



Non ST-elevation acute coronary syndromes: New Zealand management guidelines

Non ST-Elevation Acute Coronary Syndrome Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand

Glossary

ACC	American College of Cardiology
ACE	Angiotensin converting enzyme
ACS	Acute coronary syndromes
AHA	American Heart Association
BNP	Brain natriuretic peptide
CAD	Coronary artery disease
CABG	Coronary artery bypass grafting
CAPRIE	Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events
CREDO	Clopidogrel for the Reduction of Events During Observation
CURE	Clopidogrel in Unstable Angina to Prevent Recurrent Events
ECG	Electrocardiogram
ESC	European Society of Cardiology
FRISC-II	Fragmin and Fast Revascularisation During Instability in Coronary Artery Disease
hsCRP	High sensitivity C-reactive protein
HPS	Heart Protection Study
ICTUS	Invasive versus conservative treatment in unstable coronary syndromes
IHD	Ischaemic heart disease
ISAR	Intracoronary Stenting and Antithrombotic Regimen trials
LMWH	Low-molecular weight-heparin
LV	Left ventricular
MI	Myocardial infarction
NSTEACS	Non ST-elevation acute coronary syndromes
NT-proBNP	N-terminal pro-B-type natriuretic peptide
PCI	Percutaneous coronary intervention
RITA	Randomised Intervention Trial of Unstable Angina (RITA-3)
SYNERGY	Superior Yield of the New Strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa Inhibitors (SYNERGY) trial
TACTICS	Treat Angina With Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction
TNI	Troponin I
TNT	Troponin T
UFH	Unfractionated heparin

Purpose

These guidelines apply to the management of patients with non-ST elevation acute coronary syndromes (NSTEACS). The purpose of these guidelines is to provide a summary of the most up to date New Zealand and overseas evidence and to make recommendations based on the evidence that will lead to the best practice for patients with NSTEACS in New Zealand. The guideline is aimed at all health providers who care for patients with NSTEACS.

These guidelines are based on the Cardiac Society of Australia and New Zealand (2000) Guidelines on the Management of Unstable Angina¹ as well as a meeting held in Queenstown in May 2001, to which doctors from every major New Zealand hospital, recommended by the Head of Department, were invited to attend. The aim of

this meeting was to discuss the management of patients with NSTEMACS, to define guidelines and to develop a New Zealand Audit. The meeting was initiated by the Cardiac Society of New Zealand with a Grant from Roche Pharmaceuticals. The choice of content of the meeting and the organisation was completely independent.

For a detailed description of the levels of evidence cited in this guideline please see Appendix 2. These guidelines are intended for best clinical practice. Where physicians or hospitals are not able to meet the guidelines it is important that there is documentation that there have been communications between clinicians and managers clearly defining the clinical implications of any resource shortages.

Early risk stratification

Introduction

Risk assessment of patients with NSTEMACS plays an important role in predicting patient prognosis. This also enhances the cost-effectiveness of patient care by enabling evidence-based treatments including antiplatelet, antithrombotic, and revascularisation therapies to be targeted at the patients who are most likely to benefit from their use. The clinical history, examination findings, electrocardiographic changes, and blood levels of cardiac marker and troponins are all critical factors in determining risk.²⁻⁹

Risk assessment should be considered a dynamic process and patients should be assessed when first seen, after several hours, 6–8 hours, 24 hours and prior to discharge. The presence of continuing symptoms and response to therapy are important in risk assessment. Refractory ischaemia or evidence of ongoing (including silent) ischaemia on electrocardiogram (ECG) monitoring should mandate early angiography. Risk assessment may be enhanced by determining the number and severity of flow-limiting coronary artery stenoses and the presence or absence of left ventricular impairment. Risk assessment in patients with NSTEMACS allows prediction of the low, intermediate or high risk of death or nonfatal myocardial infarction (MI) and particularly the risk of events occurring in the short term.

The important features contributing to risk assessment are shown in Table 1. Various risk scores can also be used—e.g. The Thrombolysis In Myocardial Infarction TIMI risk score (Table 2).¹⁰

Measurement of markers of myocardial necrosis, inflammation, and natriuretic peptides

Cardiac markers

In patients presenting with symptoms within the last 24 hours suggestive of acute myocardial ischaemia cardiac troponins T or I have the best sensitivity and specificity for the diagnosis of MI and these are the markers of choice.^{11,12} In both short- and long-term follow-up studies, the magnitude of troponin elevations has correlated consistently with the risk of death and the composite risk of death or nonfatal MI^{2,8,13,14} and troponin levels have been shown to be more powerful prognostic indicators than CKMB levels (Table 3).^{13,15}

Table 1. Short-term risk of death or nonfatal MI in patients with unstable angina³

Feature	High Risk (At least 1 of the following features must be present)	Intermediate Risk (No high-risk features but must have 1 of the following features)
History	Accelerating tempo of ischaemic symptoms in preceding 48h	Prior MI, peripheral or cerebrovascular disease, or CABG; prior aspirin use
Character of pain	Prolonged ongoing (>20 min) rest pain PCI last 6 months	Rest angina (<20 min or relieved with rest or sublingual nitroglycerine)
Clinical findings	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD. Pulmonary oedema, most likely related to ischaemia. New or worsening mitral regurgitation murmur S3 or new/worsening rales. Hypotension, bradycardia, tachycardia Age >75yrs Diabetes Associated syncope Associated haemodynamic instability (Systolic BP <90mmHg, cool peripheries, diaphoresis) Known poor LV function (EF <40%)	Age >65-75yrs
ECG findings	Angina at rest with transient ST-segment changes >0.05mV Bundle-branch block, new or presumed new Sustained ventricular tachycardia Deep T wave inversion (≥ 3 min in ≥ 3 leads)	T-wave inversions ≥0.2mV in 3 leads Pathological Q waves
Cardiac markers	Elevated troponins (eg, TnT ≥0.03µg/L)	

Table 2. Thrombolysis in myocardial infarction (TIMI) risk score¹⁰

Factor	Points
Age >65 years	1
>3 Risk Factors for IHD	1
Prior coronary stenosis >50%	1
>0.5mm ST deviation on ECG	1
>2 anginal events in prior 7 days	1
Aspirin use in prior 7 days	1
Elevated cardiac markers	1

Table 3. Serum markers for non-ST acute coronary syndromes

- Cardiac troponin T or I are considered the serum markers of choice.
- The presence in the serum of cardiac troponin T or I indicates myocyte necrosis.*
- The levels of cardiac troponins correlate with early risk of cardiac death and myocardial infarction.
- Measurements of cardiac troponin levels should be repeated after 6-8 hours, particularly if the baseline levels are normal.
- Myoglobin, heart fatty acid binding protein and CKMB (mass) are earlier markers of myocardial damage.
- Elevated cardiac troponin levels predict response to therapy with LMWHs, glycoprotein IIb/IIIa antagonists, and the benefit of an early invasive strategy.
- In patients with a recent (<14 days) MI, elevated troponins could be due to myocardial damage sustained in the initial MI. CK or CKMB is more useful in this setting to diagnose recurrent MI.

*See Table 4 for exceptions

Troponins may be the only markers required if utilised in a chest pain pathway with patients undergoing a 6-8 hour observation period.¹⁶ Point of care testing is recommended when hospital logistics cannot consistently deliver laboratory-assayed results within 1 hour.¹⁷

Troponins are very sensitive markers of myocyte necrosis, and elevated levels can occur in settings other than spontaneous myocardial ischaemia or percutaneous coronary intervention (PCI) (Table 4).⁵ Apart from acute coronary syndromes (ACS), the most frequent causes of elevated troponin levels are atrial or ventricular tachycardia (often with hypotension and an increased myocardial oxygen demand), pulmonary emboli with right ventricular infarction, and cardiac failure¹⁸ with myocardial necrosis due to neurohumoral changes and elevated left ventricular end-diastolic pressure. Other causes of elevated troponin levels include cardiac surgery, myocarditis, and renal failure.

The diagnostic criteria for MI for troponin T is a discrimination level of 0.03µg/L, there are different cutpoints for troponin I.¹⁹ The levels of troponins predict the benefits of therapy with low molecular weight heparins (LMWH),²⁰ glycoprotein IIb/IIIa antagonists,²¹ and of an early invasive/revascularisation strategy.²² The use of troponins to diagnose reinfarction is problematic in the 2 weeks after an initial MI as these markers have a long half-life (up to 14 days) and CKMB or CK should be measured in these circumstances.**D4**

Inflammatory markers

There has been extensive research into the roles of inflammation and inflammatory markers in NSTEMI. The levels of high sensitivity C-reactive protein (hsCRP), interleukin-6 and more recently CD-40 ligand (which has prothrombotic effects) have been shown to have independent prognostic information.²³ Elevated levels of other inflammatory markers such as adhesion molecules,²⁴ interleukin-7²⁵ and matrix-metalloproteinases (including pregnancy associated plasma protein A)²⁶ also have been observed in patients with NSTEMI. Conversely, levels of the anti-inflammatory cytokine, interleukin-10 have been shown to be reduced and patients with higher levels of interleukin-10 suffer fewer events during follow-up.²⁷ There have been no prospective trials of therapies aimed at modulating the levels of these markers. Neither the current ACC/AHA,³ ESC treatment guidelines for NSTEMI²⁸ or the guidelines of The Australian and New Zealand Cardiac Society¹ recommend the measurement of inflammatory marker levels. Nor does this guideline recommend measurement, but recognises that in the near future with further evidence inflammatory markers may have an important role in risk assessment and choice of therapy.

Natriuretic peptides

In observational studies of patients with NSTEMI, brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels have been shown to be independent prognostic factors for mortality and myocardial infarction. Elevation of BNP levels may be related to ischaemia causing myocardial stretch.²⁹⁻³¹ In the FRISC-II substudy NT-proBNP levels measured at admission predicted the benefit of revascularisation and added prognostic information to that obtained from clinical and ECG information and from markers of myocyte necrosis and

inflammation.³⁰ However in the TACTICS trial revascularisation did not provide more benefit for patients with elevated BNP levels (>80 ng/L) at admission.³² The results may relate to the enrolment of higher risk patients in FRISC-II and issues of statistical power. To enhance risk stratification and targeting of therapies, measurement of BNP or NT-proBNP levels may be considered but are not currently recommended.²⁹

Initial medical management

The recommended pathway of triage and indications for hospitalisation in patients with NSTEMACS is summarised in Figure 1. An ECG and bloods for troponins, full blood count and lipids should be obtained within 10 minutes of presentation. If a chest pain unit pathway is used patients should be observed and have repeat measurements of troponins at 6–8 hours. Some patients will develop elevated troponins up to 12 hours after symptom onset. Early discharge decisions can then be made based on clinical features, including the presence or absence of recurrence of ischaemia, troponin levels, electrocardiographic changes, and testing for inducible ischaemia as appropriate, usually with exercise testing. Table 5 summarises the recommended dosage regimens for various antiplatelet and antithrombotic therapies (for more details see Appendix 2). Where to manage patients is an important consideration. It is recommended that all high risk patients should be managed in a CCU or CCU step-down until further risk stratification shows them to be at lower risk or revascularisation is performed.

The very important role of nurses in the management of these patients is acknowledged and highly valued.

Analgesia

Sub-lingual nitroglycerine is recommended for symptoms of ischaemia.**D4** Morphine or omnipon together with an antiemetic should be used to relieve severe pain.**D4** Intravenous nitroglycerine can also achieve symptomatic relief and be used for blood pressure lowering.**D3**

Antiplatelet agents

Aspirin—Aspirin reduces progression to MI and cardiac mortality by about 50%³³ and all patients without contraindication should immediately receive aspirin 150–300mg, 1++A which should be chewed if enteric coated. Long-term, lower doses of 75–100mg in enteric coated formulations to maintain efficacy and to minimise bleeding risk should be given indefinitely.^{33,34}

Clopidogrel—The CURE trial³⁵ and the separately reported PCI-CURE³⁶ results provide important evidence for the use of clopidogrel in patients with NSTEMACS regardless of whether they are managed conservatively or invasively. In the CURE trial which randomised 12,562 patients (77% managed conservatively), clopidogrel reduced the incidence of death, non-fatal MI and stroke by 20% over an average 9-month follow-up period (9.3% with clopidogrel vs 11.5% with placebo, $P < 0.001$). There were also reductions in the rates of revascularisation, as well as need for thrombolytic therapy and intravenous glycoprotein IIb/IIIa inhibitors in the clopidogrel group.

Figure 1. Early triage of patients presenting with probable/possible ischaemic symptoms including chest discomfort

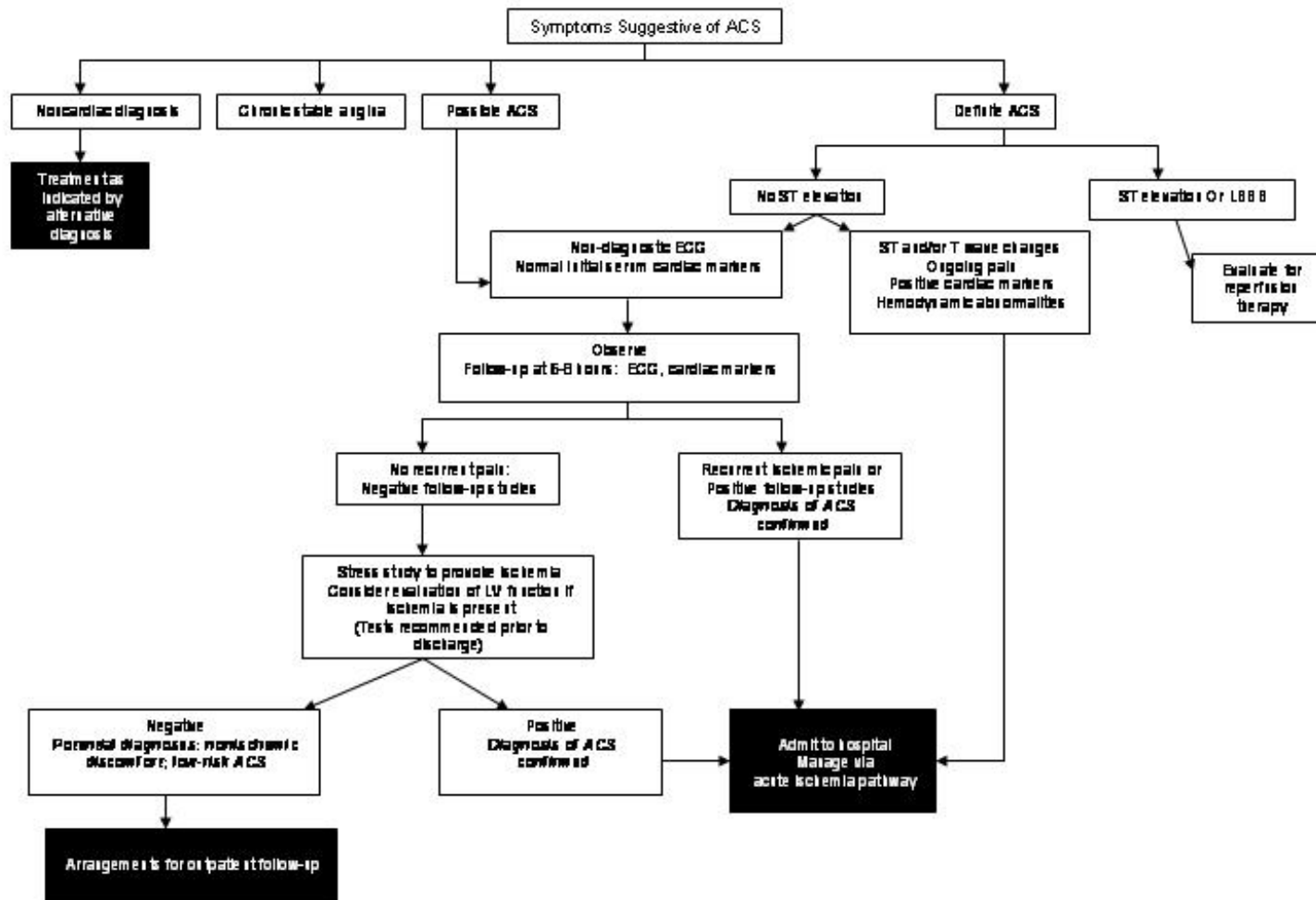


Table 4. Causes of elevated troponin levels in clinical settings other than ACS or PCI⁵

<p>Ischaemic causes other than plaque fissuring or rupture</p> <ul style="list-style-type: none"> • Coronary embolism (red cell or platelet thrombi, vegetation, atrial myxoma, calcification) • Coronary spasm • Coronary dissection • Aortic dissection • Transplant vasculopathy 	<p>Myopericarditis</p> <ul style="list-style-type: none"> • Rheumatic fever • Rheumatoid arthritis • Systemic vasculitis • Post-viral
<p>Cardiac surgery</p> <ul style="list-style-type: none"> • Left ventricular venting • Inadequate cardioplegia • Traumatic atrial cannulation • Manipulation of the heart • Ischaemia-related causes such as conduit or native vessel occlusion 	<p>Infiltrative diseases of the myocardium</p> <ul style="list-style-type: none"> • Amyloidosis • Sarcoidosis
<p>Miscellaneous</p> <ul style="list-style-type: none"> • Tachyarrhythmia • Hypertension • Congestive heart failure • Renal failure • Drug toxicity (e.g. adriamycin, 5-fluorouracil, etc) • Hypothyroidism • Pulmonary embolism with right ventricular infarction • Sepsis (including sepsis occurring with shock) • Transient ischaemic attack, stroke or subarachnoid haemorrhage • Pheochromocytoma • Rhabdomyolysis with myocyte necrosis 	<p>Traumatic</p> <ul style="list-style-type: none"> • Atrioventricular ablation • Defibrillation • Chest wall trauma

Table 5. Clinical use of antithrombotic therapies

Oral antiplatelet therapies	
Aspirin	Initial dose of 150-300mg nonenteric formulation followed by 75-150 mg/day of an enteric formulation
Clopidogrel (Plavix)	A loading dose of 4-8 tablets (300-600 mg) should be used when rapid onset of action is required, followed by 75 mg/day.
Heparins	
Heparin (UFH)	Bolus 60U/kg (maximum 4000 U) IV followed by infusion of 12U/kg/h (modified to achieve an aPTT of 50-75 seconds) with laboratory measurements and 60-85 with bedside measurements.
Enoxaparin (Lovenox)	1 mg/kg subcutaneously every 12 h; the first dose may be preceded by a 30 mg IV bolus.‡
Dalteparin (Fragmin)	120 IU/kg subcutaneously every 12 h (maximum 10,000 IU twice daily)
Glycoprotein IIb/IIIa antagonists	
Tirofiban (Aggrastat)	0.4 µg/kg/min for 30 minutes followed by infusion of 0.1 mcg/kg/h for 48 to 96 h* and for 12-24 hours post PCI
Eptifibatide (Integrilin)	180 mcg/kg bolus followed by infusion of 2.0 µg/kg/min for 72 to 96 h* and for 12.24 hours post PCI
Abx cimab (ReoPro)	0.25 mg/kg bolus followed by infusion of 0.125 mcg/kg/min (maximum 10 mcg/min) for 12 to 24 h post PCI. Abx cimab should not be used as upstream treatment unless coronary anatomy is known and the patient is scheduled for PCI

* Different dose regimens were tested in recent clinical trials before percutaneous interventions

‡ Adjustment required for age ≥75 years and renal dysfunction – see pharmacy guidelines.

There was an excess of major bleeding with clopidogrel (3.7% vs 2.7%, P=0.003) but life-threatening bleeding was not increased. In patients undergoing CABG within 5 days of receiving clopidogrel, there was an increase in major bleeding from 6.3% to 9.6%, p=0.05. This compares with 7 major events per 1 000 patients (cardiovascular death, MI or stroke) prevented within the first 24 hours with clopidogrel.

In the PCI-CURE trial with 2658 patients, pre-treatment with clopidogrel for 10 days prior to PCI reduced 30-day composite of death, non-fatal MI and urgent target vessel revascularisation by 30% after PCI (4.5% vs 6.4%, P=0.03).³⁶ Long-term administration of clopidogrel after PCI for 12 months was associated with a lower rate of cardiovascular death, MI, or any revascularisation (p=0.03), and of cardiovascular death or MI (p=0.047). Overall (including events before and after PCI) there was a 31% reduction cardiovascular death or MI (p=0.002). Long-term benefit of clopidogrel plus aspirin after PCI in patients with chronic stable angina was also shown in the CREDO trial.³⁷ At 1 year, the composite endpoint of death, myocardial infarction or stroke was reduced by 27% in the clopidogrel group. Greater benefit was achieved in patients receiving clopidogrel >6 hours prior to PCI.

In the CAPRIE trial³⁸ in patients with previous MI, stroke or peripheral vascular disease clopidogrel had an 8.7% greater benefit than aspirin on reducing vascular death, MI and ischaemic stroke. Clopidogrel is therefore a useful alternative to aspirin when there is intolerance to aspirin.1++A

Clopidogrel (300-600mg orally and then 75 mg daily) should be considered in all patients at intermediate or high risk in addition to aspirin or as an alternative to aspirin and continued for 9 months according to appropriate funding.1+A There are two approaches, one is to give clopidogrel at the time of stenting after the coronary anatomy is known and the other is to give it to all patients prior to angiography, except those in whom urgent coronary artery bypass grafting (CABG) is likely as there is increased bleeding if clopidogrel has been given within 5 days of surgery.³⁵ These patients include those with ECG changes suggestive of $\geq 50\%$ left main stenosis (i.e. ST deviation in ≥ 2 coronary artery territories), known coronary anatomy from a previous angiogram which is inappropriate for PCI, the presence of multiple regional wall motion abnormalities on echocardiography, haemodynamic instability or heart failure. All of these patients should be considered for expeditious angiography.

Clopidogrel is expensive but several studies have shown it to be cost effective.³⁹⁻⁴¹ It is not currently funded except for patients undergoing stenting.

Glycoprotein IIb/IIIa antagonists—Patients with ischaemic ST depression on an ECG (≥ 0.5 mm), those with elevated troponin levels and those with diabetes have a worse prognosis and have been shown to have better outcomes with administration of intravenous glycoprotein IIb/IIIa antagonists. In a meta-analysis of glycoprotein IIb/IIIa inhibitors involving a total of 31,402 patients not routinely scheduled for PCI a 9% reduction of death or non-fatal MI was reported in the active treatment group (10.8% vs 11.8%, P=0.015).⁴² Patients with elevated troponins had an 18% reduction in death and MI equating to 20 events reduced for 1000 patients treated.

Diabetics have been shown to have a reduction in mortality with glycoprotein IIb/IIIa administration.⁴³ It is recommended that administration of either tirofiban or eptifibatide be considered in these high risk groups of patients as well as in patients

with recurrent ischaemic symptoms and continued until the time of early coronary angiography.^{1++A} These agents have been shown to be cost effective but are not available in some hospitals.^{13,44-46}

Combination of antiplatelet therapy—The optimal antiplatelet therapy for patients with non ST-elevation acute coronary syndromes is not defined. There are no randomised clinical trial data comparing triple therapy (aspirin, clopidogrel and a glycoprotein IIb/IIIa antagonist) with double therapy—i.e. with aspirin plus clopidogrel or with aspirin plus a glycoprotein IIb/IIIa antagonist. There is in-vitro evidence showing greater inhibition of platelet function with combined therapy and there is non-randomised information⁴⁷ in non-ACS⁴⁸ and³⁶ in ACS showing improved efficacy with modest increases in bleeding.

Other antiplatelet agents—Dipyridamole does not confer any additional reduction in coronary events when added to aspirin and is not recommended.**D4**

Antithrombotic agents

Antithrombotic therapy is recommended in intermediate or high risk patients with either unfractionated heparin (UFH) or LMWH^{1++A} with the preferred therapy being enoxaparin because a meta-analysis of all enoxaparin trials shows a 9% reduction in death and MI at 30 days compared to therapy with UFH (see Table 5 for suggested doses noting that APTT ranges are reagent specific and individual hospitals may have a different target range).⁴⁹

The recent SYNERGY (Superior Yield of the New Strategy of Enoxaparin, Revascularisation and glycoprotein IIb/IIIa Inhibitors) trial showed similar outcomes with UFH compared with enoxaparin on a background of high usage of clopidogrel and glycoprotein IIb/IIIa antagonists and an invasive strategy with a modest increase in bleeding. There was no significant increase in transfusions but there was an increase in TIMI major bleeding (See Appendix 3) (non CABG related) in all patients 1.7% UFH, 2.4% enoxaparin; p=0.025. In patients undergoing PCI there were similar TIMI major bleeding rates of 2.8% in patients receiving UFH vs 2.7% in patients receiving enoxaparin on a background of aspirin, clopidogrel, and glycoprotein IIb/IIIa inhibitors. Either enoxaparin or UFH should be continued until catheterisation or for 48 hours but in view of increased bleeding and events if patients are switched from one antithrombotic agent to another, patients should continue on the initial antithrombotic agent.^{1++A}

β-blockers

Although there is no strong evidence base in NSTEMI patients β-blockers may reduce progression to MI. IV β-blockers are recommended for patients at high risk and for those with continuing ischaemia if there are no contraindications (asthma, systolic BP <110 mmHg, heart rate <50 min or AV block) and oral therapy should be continued indefinitely.^{++B}

Calcium channel blockers

If β-blockers are contraindicated, diltiazem should be given.**D4** Calcium channel blockers that increase heart rate should not be used without concomitant β-blockers therapy.**D4**

Lipid modifying therapy

Initiation of statin therapy should begin in hospital in all ACS patients in order to enhance compliance and to reduce events.**1++A** Use of a fixed dose of simvastatin (40 mg) has been shown to reduce events by over 20% in HPS in non ACS patients.⁵⁰ Achievement of an LDL level of 1.6mmol/L with atorvastatin (80 mg) has been shown to reduce by 16% a composite endpoint of death, MI, readmission with unstable angina, revascularisation and stroke compared to an LDL level of 2.5mmol/L achieved with pravastatin therapy (40 mg).⁵¹

ACE inhibitors

All patients with evidence of heart failure, should receive oral ACE inhibitors beginning 2 hours after admission if the systolic BP is >100 mmHg using (e.g. 6.25 mg tds, or equivalent medication) and then increasing over several days to maximally tolerated doses.**1++A** In patients who are at high risk, ramipril and perindopril have been shown to reduce death and MI.^{52,53} In patients at low risk because of low cholesterol levels, non smoking, controlled blood pressure, previous revascularisation, and high usage of aspirin, beta-blockers, and statins, trandolapril has been shown not to be beneficial.^{53,54} ACE inhibitors should be commenced during hospitalisation and continued indefinitely.**1++C**

Early angiography and revascularisation

The FRISC-II trial demonstrated superiority in higher risk patients of an invasive approach with PCI or CABG after initial medical treatment with the low molecular weight heparin dalteparin and aspirin for 4-7 days with a reduction in mortality at 1 year from 3.9% to 2.2% p=0.01612. The TACTICS trial⁴ randomised 2220 high risk patients with aspirin, unfractionated heparin and tirofiban to an early invasive strategy with angiography within 4–48 hours followed by revascularisation if the anatomy was suitable, or to a more conservative strategy with catheterisation only for recurrent ischaemia or a positive stress test. Death, non-fatal MI and rehospitalisation for ACS at 6 months occurred in 15.9% of patients in the invasive arm and 19.4% in the conservative arm (P=0.025). The benefit of an invasive approach was confined to medium and high-risk patients who had elevated troponins, ST segment changes or diabetes.

RITA 3⁵⁵ also showed benefit of an invasive strategy in high risk patients treated with enoxaparin for 3 days prior to intervention. The ISAR Cool study⁵⁶ showed that an immediate invasive approach in 410 patients with either ST depression or elevated troponins (time to angiography of 2.4 hours) together with aspirin, clopidogrel, UFH and tirofiban resulted in lower rates of MI (5.9% vs 10.1%) compared with delaying PCI while on the same therapy for 72 hours. In the ICTUS (Invasive vs Conservative Treatment in Unstable Coronary Syndromes) study (Hot Lines ESC Munich 2004) a very high rate of intervention (73%) showed no advantage over a selective invasive strategy (47%).

An early invasive strategy within 48–72 hours together with intensive antithrombotic therapy is strongly recommended for patients with elevated troponin levels (or other cardiac markers of myocardial necrosis) **1++A**, patients with ST segment changes, diabetes, patients with recurrent or continuing ischaemic symptoms at rest or on mild

exertion despite medical therapy (beta-blocker or calcium channel blockers) and patients with interstitial or pulmonary oedema.**D4**

Several comorbidities such as renal failure are relative contraindications for angiography and revascularisation. Advanced age is not an absolute contraindication for angiography and PCI. Because of data²² showing reduced readmissions, PCI may be of particular value in the elderly.⁵⁷ Increasing stroke rates with surgery makes surgery unattractive in the very elderly.

In patients going to the catheterisation laboratory without pre-treatment with glycoprotein IIb/IIIa antagonists, it is recommended that administration of eptifibatid or abxiciamab in the laboratory be considered, especially in patients with diabetes or the presence of angiographic thrombus.**1++A**

It is recommended that troponin positive patients waiting for surgery should be on clopidogrel and have it stopped 5 days before surgery.**1++B**

Secondary prevention

All patients should be referred to rehabilitation services. All patients without contraindication should be on aspirin, a β -blocker, a statin and an ACE inhibitor indefinitely and if funding allows clopidogrel for 9 months. Patients should also stop smoking, achieve ideal weight, and exercise 30 minutes/day.

Resource availability

It is recognised that in New Zealand that providing expensive pharmaceuticals and equitable provision of an invasive strategy for Maori and in rural populations will be challenging.⁵⁸ However, it is recognised that an invasive approach has been shown to be cost effective^{44,46} and it is expensive to keep patients in hospital for long periods awaiting diagnostic testing or to have these patients discharged with a high risk of reinfarction or readmission to hospital. Extensive cost effective analyses are planned to determine appropriate levels of funding in the New Zealand setting for patients with NSTEMACS.

Conclusion

In New Zealand cheap and readily available therapies such as aspirin, beta blockers and ACE inhibitors are under prescribed.⁵⁹ It is important that these treatments are used in as many patients as possible and treatment such as PCI in patients at high risk should also be equitably available to all New Zealanders.

Author information: Non ST-Elevation Acute Coronary Syndrome Guidelines Group (refer to Appendix 1 below), nationwide; The New Zealand Branch of The Cardiac Society of Australia and New Zealand, Wellington

Appendix 1. Non ST-Elevation Acute Coronary Syndromes Guidelines Group

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Appendix 2

LEVELS OF EVIDENCE	
1++	High quality of meta-analysis, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.

2++	High quality systematic reviews of case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is casual.
2+	Well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is casual.
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not casual.
3	Non-analytic studies—e.g. case reports, case series.
4	Expert opinion.

Following assessment of the level of evidence for individual papers, recommendations were given a grade from A to D as below. This grading system departs from the Scottish Intercollegiate Guidelines Network (SIGN) system which was derived primarily for treatment guidelines and revises ranking according to therapy or prognosis. Questions relating to prognosis were considered a feature of this guideline to determine how to tailor cardiac rehabilitation services according to individual patient needs. For further details on the SIGN system see www.sign.ac.uk.

Grades of Recommendation	
A	<p>For therapy: At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population, OR</p> <p>A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.</p> <p>For prognosis: At least one meta-analysis, systematic review, or large high quality cohort study rated as 2++ and directly applicable to the target population, OR</p> <p>A body of evidence consisting principally of studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results.</p>
B	<p>For therapy: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results, OR</p> <p>Extrapolated evidence from studies rated as 1++ or 1+.</p> <p>For prognosis: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results.</p>
C	<p>For therapy: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, OR</p> <p>Extrapolated evidence from studies rated as 2++</p>
D	<p>Evidence levels 3 or 4, OR</p> <p>For therapy: Extrapolated evidence from studies rated as 2+, or expert opinion.</p>

Appendix 3. TIMI major bleeding criteria—Bleeding is associated with ≥ 5 g/dL decrease in haemoglobin (each unit of packed red blood cells or whole blood transfused counting as 1g of haemoglobin) or a $\geq 15\%$ absolute decrease in haematocrit (each unit of packed red blood cells or whole blood transfused will count as 3% points) or it is intracranial (confirmed by magnetic resonance imaging or computer tomography).

Acknowledgement: We are extremely grateful to Charlene Nell for secretarial assistance.

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