AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council
Whakahauora, Aotearoa

GUIDELINE 14

ACUTE CORONARY SYNDROMES

OVERVIEW AND SUMMARY

As a part of the International Liaison Committee on Resuscitation (ILCOR) process that led to the International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with treatment recommendations (COSTR) document for 2005 it became clear that there was an increasing need to address questions related to the initial management of acute coronary syndromes (ACS) in the pre hospital and emergency setting[1, 2].

The management of patients in this setting has been an area of increased research activity over the last 10 years. It is an area that has often been overlooked in guidelines focused on the management of acute coronary syndrome that have tended to focus on immediate and definitive therapeutic interventions once a clear diagnosis has been established. The area of pre hospital and emergency management then was added somewhat belatedly to the 2005 ILCOR and the COSTR 2005 represented the first foray into this area of Resuscitation medicine[2]. The current COSTR process devoted a dedicated Task Force formed from the outset to address 25 topics related to the acute initial management of acute coronary syndromes drawing on expert reviewers from Africa, Asia, Australia, Europe, North America, and South America. The 2010 COSTR has produced an expanded review the available evidence in the area of out of hospital and emergency care of ACS[3]. A complete systematic review of all literature is contained in this document. For the first time the Australian Resuscitation Council has decided to develop guidelines in this area based on the 2010 COSTR on ACS. Comprehensive guidelines for the diagnosis and treatment of ACS with and without ST elevation have been published by the Cardiac Society of Australia and New Zealand (CSANZ) and the National Heart Foundation (NHF) [4, 5]. This section on ACS has been developed to complement the CSANZ and NHF guidelines.

INTRODUCTION AND DEFINITIONS

The hallmark of acute coronary syndromes (ACS) is a common pathophysiology. The pathophysiology is thought to be related to a ruptured or eroded atherosclerotic plaque that then leads to thrombosis at the site and thromboembolism and ischaemia to the downstream myocardium[6]. This is often associated with the subsequent production of myocardial necrosis. Clinically it is divided into syndromes that are characterised by the presence of ST elevation on the ECG or the absence of ST elevation on the ECG.

In the absence of ST elevation other changes such as ST depression, non-specific ST-T wave abnormalities or even a normal ECG may be noted[4]. These syndromes are related but do have different clinical behaviour, outcomes and therapeutic management.

The term ACS includes ST Elevation Myocardial Infarction (STEMI), non ST elevation myocardial infarction (NSTEMI) and unstable angina pectoris. The term non ST elevation myocardial infarction – acute coronary syndrome or non STEACS has also been introduced to cover both non-STEMI and unstable angina pectoris because the differential diagnosis is dependent on biomarkers that may not be available at the time of initial assessment and treatment[4]. The term covers the suspected diagnosis based on clinical signs and symptoms and electrocardiograph (ECG) on presentation.

One of the best opportunities for improving survival for an acute coronary syndrome is reducing the delay from symptom onset to first medical contact and then initiation of targeted treatment. There are then real potential opportunities for improving survival in the out of hospital phase and emergency phase of care pathway[7]. This is evidenced by the fact that although in hospital from NSTEMI has been reducing significantly by improved reperfusion therapy and optimal medical therapy including risk factor modification, mortality for STEMI is virtually unchanged in the recent decade. This is thought to be because two thirds of patients who die from STEMI do so before they reach hospital for treatment for definitive treatment[7]. Further, ACS are the most common underlying cause leading to sudden cardiac arrest[3, 8, 9]. These guidelines are designed to address in the first hours after the onset of symptoms, the out of hospital treatment and the initial emergency department management, diagnosis and risk stratification.

SUMMARY OF THE GUIDELINES

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Presentation with ACS

- Symptoms and Signs
- The 12 lead ECG
- Cardiac Biomarkers
- Decision Rules
- Chest Pain Observation Units (CPUs)
- Imaging

Guideline 14.2
Initial Medical Therapy

- Oxygen and analgesia
- Anti platelet agents and Anticoagulants
- Optimal Medical Therapy for Primary and Secondary Prevention

Guideline 14.3
Reperfusion Strategy

- Introduction
- Primary Percutaneous Coronary Intervention (PCI)
- Fibrinolytic therapy
- Triage and inter facility transfer for Primary PCI
- Facilitated PCI
- Rescue PCI
- Pharmaco-invasive Strategy

There are a number of new evaluations that should be highlighted since initial 2005 COSTR that have been outlined in the 2010 document[3]. These include:

Guideline 14.1 Presentation with ACS

- In isolation the clinical history, clinical examinations, biomarkers, ECG criteria and risk scores are unreliable for the identification of patients who may be safely discharged early in the emergency setting.
- Chest Pain Observations Units (CPUs) have an important role in the safe and effective evaluation of patients presenting with possible ACS. The use of a protocol that includes serial evaluation of physical findings, symptoms, ECG, biomarker testing coupled with further provocative testing or imaging procedures are recommended to identify patients who required admission for further testing and treatment.
- The use of pre- hospital ECG for the diagnosis of ST elevation myocardial infarction is recommended and can be interpreted by a variety of methods including by trained non medical staff in the field, remote transmission or with computer assistance.

Guideline 14.2 Initial Medical Therapy

- Supplemental oxygen should be initiated for breathlessness, hypoxaemia or signs of heart failure or shock however hyperoxaemia may be harmful in uncomplicated myocardial infarction.
- Response of chest pain to nitrate therapy is not reliable for diagnostic purposes.
- Non-steroidal anti inflammatories other than aspirin should not be administered as they may be harmful in patients with suspected ACS.
- Aspirin may be given by dispatchers or bystanders provided true allergy or a bleeding disorder can be excluded.
- Newer anti-platelet agents have an important role in the early management of ACS.

Guideline 14.3 Reperfusion Strategy

- Clinical reperfusion networks that include emergency medical services and hospitals with an agreed approach to ST Elevation Myocardial Infarction (STEMI) management can be beneficial in achieving best outcomes for patients with ACS.
- Primary Percutaneous Coronary Intervention (PPCI) is the preferred reperfusion strategy for STEMI when it is performed in a timely manner by an experienced team.
- Fibrinolysis continues to be an important treatment modality for many patients when PPCI is not available.
- Acceptable first medical contact to PPCI delays varies depending on the infarct territory, age of the patient, and duration of symptoms.
- Rescue Percutaneous Coronary Intervention (PCI) should be performed if fibrinolysis fails.
- Patients may be directed to PPCI capable facilities in the pre hospital setting bypassing closer Emergency Departments if PPCI can be delivered in a timely manner.
- Patients with successful fibrinolysis but not in a PCI-capable facility should be transferred for angiography and possible PCI at ideally 6–24 h after fibrinolysis.

- However immediate routine PCI after fibrinolysis or combination fibrinolysis ('facilitated') is not recommended.
- Immediate angiography and PCI is a reasonable approach to patients with return of spontaneous circulation (ROSC), even in patients without ST elevation on the electrocardiograph, and may be a part of a standardised protocol for the post arrest care of patients.

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AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council WHAKAHAUORA AOTEAROA

ANZCOR Guideline 14.1 – Acute Coronary Syndromes: Presentation

Guideline

Who does this guideline apply to?

This guideline applies to adult victims.

Who is the audience for this guideline?

This guideline is for use by first responders and health professionals.

1 Symptoms and Signs

While it is important that patients who are at risk and their families should be able to recognise characteristic symptoms that may be indicative of ACS, it is important to note that signs and symptoms alone are neither sufficiently sensitive nor specific. (LOE IV). (See Guideline 9.2.1 Chest Pain)

Even amongst trained health care providers, signs and symptoms alone should not be used without other information for making the diagnosis of ACS[1,2]. (LOE IV) Signs and symptoms may be useful when used in combination with other information such as biomarkers, risk factors, an ECG and other diagnostic tests, in making triage and some treatment decisions in the out of hospital and emergency department (ED) setting.

A cautionary note also applies to the use of a response to sublingual nitroglycerine therapy as a diagnostic manoeuvre[3-6]. Although it is reasonable to consider nitroglycerine in select patients without contraindications, there is really insufficient data to recommend relief of chest pain with nitroglycerine as a diagnostic test for ACS. (LOE IV)

There are various patient related factors which impede seeking medical help. These factors include older age, belonging to racial and ethnic minorities, female gender, lower social status and social isolation[7-13]. This is particularly important to recognise these issues when providing care to the Australian indigenous, Maori and Pacific Islander population. (LOE IV) It is important that the health care providers are trained to expeditiously identify ACS irrespective of these factors.

2 The 12 Lead Electrocardiograph

The acquisition and interpretation of the ECG is the critical step for the diagnosis, triage and initiation of revascularisation therapy in patients with suspected high risk ACS and STEMI. This early recognition of STEMI patients has the potential to reduce delays to reperfusion and thus improve patient survival.

Therefore in patients with suspected ACS a 12 lead ECG should be acquired and interpreted in the pre-hospital emergency setting as soon as possible after first medical contact[14-18]. Acquisition and interpretation should then result in hospital notification of suspected STEMI with prehospital activation of the cardiac catheterisation laboratory if PPCI is the planned reperfusion strategy[19] (CoSTR 2015, strong recommendation, low-quality evidence).

It is important that the system in place for the interpretation of the prehospital ECG has optimal diagnostic performance with low false positive and false negative rates. This is important to balance the risk of missing the diagnosis of STEMI against the costs of inappropriate activation of resources[19]. If the interpretation for pre-hospital usage is not available by medical staff by field transmission of the ECG for expert interpretation, then interpretation of the ECG by non-physicians trained in ECG interpretation is suggested[20-32] (CoSTR 2015, weak recommendation, very-low-quality evidence)[19].

Further computer assisted interpretation of the ECG may be used as an adjunct or in conjunction to physician or non-physician interpretation in STEMI [33-35]. Whilst computer assisted ECG interpretation is highly specific for STEMI, it is not recommended that it be used as the sole strategy for ruling out STEMI as sensitivity is poor (CoSTR 2015, weak recommendation, very-low-quality evidence)[19].

3 Cardiac Biomarkers

All patients who present to the ED with symptoms suspicious of cardiac ischaemia should be evaluated with cardiac biomarkers as part of the initial evaluation[36,37]. Cardiac specific troponin (cTnI or cTnT) has become the most widely utilized and validated diagnostic biomarker for myocardial infarction and is the preferred laboratory test. (LOE I). Given the burden of presentations of chest pain to emergency departments it is important to rule out the diagnosis of ACS to allow early appropriate discharge of patients. An acceptably low risk at 30 days is defined as a MACE event rate of <1%. To achieve such outcomes, cTn should not be used alone to exclude a diagnosis of ACS but should be combined with a validated clinical risk score (Vancouver rule, TIMI score, HEART score or North American Chest Pain rule) (CoSTR 2015, strong recommendation, very-low-quality evidence)[19].

As cTn may be initially negative if the presentation is very soon after the symptom onset, it is recommended paired biomarker testing (c TnI or c TnT) be performed at 0 and 3-6 hours after symptom onset and combined with a very low clinical risk score to reliably exclude myocardial necrosis[37-39] (CoSTR 2015, weak recommendation, low-quality evidence)[19].

Highly sensitive cardiac troponin assays (10% coefficient of cardiac variation at the 99th percentile) have been shown to have increased sensitivity and become positive at an earlier time after onset of ischaemia when compared to conventional assays[40-43]. This supports their use in the diagnosis of AMI. These assays are able to determine the presence of a positive biomarker reliably at 2 hours[19,44,45]. (LOE II). A negative hs-cTnI at 0 and 2 hours combined with a low clinical risk score (Vancouver or TIMI score) can be used to exclude the diagnosis of ACS (CoSTR 2015, weak recommendation, low-quality evidence)[19].

There has been a lack of evidence of supporting the routine use of point of care troponin testing in isolation as the primary test in a pre-hospital setting to evaluate patients with ACS[46].

It is important to note that not all troponin elevations are related to acute coronary syndromes.

Elevated troponin values have been described in a variety of conditions not at all related to acute coronary syndromes. These include myocarditis, pulmonary embolism, acute heart failure, septic shock, secondary to cardiotoxic drugs as well as after therapeutic procedures like coronary angioplasty, electrophysiological ablations, or electrical cardioversions[47].

There are a variety of biomarkers that have become available including myoglobin and brain natriuretic peptide (BNP), NT-proBNP, D-dimer, C-reactive protein, ischaemia-modified albumin, pregnancy-associated plasma protein A and interleukin 6. These tests however are not supported by sufficient evidence to allow their use in isolation to evaluate patients with symptoms or signs of myocardial ischaemia[48-51].

4 Chest Pain Observation Units

The use of Chest Pain Observation Units (CPUs) and accelerated chest pain assessment pathways using protocols outlined above are recommended in the evaluation of patients with possible ACS. CPUs usually incorporate a protocol or pathway based strategy involving the measurement of serial biomarkers, serial ECG or continuous ECG monitoring to allow for a period of clinical observation integrated with more advanced diagnostic testing[1,2,46,56-63].

This strategy involving biomarker testing with associated protocols and pathways may be recommended as a means to reduce the length of stay, reduce hospital admissions, reduce health care costs and improve diagnostic accuracy in patients who are suspected as suffering ACS[1,2,56-62]. (LOE III-1).

5 Imaging Techniques

In patients with suspected ACS there are a variety of imaging techniques which may be utilised to diagnose acute coronary syndrome. These include CT angiography, MRI, nuclear cardiography and echocardiography[64-78]. A non-invasive test may be considered in selective patients who present to the ED with chest pain and initial non-diagnostic conventional work-up. However it is important to consider both the exposure radiation and iodinated contrast when utilising these imaging modalities. (LOE II).

These non-invasive tests may help to improve the accuracy of the diagnosis and they may also, in select groups, decrease cost, length of stay and time of diagnosis. They may provide valuable short and long term prognostic information about the incidence of future major cardiac events[64-84]. (LOE II).

6 Risk Stratification

There are a number of factors determined from the patient history, physical examination, initial ECG and biomarker testing, that allow the clinician to risk stratify patients. (LOE II).

The Australian indigenous, Maori and Pacific Islander population are at high risk for ischaemic heart disease and present at a younger age with more advanced disease[85]. Features associated with high-risk, intermediate-risk and low-risk non-ST-segment-elevation acute coronary syndromes (NSTEACS).

7 High-risk Features

Presentation with clinical features consistent with acute coronary syndromes (ACS) and any of the following high-risk features[86]:

- Repetitive or prolonged (> 10 minutes) ongoing chest pain or discomfort
- Elevated level of at least one cardiac biomarker (troponin or creatine kinase-MB isoenzyme)
- Persistent or dynamic electrocardiographic changes of ST-segment depression ≥ 0.5 mm or new T-wave inversion ≥ 2 mm
- Transient ST-segment elevation (≥ 0.5 mm) in more than two contiguous leads
- Haemodynamic compromise — systolic blood pressure < 90 mmHg, cool peripheries, diaphoresis, Killip Class > I, and/or new-onset mitral regurgitation
- Sustained ventricular tachycardia
- Syncope
- Left ventricular systolic dysfunction (left ventricular ejection fraction < 0.40)
- Prior percutaneous coronary intervention within 6 months or prior coronary artery bypass surgery
- Presence of known diabetes (with typical symptoms of ACS)
- Chronic kidney disease (estimated glomerular filtration rate < 60 mL/minute) (with typical symptoms of ACS).

8 Intermediate-risk Features

Presentation with clinical features consistent with ACS and any of the following intermediate risk features AND NOT meeting the criteria for high-risk ACS:

- Chest pain or discomfort within the past 48 hours that occurred at rest, or was repetitive or prolonged (but currently resolved)
- Age > 65 years
- Known coronary heart disease — prior myocardial infarction with left ventricular ejection fraction ≥ 0.40, or known coronary lesion more than 50% stenosed
- No high-risk changes on electrocardiography (see above)
- Two or more of the following risk factors: known hypertension, family history, active smoking or hyperlipidaemia
- Presence of known diabetes (with atypical symptoms of ACS)
- Chronic kidney disease (estimated glomerular filtration rate < 60 mL/minute) (with atypical symptoms of ACS)
- Prior aspirin use.

9 Low-risk Features

Presentation with clinical features consistent with an acute coronary syndrome *without* intermediate-risk or high-risk features includes onset of angina symptoms within the last month, *or* worsening in severity or frequency of angina, *or* lowering of angina threshold.

A number of risk scores have been developed to assist in risk stratification using simple risk variables that can be calculated on information easily available to clinicians. These scores have been validated in large studies and predict major adverse cardiovascular outcomes in a robust fashion.

10 The Thrombolysis in Myocardial Infarction (TIMI) score is one such score[87] (Table 1)

Predictor Variable	Point Value of Variable
Age ≥65 years	1
≥3 risk factors for CAD	1
Risk factors ● Family history of CAD ● Hypertension ● Hypercholesterolemia ● Diabetes ● Current smoker	
Aspirin use in last 7 days	1
Recent, severe symptoms of angina • ≥2 angina events in last 24 hours	1
Elevated cardiac markers • CK-MB or cardiac-specific troponin level	1
ST deviation ≥0.5 mm	1
Prior coronary artery stenosis ≥50%	1

Calculated TIMI Risk Score:

Risk Status	Risk of ≥1 Primary End Point* in ≥14 Days
0 or 1	5% Low
2	8% Low
3	13% Intermediate
4	20% Intermediate
5	26% High

*Primary end points: death, new or recurrent MI, or need for urgent revascularization

Patients without high risk features may be managed with a conservative strategy that does not include routine invasive assessment with coronary angiography and PCI where indicated. (LOE I).

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AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council WHAKAHAUORA AOTEAROA

GUIDELINE 14.1.2

ACUTE CORONARY SYNDROMES:
THE USE OF A GASTRO INTESTINAL COCKTAIL FOR THE DIAGNOSIS OF ACUTE CORONARY SYNDROME IN ADULT EMERGENCY DEPARTMENT PATIENTS PRESENTING WITH CHEST PAIN

INTRODUCTION

The Gastrointestinal (GI) cocktail (a mixture of liquid antacid, viscous lignocaine, and often an anticholinergic agent) or 'pink lady' has been suggested to be effective in treating symptoms of dyspepsia in patients presenting to the emergency department[1]. The GI cocktail however, has been proposed to be useful not only for the therapy of patients with indigestion (gastro oesophageal reflux), but has also been used as a diagnostic aid for differentiating cardiac ischemic chest pain from chest pain of gastroesophageal origin.

ACCURACY OF DIAGNOSIS

It is important that health care professionals, patients who are at risk and their families should be able to recognise characteristic symptoms that may be indicative of ACS. The signs and symptoms alone are neither sensitive nor specific[2]. (Class B;LOE IV). (See Guideline 9.2.1 Recognition and First Aid Management of Heart Attack, Guideline 14.1 ACS: Presentation with ACS).

Distinguishing ischemic from oesophageal chest pain can be difficult on clinical grounds. Both ischemic cardiac chest pain and the pain associated with gastro oesophageal reflux can share very similar characteristics such as sense of dyspepsia and response to nitrates or antacid cocktail[3 4].

The available evidence to support the use of a GI cocktail (oral viscous lignocaine/antacid/ +/- anticholinergic) compared with standard diagnostic protocols (Serial ECG and biomarkers and provocative testing or imaging) to improve accuracy of diagnosis is sparse and inconclusive[1-14].

In patients with chest pain and suspected ACS, the use of a GI cocktail (oral viscous lignocaine/antacid/ +/- anticholinergic) compared with standard diagnostic protocols (Serial ECG and biomarkers and provocative testing or imaging) is not proven to improve the accuracy of diagnosis.

A number of these studies suggest a potential for harm in using antacid cocktail to improve the accuracy of diagnosis of ACS because myocardial ischaemia may be incorrectly excluded from the diagnosis[4 7 9 11]. A symptomatic response to a GI cocktail in proven ACS has been well documented.

The signs and symptoms alone should not be used without other data for making the diagnosis of ACS. (Class B;LOE IV) (See Guideline 14.1).

These symptoms cannot be used in isolation but may be useful when used in combination with other information such as biomarkers, risk factors, an ECG and other diagnostic tests, in making triage and some treatment decisions in the out of hospital and emergency department (ED) setting. (Guideline 14.1)

RECOMMENDATION

It is recommended that the GI cocktail not be used in the emergency department to assist in the diagnosis of ACS.

LEVEL OF EVIDENCE

III Case series and observational studies

CLASS OF RECOMMENDATION

Class A - Recommended

FURTHER READING

ARC Guideline 9.2.1 Recognition and First Aid Management of Heart Attack
ARC Guideline 14.1 ACS: Presentation with ACS

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ANZCOR Guideline 14.2 – Acute Coronary Syndromes: Initial Medical Therapy

Guideline

Who does this guideline apply to?

This guideline applies to adult victims.

Who is the audience for this guideline?

This guideline is for use by health professionals.

1 Symptomatic Therapy

There are a number of therapies in patients with Acute Coronary Syndromes (ACS) that provide relief for symptoms.

Supplemental oxygen should be initiated only if the patient has breathlessness, hypoxaemia (SpO2<94%), or signs of heart failure or shock. The use of oxygen saturation monitoring by non-invasive techniques such as pulse oximetry, may be very useful in guiding oxygen therapy[2] (weak recommendation, very-low-quality evidence)[3]. However, it is important to understand that there is evidence that hyperoxaemia is potentially harmful in uncomplicated myocardial infarction[3,4]. (LOE IV). Oxygen may have a separate indication in other emergency situations at times associated with ACS however (e.g. water accidents, gas embolism etc.).

Morphine analgesia is also important symptomatic relief for patients with chest pain. Morphine may be considered for patients with ongoing symptoms of chest discomfort[5] and titrated to relieve pain. (LOE IV). Value is placed on relieving pain and distress understanding that the evidence of benefit is lacking and further research is required regarding the possibility of harm suggested in some registry data[5].

While anxiolytics may be administered to relieve anxiety in patients with ACS but there is no evidence that it improves outcomes for patients in terms of ECG resolution, reduced infarct, decreased mortality or morbidity in patients with suspected ACS[6]. (LOE IV)

Nitroglycerine administration may be of benefit within 3 hours of the onset of symptoms in patients with infarction in the era prior to the advent of reperfusion therapy (based on extrapolation from other contexts)[7-9]. In the current era no trial has specifically evaluated patients in the Emergency Department (ED) or prehospital settings. It is reasonable to consider the early administration of nitroglycerin in selected patients without contraindications, particularly if this provides pain relief.

There is however a lack of evidence to support or refute the routine administration of nitroglycerin in the ED or prehospital setting in patients with a suspected ACS. (LOE IV)
Specifically in cocaine-associated chest pain lorazepam and nitroglycerine may be useful in the alleviation of chest pain in this specific setting.

In general non-steroidal anti-inflammatory drugs (NSAIDs) should not be administered in patients with suspected ACS as they could be harmful[10]. Further, patients with suspected ACS who are taking NSAIDS should have these discontinued if it is feasible. (LOE I).

2 Antiplatelet and Anticoagulant Therapy

2.1 Aspirin administration

The early administration of aspirin in an antiplatelet dose of 300 mg is recommended in patients with suspected ACS where contraindications such as true anaphylaxis or bleeding disorder have been excluded[11]. The patients should be directed to chew the tablet (which should not be enteric coated). Dissolvable aspirin is preferred[12-15].

There is currently limited evidence to directly support the strategy of dispatcher directed or bystander administration of aspirin, however, it is considered to be a reasonable approach if the carer is able to exclude a history of true anaphylaxis or bleeding disorder[15-18]. (LOE IV).

2.2 Antiplatelet Agents

Clopidogrel: Clopidogrel is a thienopyridine that inhibits $P2Y_{12}$ platelet receptor. The drug requires activation by a two stage biotransformation within the liver. This is a process that is modulated by genetic polymorphisms resulting in variability in clinical effect[19]. Benefit has been demonstrated when added to aspirin in non-ST elevation acute coronary syndrome (NSTEACS) patients, including those treated with percutaneous coronary intervention (PCI). Reductions in cardiovascular death, myocardial infarction (MI) and stroke have been observed but with an increase in major bleeding [20]. It is recommended that patients who have moderate to high risk NSTEACS and ST-elevation myocardial infarction (STEMI) receive clopidogrel in addition to the standard care (aspirin, anticoagulation and/or a reperfusion). The ideal dose in older patients has not yet been determined. However, in patients under the age of 75 years the loading dose of clopidogrel is 600 mg if PCI is planned or 300 mg if a non-invasive strategy with fibrinolysis is the planned treatment option[21,22]. (LOE II).

Prasugrel: Prasugrel is a new thienopyridine, that produces more rapid and consistent platelet inhibition[19]. In the clopidogrel naïve patient, prasugrel (compared to clopidogrel) reduced the incidence of myocardial infarction in patients with moderate to high risk NSTEACS and patients with STEMI planned for primary PCI. Prasugrel has been associated with a higher rate of bleeding complications in patients >75 years of age, those with a history of stroke or transient ischaemic attack and body weight less than 60 kg. Prasugrel is not recommended in patients with STEMI who have received fibrinolysis. It may be used in place of clopidogrel in patients with STEMI of less than 12 hours duration where PPCI is planned[23]. (LOE II)

In patients with NSTEMI, prasugrel may be administered after angiography when the coronary anatomy is known and the plan is to proceed to PCI.

Prasugrel may be administered as a loading dose of 60 mg in place of clopidogrel in these patients with ACS as long as they are not at high risk from bleeding. (LOE II).

Ticagrelor is a pyrimidine derivative, which binds reversibly to the $P2Y_{12}$ receptor without the need for biotransformation. Like prasugrel, it has a more rapid and consistent onset of action compared with clopidogrel, but additionally it has a quicker offset of action so that recovery of platelet function is faster[19].

Ticagrelor has demonstrated some benefits over clopidogrel in patients with moderate to high risk NSTEACS (treated conservatively or invasively) and patients with STEMI planned for primary PCI (PPCI) in terms of a reduction in death from vascular causes and MI. There was no increase in major bleeding observed but an increase in minor bleeding was seen[24].

The adverse effects of ticagrelor include dyspnoea, increased frequency of mostly asymptomatic ventricular pauses, and asymptomatic increases in uric acid.

Ticagrelor is recommended for patients at moderate-to-high risk of ischaemic events (e.g. troponin positive ACS) , regardless of initial planned treatment strategy and including those pre-treated with clopidogrel. The dose is 180-mg loading dose and then 90 mg twice daily. (LOEII). Ticagrelor may be used then in place of clopidgrel in patients with ACS.

The risks and benefits of combinations of the newer antiplatelet agents are undetermined. It is expected that whilst patients may be switched from one agent to another, the drugs should not be used in combination with each other on an ongoing basis. They are expected to be used in combination with aspirin on an ongoing basis.

Prehospital administration of these agents in the setting of STEMI in recent studies has shown no mortality benefit or harm in the administration of either ticagrelor or clopidogrel(ref 14.2 NA). ANZCOR suggest that when ADP-receptor antagonists are given to suspected STEMI patients with a planned primary PCI approach, administration can occur in either the prehospital or in-hospital setting, but there is insufficient evidence to change existing practice (CoSTR 2015, very-low-quality evidence, weak recommendation)[3]. The pre hospital administration of ticagrelor when compared with placebo, showed evidence of reduced subacute stent thrombosis.[25] Typically the delays between first medical contact and PPCI are relatively short and the administration of these agents can occur either prehospital or in-hospital. It is important that the initial management of STEMI including the prehospital use of these agents is undertaken within an appropriate model of care with close communication between physicians, PCI facility cardiologists and emergency staff. This will also need to take into account geographic, population and resource factors and local systems of care.

3 Anticoagulants

3.1 Anticoagulants in NSTEACS

In patients presenting with NSTEACS, anticoagulation with enoxaparin or unfractionated heparin (UFH) is a reasonable treatment strategy[26]. (LOE I) This recommendation includes patients managed with an initial conservative approach or a planned invasive approach.

Recent studies have suggested that bivalirudin is an alternative anticoagulant to heparin. It is considered an effective alternative[27-30]. (LOE II). There is however, no definite evidence that it offers an advantage over UFH or enoxaparin where these agents are used without a glycoprotein IIB/IIIA inhibitor. When heparin is used routinely combined with a glycoprotein IIB/IIIA inhibitor, composite ischaemic end points are similar but bleeding is increased compared to bivalirudin and the provisional use of a glycoprotein IIB/IIIA inhibitor.

In patients with renal impairment, those at increased bleeding risk but where anticoagulation therapy is not contraindicated, it may be a reasonable option to treat with bivalirudin. UFH may also be considered while, enoxaparin may be best avoided with renal impairment. There is no specific evidence for or against anticoagulant use in non-ST elevation ACS in the pre-hospital setting. (LOE II).

3.2 Anticoagulants in STEMI treated with Fibrinolysis

In patients with STEMI in the pre-hospital and ED setting, the issue of anticoagulant choice needs to be considered. In patients with STEMI managed with fibrinolysis, anticoagulation with either enoxaparin or UFH is reasonable[31-35]. (LOE I).

However, in all situations these agents should not be switched from enoxaparin to UFH or vice versa as this has been shown to be associated with an increased bleeding risk. (Class B;LOE II).

3.3 Anticoagulants in STEMI treated with PCI

In patients with suspected STEMI in the pre-hospital and ED setting there are a number of anticoagulants available to treat patients including bivalirudin and enoxaparin. Enoxaparin may be considered a safe and effective alternate to UFH in the patient with STEMI undergoing contemporary PCI[3] (CoSTR 2015, weak recommendation, low-quality evidence). However, to avoid increased bleeding risks, patients initially treated with enoxaparin or UFH should not be switched[36-38]. (LOE II). The administration of anticoagulant in patients with suspected STEMI and a planned PPCI can occur in-hospital or in the pre-hospital setting (CoSTR 2015, weak recommendation, very-low-quality evidence)[3].

Bivalirudin may be superior to UFH plus glycoprotein IIB/IIIA inhibitors with respect to bleeding complications and reduces adverse cardiac events and mortality in STEMI patients undergoing primary PCI[39]. There is however, increased rate of stent thrombosis observed in patients treated with bivalirudin in the first 24 hours[40-44]. There is insufficient data to speculate on the use of bivalirudin versus UFH or enoxaparin alone in patients undergoing PCI. We do not recommend change to exsiting practice of using UFH or enoxaprin. (CoSTR weak recommendation, very-low-quality evidence)[3]. (LOE II).

3.4 Glycoprotein IIBIIIA inhibitors

There have been recent studies that have called into question the value of the routine use of glycoprotein IIBIIIA inhibitor use in patients with suspected STEMI or non-STEMI in the pre-hospital and ED setting[45]. There may still be a role for glycoprotein IIBIIIA inhibitors in selected high risk patients with NSTE-ACS in whom a PCI is planned. There are increased bleeding risks with the routine use of these agents. (LOE II).

3.5 Fondaparinux

Fondaparinux has no indication for ACS in Australia and New Zealand.

4 Optimal Medical Therapy for Primary and Secondary Prevention

There are a number of additional medical therapies that have been proposed for ACS patients to reduce myocardial ischaemia and recurrent major cardiovascular events, and improve long-term survival. Therapeutic options in the pre-hospital and emergency setting that should be specifically addressed include the routine use of antiarrhythmics, beta blockers, angiotensin converting enzyme (ACE) inhibitors and HMG CoA-reductase inhibitors.

4.1 Antiarrhythmics

There is little evidence to suggest that the prophylactic use of antiarrhythmics improves outcomes in patients with ACS[46-49]. The prophylactic use of antiarrhythmic agents is not recommended. (LOE II).

4.2 Beta Blockers

Routine use of IV beta blockers in the pre-hospital setting or during initial assessment in the ED is not supported by the available evidence[50-52]. It may be useful to administer IV beta blockers in specific settings such as severe hypertension or tachycardia when no contraindication exists. (LOE I).

4.3 ACE Inhibitors

ACE inhibitors and angiotensin receptor blocker agents reduce mortality in patients with acute myocardial infarction[53,54]. However there is insufficient evidence to support the routine initiation of these in the pre-hospital or ED setting. (LOE IV)

4.4 Lipid Lowering Therapy

Statins should be considered early after the onset of ACS. In patients presenting with ACS, unless it is contraindicated, pre-existing statin therapy should be continued[55-57]. There are no reports on the risk or safety of an early administration of statins. Most studies document treatment within the first 24 hours after presentation. (LOE IV)

4.5 Calcium channel blockers

There is little data to support the routine use of calcium channel blockers in the pre hospital and emergency setting. Reductions in mortality have not been reported in this setting[58].

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ANZCOR Guideline 14.3 – Acute Coronary Syndromes: Reperfusion Strategy

Guideline

Who does this guideline apply to?
This guideline applies to adult victims.

Who is the audience for this guideline?
This guideline is for use by health professionals.

1 Introduction

STEMI occurs in the majority of the patients due to the acute thrombotic occlusion of a major epicardial artery[1-3]. This is part of a spectrum of acute syndromes that are the result of disruption or erosion of typically lipid rich atherosclerotic plaque which leads to thrombus formation that occludes the vessel. Myocardial necrosis ensues in a time dependent fashion. Therefore strategies aimed at restoring myocardial perfusion at the earliest possible moment are an important part of the management of these patients. The longer the vessel remains occluded the higher the mortality for this patient group. Restoring coronary blood flow and myocardial reperfusion either by percutaneous coronary intervention (PCI) or fibrinolytic therapy has been demonstrated to improve outcomes in patients presenting within 12 hours of symptom onset[4,5]. It has also been shown to be beneficial in other patient groups beyond 12 hours of symptom onset such as those with cardiogenic shock[1,3,6,7].

In general the creation of cardiac clinical networks including emergency and medical providers, non capable and capable PCI hospitals is important to facilitate a regional strategy for the delivery of timely revascularisation[3,6-13]. The development of these networks has allowed timely institution of reperfusion therapy and reduced mortality from STEMI over the last decade[14].

Related to the issue of STEMI systems of care is a growing body of observational data suggesting out of hospital cardiac arrest (OHCA) patients should be considered for transport to a specialist cardiac arrest centre as part of wider regional system of care for management of patients with OHCA. Such centre would need to have capacity to undertake Primary PCI[15].

1.1 Primary PCI

Primary PCI (PPCI) is the preferred perfusion strategy with the best outcomes demonstrated in a number of large meta-analyses provided it is performed in a timely manner by an experienced team[16,17]. The benefit is mostly driven by reduced rates of recurrent myocardial infarction and reduced rates of intracranial haemorrhage (ICH) in the PPCI treated patients compared to those receiving fibrinolysis. (LOE I).

Hence where immediate PCI is available the combination of routine administration of fibrinolysis in conjunction with PPCI is without benefit and is associated with increased risk of ICH. It is not recommended (CoSTR 2015, strong recommendation, moderate-quality evidence)[14].

In many parts of Australia and New Zealand, PPCI is not widely available. PPCI is limited by accessibility to a catheterisation laboratory facility, access to appropriate skilled clinician and delays related to the time taken to obtain reperfusion[18].

For PPCI to maintain superiorly over fibrinolytic therapy the PCI related delay must be between 45 and 180 minutes depending on the patient's condition e.g. patient age, site of infarction and duration of symptoms[19-21]. (LOE II).
The Cardiac Society of Australia and New Zealand recommends in general, the maximum acceptable delay from presentation to balloon inflation is[22]:

- 60 minutes if a patient presents within 1 hour of symptom onset; or
- 90 minutes if a patient presents later.

(LOE II)

There are a number of strategies that can be undertaken to reduce the time delay to PPCI[11]. These are strategies to improve the systems of care arising from and they include pre-hospital 12 lead ECGs to facilitate earlier diagnosis, advanced notification of the results of the 12 lead ECG at the receiving institute for rapid reperfusion on arrival of the STEMI patient. Techniques that have evidence to support implementation include[23-29] (LOE III-2):

- Arranging suitable activation of the catheter laboratory
- Requiring the catheter laboratory to be ready in 20 minutes
- Having the interventional cardiologist immediately available at the hospital
- Providing real time data feedback
- Support for the treatment strategy by senior medical clincians
- Encouraging a team based approach.

Where PPCI capable facilities are available as part of a system of care, direct triage and transport to those centres for PCI is preferred (CoSTR 2015, weak recommendation, low-quality evidence)[14].

In addition to patients with contraindications for fibrinolysis, PCI should be pursued even if there is a delay rather than opting for a no treatment strategy[3,6].

For patients with STEMI presenting with shock, primary PCI or coronary artery bypass is clearly a preferred treatment option. Treatment with fibrinolysis should only be considered if there is a substantial delay to PCI[30,31]. (LOE II).

1.2 PCI in patients with ROSC

We recommend performing immediate angiography and if necessary PCI in patients with ST elevation or new left bundle branch block on the standard 12 lead electrocardiograph who respond to cardio-pulmonary resuscitation with spontaneous return of circulation after cardiac arrest[32-35] (LOE II) (CoSTR 2015, strong recommendation, low-quality evidence)[14]. Coma is common and should not be a contraindication to angiography and PCI. We suggest immediate angiography and if necessary PCI in selected patients who do not have evidence of ST elevation on their ECG nor prior clinical features such as chest pain, if coronary ischaemia is considered the likely cause on clinical grounds . (LOE III-1) (CoSTR 2015, weak recommendation, very-low-quality evidence)[14].

Targeted temperature management is recommended in combination with PCI and can be commenced as part of the initial treatment preferably prior to PCI[36]. Angiography and PCI can be incorporated as part of a standardised post cardiac arrest protocol[37]. (LOE III-3).

Immediate angiography implies these patients should be managed to minimize door-to-reperfusion times in a manner similar to the general STEMI patient population. However, the complexity and heterogeneity of this patient group may delay their resuscitation, management and time to angiography[14].

A number of complex clinical factors may influence the decision to proceed to angiography and intervention. These include patient age, the presenting rhythm, whether the arrest was witnessed, the requirement for haemodynamic support and the known presence of co morbidities such diabetes mellitus, renal failure, and chronic heart failure[14].

1.3 Fibrinolytic Therapy

Fibrinolytic therapy is more widely available and is beneficial in a wider range of patients who may not have access to PPCI[38-40]. Fibrinolytic therapy can be safely given by a trained paramedic, nurse or physician using established protocols[41-45]. (LOE I) The efficacy is greatest given the first three hours of the onset of symptoms. Without timely access to primary PPCI, patients with symptoms of ACS and ECG evidence of ST elevation infarction or true new bundle branch block or true posterior infarction should be treated with fibrinolytic therapy as soon as possible.

In patients presenting early after the onset of chest pain (<1-2 hours) and in certain clinical subsets (<65 years-of-age, anterior STEMI), prehospital fibrinolysis may offer similar outcomes compared to PPCI[20,46,47]. (LOE II)

There are a number of contraindications to fibrinolysis that health care practitioners need to be well aware of (see Table 1)[1,48]. In addition, the older patients are a difficult patient group. They have a high absolute risk of death from their STEMI, have an increased absolute benefit from fibrinolytic therapy but the risk of intracranial bleeding from fibrinolysis is also higher. This is increased in the presence of systolic hypertension of over 180 mmHg. The benefits of fibrinolytic therapy are less impressive in areas of infarction other than an anterior STEMI location.

2 Table 1

Contraindications for fibrinolysis[48]

2.1 Absolute contraindications

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage, neoplasms or structural vascular lesions (e.g. ateriovenous malformation)
- Recent major trauma/surgery/head injury (within the preceding 3 weeks)
- Gastro-intestinal bleeding within the last month
- Known bleeding disorder (excluding menses)
- Aortic dissection

2.2 Relative contraindications

- Transient ischaemic attack in preceding 6 months, dementia
- Oral anticoagulant therapy
- Pregnancy within 1-week post-partum
- Non-compressible punctures

- Traumatic resuscitation
- Refractory hypertension (systole. blood pressure >180mmHg
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

In patients with STEMI diagnosed in the pre-hospital setting, reperfusion can be achieved by the administration of fibrinolytics by health care providers in the field. If fibrinolysis is chosen as a reperfusion strategy and transport to hospital estimated to be greater than 30 min from first medical contact, we recommend prehospital fibrinolysis if this capability exists (CoSTR 2015, strong recommendation, moderate-quality evidence)[14]. This requires paramedics, nurses or doctors to use well established protocols, have competency based training programs, a quality assurance program and be under medical oversight[43,49,50]. (LOE II).

This strategy may be particularly important in rural areas where there are long transit times to hospital[44,51-53].

2.3 Triage and inter facility transfer for PPCI

It is reasonable to consider direct transport to PCI capable facilities for PPCI for patients diagnosed with STEMI by emergency medical services in the prehospital setting, bypassing closer hospitals as necessary, in systems where time intervals between first medical contact and balloon time are brief (<2 hours) [4,26,54-56].

Transfer of STEMI patients for PPCI from community hospitals is reasonable for those presenting more than 3 h but less than 12 h after the onset of symptoms, provided that the transfer can be achieved rapidly (<2 hrs). The risk of death, reinfarction or stroke is reduced if patients with STEMI are transferred promptly from community hospitals to tertiary care facilities for PPCI[55-57]. (LOE I) (CoSTR 2015, strong recommendation, moderate-quality evidence)[14].

When long delays to PPCI are anticipated (more than 120 minutes), a strategy of immediate fibrinolysis followed by routine early (within 3–24 hours) angiography and PCI, if indicated, is reasonable (CoSTR 2015, weak recommendation, very-low-quality evidence)[14]

2.4 Rescue PCI

It is reasonable to perform coronary angiography and PCI in patients who have failed fibrinolysis according to clinical signs and insufficient ST segment resolution[58-63].
(LOE I).

2.5 Pharmaco-Invasive Strategy

Patients with successful fibrinolysis but are not treated at a PCI capable centre should be encouraged to be routinely transferred for angiography and PCI performed within 3-24 hours after fibrinolysis. The optimal timing has not been determined but intervention in under 24 hours has been shown to reduce re-infarction rates. It is recognised that there may be situations and geography where transfer within 24 hours may be difficult or not available.[64-68] (LOE II) (CoSTR 2015, weak recommendation, very-low-quality evidence)[14] .

2.6 Facilitated PCI

Facilitated PCI refers to the routine use of fibrinolysis prior to PPCI. The strategy of facilitated PCI compared with PPCI is not recommended in STEMI.

A number of studies have examined the strategy of facilitated PCI and they have shown no benefit of PPCI and some studies have shown poor outcomes with routine PCI shortly after fibrinolysis[69,70]. (LOE II) (strong recommendation, moderate-quality evidence)[14]

2.7 Cardiac Arrest Centres

A cardiac arrest centre is a hospital that has the facilities to provide a comprehensive package of post resuscitation care including percutaneous coronary intervention and targeted temperature management. There is evidence from observational studies that such centres appear to have better survival and better neurologically intact survival. The evidence supporting triaging to such centres is however weak with an absence of randomised studies supporting such a strategy. It is reasonable to consider transport patients with OHCA directly to a cardiac arrest centre. This would need to take into account geographic, population and resource factors. (CoSTR 2015, weak recommendation, low level of evidence)[15]

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