Cardiovascular Society. Campeau L. Grading of angina pectoris. Circulation 1976; 54: 522–523.

PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft

Adapted from Management of Unstable Angina Guidelines - 2000. NHF/CSANZ. MJA 2000; 173 (supplement): S95–S98. Available at www.heartfoundation.com.au Printed with the support of an unrestricted educational grant from Sanofi-Synthelabo and Merck Sharp & Dohme. For general heart health information contact the Heart Foundation's national telephone information service, Heartline, on 1300 36 27 87 for the cost of a local telephone call or visit the Foundation's website www.heartfoundation.com.au Published by IntraMed Educational Group, Level 15, 65 Berry Street, North Sydney, NSW 2060 (a division of Sudler & Hennessey Australia Pty Limited) ABN 42 000 695 049.

Heart Foundation

Aboriginal and Torres Strait Islander
Acute Coronary Syndromes
Blood Pressure
General
Heart Failure
Lipid Management
Nutrition
Physical Activity
Psychological and Social
Publications
Rehabilitation
Tobacco

ACUTE CORONARY SYNDROMES

The Heart Foundation produces a comprehensive range of independent, evidence-based cardiovasc information.

These policies, information sheets, guidelines and other professional resources are developed by th with generous input from a network of leading cardiovascular health experts who voluntarily serve committees. The information is subject to extensive review prior to publishing and is also professio the most effective communication of the subject matter.

Please refer to the table below for the Heart Foundation's latest acute coronary syndrome clinical g

Unstable Angina Guidelines 2000
(PDF format-505K)
These Guidelines are supported by the Addenda below:

Unstable Angina Guidelines Addenda (Aug 2001, Oct 2001, July 2002)
(PDF format-93K)

Management of Non-ST Elevation Chest Pain/Discomfort Flow Chart (August 2002)
(PDF format-89K)

Reperfusion Therapy for Acute Myoca Guidelines (2002)
(PDF format-40K)
Supported by Reperfusion Manageme listed below:

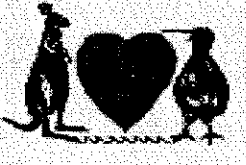
Reperfusion Management Flow Chart
(PDF format-67K)

0402

MJA

Heart Foundation

The National Heart Foundation of Australia



The Cardiac Society of Australia and New Zealand

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Management of Unstable Angina Guidelines 2000 – Addenda

These addenda accompany the *Management of Unstable Angina Guidelines 2000.*

National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Management of Unstable Angina Guidelines – 2000. Med J Aust 2000; 173 (Suppl.): S65-S88.

ADDENDUM AUGUST 2001

The Myocardial Ischaemia Reduction with Aggressive Cholesterol Lowering (MIRACL) study is the largest of the reported randomised control trials which have examined the effects of cholesterol lowering early after acute coronary syndromes.

The MIRACL study included 3086 adults aged 18 years or older with unstable angina or non-ST elevation myocardial infarction who were randomly assigned to receive atorvastatin (80mg daily) or placebo commencing 24 to 96 hours after a hospital admission.

Over 16 weeks, there was a significant reduction in the composite primary end-point of death, non-fatal acute myocardial infarction, resuscitated cardiac arrest or recurrent symptomatic myocardial ischaemia with objective evidence and requiring emergency rehospitalisation; from 17.4% in the placebo group (269 patients) to 14.8% in the atorvastatin group (228 patients) (RR 0.84, 95% CI 0.70-1.00, p=0.048).

Of the individual components of the composite end-point, only the reduction in symptomatic ischaemia was significant (6.2% versus 8.4%, RR 0.74, 95% CI 0.57-0.59, p=0.02). There was no change in the rate of revascularisation. Total stroke was also reduced in those assigned atorvastatin (1.6% versus 0.8%, RR 0.50, 95% CI 0.26-0.99). The extent of LDL reduction was not correlated with the reduction in the primary end-point.

Recommendation

Commencement with statin therapy is recommended during hospital admission with unstable angina or non-ST elevation myocardial. E2

Reference

1. Schwartz GG, Olsson AG, Ezekowitz MD, et al. Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Study Investigators. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA* 2001;285:1711-1718.

INFORMATION

0400

ADDENDUM OCTOBER 2001

A randomised trial[1] of clopidogrel or placebo in addition to aspirin was performed in 12,562 patients with non-ST elevation acute coronary syndrome (CURE). Clopidogrel use led to a significant reduction in the composite primary end-point of cardiovascular death, myocardial infarction or stroke from 11.4% to 9.3% (RR 0.80, CI 0.72-0.90, p<0.001). This was primarily due to a reduction in myocardial infarction from 6.7% to 5.2% (RR 0.77, CI 0.67-0.89) and particularly a reduction in Q wave MI from 3.1% to 1.9% (RR 0.60, CI 0.48-0.76). Refractory ischemia during admission was also reduced and led to a lower requirement for glycoprotein IIb/IIIa receptor inhibitors from 7.2% to 5.9% (RR 0.82, CI 0.72-0.93) and for revascularisation (22.7% to 20.8%, RR 0.92, p=0.03). These benefits were at a cost of increased major bleeding from 2.7% to 3.7% (RR 1.38, CI 1.13-1.67) predominantly from the gastrointestinal tract. There was a trend to excess bleeding after coronary bypass surgery only in those patients who were still taking clopidogrel within 5 days of their surgery.

A randomised trial[2] of an early (4–48 hours) interventional strategy compared with a conservative strategy was performed in 2220 patients with high risk ACS (TACTICS). All patients had initial therapy with tirofiban/heparin. At 6 months there was a significant reduction in the primary end-point (death/MI/recurrent hospitalisation) from 19.4% to 15.4% (RR 0.78, CI 0.62-0.97). Death and MI at 6 months were also reduced from 9.5% to 7.3% (RR 0.74, CI 0.54-1.00).

Considered together, the CURE and TACTICS results raise questions regarding the optimal combination of treatments for therapy prior to planned PCI (*upstream therapy*) of non-ST elevation ACS. Combined treatment of aspirin, clopidogrel and IIb/IIIa receptor antagonists are commonly used at the time of PCI or subsequent to this (*downstream therapy*), and are generally well tolerated. Non-randomised post-hoc studies of upstream therapy with ticlopidine combined with downstream abciximab[3] or pre-treatment with clopidogrel and downstream abciximab or tirofiban[4] have demonstrated the safety and potential benefits of the combination. An observational study[5] of that subgroup of patients in the CURE study who underwent percutaneous coronary intervention (PCI) demonstrated that those patients pre-treated with clopidogrel had a significant reduction in cardiovascular death and MI at 8 months follow-up (8.8% vs. 12.6%, RR 0.69, CI 0.54-0.87). There was lower utilisation of IIb/IIIa receptor antagonists in the clopidogrel group. Bleeding was not increased in the clopidogrel treated group.

Recommendations

1. Early treatment with aspirin, clopidogrel and tirofiban/heparin should be considered in patients with non-ST elevation ACS and high-risk features (ST depression or elevated serum markers). E2
   - The use of clopidogrel should be avoided in patients likely to require emergency coronary bypass surgery (patients with severe widespread ST depression or hemodynamic instability). E2
   - If possible, clopidogrel should be discontinued 5 days prior to coronary bypass surgery. E2
2. An early invasive strategy (4–48 hours) is recommended in patients without ST elevation who have high-risk features. E2

References

1. CURE Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001; 345:494-502.
2. Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001; 344:1879-1887.
3. Steinhubl SR, Ellis SG, Wolski K, Lincoff AM, Topol EJ Ticlopidine pretreatment before coronary

stenting is associated with sustained decrease in adverse cardiac events: data from the Evaluation of Platelet IIb/IIIa Inhibitor for Stenting (EPISTENT) Trial. Circulation 2001; 103:1403-1409.
4. Topol EJ, Moliterno DJ, Herrmann HC, Powers ER, Grines CL, Cohen DJ, et al. Comparison of two platelet glycoprotein IIb/IIIa inhibitors, tirofiban and abciximab, for the prevention of ischemic events with percutaneous coronary revascularization. N Engl J Med 2001; 344:1888-1894.
5. Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, Natarajan MK, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001; 358:527-533.

File Note

040036

Consumer: Mrs Doreen CONNELLY (DEC'D) Provider: Bundaberg Base Hospital - Mr Peter LECK — Assessment Extension

Encryption Key:
Date Composed: 07/09/2004 02:16 PM Composed By: Karen Harbus/HRC

Body Text:

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The adviser agreed with previous independent advice obtained that (a) the stress test was contraindicated and (b) it would only have confirmed what the hospital should have already known and he further said that, in any event, given the time frame of the woman's death, by the time the stress test had been performed, diagnosis made and arrangements made to transport the woman to a larger public hospital for surgery, it would have been "*too late*", as she died in the early hours of 03/12/03. I explained to the adviser that after its initial response, the HRC wrote back to the provider to ask who had made the misdiagnosis and how. I read him excerpts from the provider's subsequent letter as follows:

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the laboratory was testing for (i.e. T or I types). He said some laboratories tested for the I type of Troponin whereas some track for the T type. He said that by of example, Sullivan & Niccolaides in Brisbane track Troponin T and the PA Hospital tracks for Troponin I. He said he was informed by his hospital's laboratory that Logan Hospital tracks Troponin T. He said the point to make here is that the tracking of different types of Troponin was not uniform across Queensland, and stressed that there was no uniformity between the public and private sectors nor between the public to public system.

In summing up, the independent adviser stated that it appeared an "*honest mistake*" had been made and as it appeared to be a "*one off*", he did not see the error as being an issue of a breach of professional standards by the doctor involved but rather one of "*a simple error*". He stated that he could understand the man's grief and anger but "*to deprive a community of a specialist who was willing to work in both the private and public arenas*" was not the answer. He said that about 85% of doctors preferred to work in the private sector.

Thanked him and agreed to fax him a copy of the File Note for clarification.