Acute coronary syndromes: the management of unstable angina and non-ST-segment-elevation myocardial infarction

NICE guideline
Draft for consultation, July 2009

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
Contents

Introduction ...................................................................................................... 3
Patient-centred care ......................................................................................... 4
Key priorities for implementation ...................................................................... 5
1 Guidance .................................................................................................. 7
   1.1 Provision of information ...................................................................... 7
   1.2 Assessment of a patient’s risk of future adverse cardiovascular events ............................................................................................................ 7
   1.3 Antiplatelet therapy ............................................................................. 8
   1.4 Antithrombin therapy ......................................................................... 10
   1.5 Management strategies ..................................................................... 11
2 Notes on the scope of the guidance ....................................................... 13
3 Implementation ....................................................................................... 14
4 Research recommendations .................................................................. 14
   4.1 Testing for ischaemia ...................................................................... 14
   4.2 Risk assessment............................................................................... 15
5 Other versions of this guideline ............................................................. 16
   5.1 Full guideline.................................................................................. 16
   5.2 Quick reference guide..................................................................... 17
   5.3 ‘Understanding NICE guidance’ ....................................................... 17
6 Related NICE guidance ........................................................................... 17
7 Updating the guideline ........................................................................... 19
Appendix A: The Guideline Development Group ........................................... 20
Appendix B: The Guideline Review Panel ..................................................... 22
Appendix C: The algorithms........................................................................... 23
Introduction

The term 'acute coronary syndromes' encompasses a range of conditions from unstable angina to ST-segment-elevation myocardial infarction (STEMI), arising from thrombus formation on an atheromatous plaque. This guideline addresses the early management of unstable angina and non-ST-segment-elevation myocardial infarction (NSTEMI) once a firm diagnosis has been made and before discharge from hospital. If untreated, the prognosis is poor and mortality high, particularly in people who have had myocardial damage. Appropriate triage and timely use of acute interventions, whether invasive or pharmacological, are vital and are addressed in this guideline. The guideline does not cover the management of STEMI or acute heart failure not caused by NSTEMI. Timely assessment and classification of people presenting with undifferentiated chest pain are covered in the NICE clinical guideline on acute chest pain of suspected cardiac origin1, which is being developed in parallel with this guideline.

The guideline will assume that prescribers will use a drug’s summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Unlicensed or off-label use is indicated by a footnote.

---

1 More information on the NICE clinical guideline on chest pain of recent onset is available from www.nice.org.uk
Patient-centred care

This guideline offers best practice advice on the care of adults (18 years and older) with a diagnosis of unstable angina or non-ST-segment-elevation (NSTEMI).

Treatment and care should take into account patients’ needs and preferences. Patients with unstable angina or NSTEMI should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – ‘Reference guide to consent for examination or treatment’ (2001) (available from www.dh.gov.uk). Healthcare professionals should also follow the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient’s needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.
Key priorities for implementation

- As soon as the diagnosis is made, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, Global Registry of Acute Cardiac Events [GRACE]).
- Consider offering intravenous eptifibatide or tirofiban\textsuperscript{2}, in addition to aspirin, clopidogrel and an antithrombin, as part of the early management for patients who have an intermediate or higher risk of future adverse cardiovascular events (predicted 6-month mortality >3\%), and who are scheduled to undergo early angiography (within 96 hours of hospital admission).
- Offer coronary angiography within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality >3.0\%) if they have no contraindications to angiography (such as active bleeding or comorbidity).
- When the place, or choice, of revascularisation is unclear, resolve this by discussion involving the patient, an interventional cardiologist, cardiac surgeon and other relevant healthcare professionals.
- To detect and quantify inducible ischaemia, consider offering ischaemia testing before discharge to patients whose condition has been managed conservatively and who have not had coronary angiography.
- Before discharge offer patients advice and information about:
  - their diagnosis and arrangements for follow-up [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
  - cardiac rehabilitation [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
  - management of cardiovascular risk factors and drug therapy for secondary prevention [in line with 'MI: secondary prevention']

\textsuperscript{2} Eptifibatide and tirofiban are licensed for use with aspirin and unfractionated heparin. They do not have UK marketing authorisation for use with clopidogrel. This recommendation is therefore for an off-label use of these drugs. Informed consent should be obtained and documented before they are used in combination with clopidogrel.
(NICE clinical guideline 48) and 'Lipid modification' (NICE clinical guideline 67)]

- lifestyle changes [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
- health education.
1  Guidance

The following guidance is based on the best available evidence. The full guideline ([add hyperlink]) gives details of the methods and the evidence used to develop the guidance.

1.1  Provision of information

1.1.1 Offer patients clear information about the risks and benefits of the treatments offered so that they can make informed choices about management strategies. Information should be appropriate to the patient's underlying risk of a future adverse cardiovascular event and any comorbidities.

1.2  Assessment of a patient’s risk of future adverse cardiovascular events

1.2.1 As soon as the diagnosis is made, formally assess individual risk of future adverse cardiovascular events using an established risk scoring system that predicts 6-month mortality (for example, Global Registry of Acute Cardiac Events [GRACE]).

1.2.2 Include in the formal risk assessment:

- a full clinical history (including age, previous myocardial infarction [MI] and previous percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG])
- a physical examination (including measurement of blood pressure and heart rate)
- a resting 12-lead electrocardiogram (ECG) (looking particularly for dynamic or unstable patterns that indicate myocardial ischaemia)
- blood tests (such as troponin I or T, creatinine, glucose and haemoglobin).
1.2.3 Record the results of the risk assessment in the patient's care record.

1.2.4 Use risk assessment to guide clinical management and balance the benefit of a treatment against any related adverse events in the light of this assessment.

1.2.5 Use predicted 6-month mortality to categorise the risk of future adverse cardiovascular events as follows:

<table>
<thead>
<tr>
<th>Predicted 6-month mortality</th>
<th>Risk of future adverse cardiovascular events</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.5%</td>
<td>Lowest</td>
</tr>
<tr>
<td>&gt;1.5–3.0%</td>
<td>Low</td>
</tr>
<tr>
<td>&gt;3.0–6.0%</td>
<td>Intermediate</td>
</tr>
<tr>
<td>&gt;6.0–9.0%</td>
<td>High</td>
</tr>
<tr>
<td>&gt;9.0%</td>
<td>Very high</td>
</tr>
</tbody>
</table>

1.3 **Antiplatelet therapy**

**Aspirin**

1.3.1 Offer aspirin to all patients and continue indefinitely unless contraindicated by bleeding risk or aspirin hypersensitivity.

1.3.2 Offer a single loading dose of 300 mg aspirin to people who have not been on regular aspirin treatment and have not received aspirin since presentation.

1.3.3 For patients with aspirin hypersensitivity, clopidogrel monotherapy should be considered as an alternative treatment. [This

---

3 Categories are based on quartiles of risk derived from the Myocardial Infarction National Audit Process (MINAP) database.
recommendation is from ‘MI: secondary prevention’ (NICE clinical guideline 48)].

**Clopidogrel**

Recommendations in this section update and replace ‘Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome’ (NICE technology appraisal guidance 80). Recommendation 1.3.6 has been incorporated from TA80.

1.3.4 As soon as a firm diagnosis of unstable angina or NSTEMI is made, offer a loading dose of 300 mg clopidogrel in addition to aspirin to patients with a predicted 6-month mortality of >1.5% and no contraindications (for example, an excessive bleeding risk).

1.3.5 Consider offering a higher loading dose of clopidogrel to all patients with no contraindications who may undergo PCI within 24 hours of admission to hospital.

1.3.6 It is recommended that treatment with clopidogrel in combination with low-dose aspirin should be continued for up to 12 months after the most recent acute episode of non-ST-segment-elevation ACS. Thereafter, standard care, including treatment with low-dose aspirin alone, is recommended. [This recommendation has been incorporated from 'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome' (NICE technology appraisal guidance 80).]

1.3.7 Consider discontinuing clopidogrel treatment 5 days before CABG in patients who have a low risk of adverse cardiovascular events (predicted 6-month mortality ≤3.0%).

1.3.8 For patients at intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality >3.0%), discuss the continuation of clopidogrel before CABG with the cardiac surgeon.

---

4 Clopidogrel does not have UK marketing authorisation for use at doses above 300 mg. Such use is an off-label use. Informed consent should be obtained and documented.
and base the decision on the balance of ischaemic and bleeding risk.

**Glycoprotein IIb/IIIa inhibitors**

Recommendations in this section update and replace ‘Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndrome’ (NICE technology appraisal guidance 47) for unstable angina and NSTEMI.

1.3.9 Consider offering intravenous eptifibatide or tirofiban\(^5\), in addition to aspirin, clopidogrel and an antithrombin, as part of the early management for patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality >3.0%), and who are scheduled to undergo early angiography (within 96 hours of hospital admission).

1.3.10 Consider offering abciximab as an adjunct to PCI to patients at intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality >3.0%) who are not already receiving a GPI.

1.3.11 Balance the potential reduction in a patient's ischaemic risk with any increased risk of bleeding, when determining whether a GPI should be offered.

**1.4 Antithrombin therapy**

1.4.1 Routinely offer fondaparinux in addition to aspirin and clopidogrel to patients who do not have a high bleeding risk.

1.4.2 Carefully consider the choice and dose of antithrombin in patients who have a high risk of bleeding associated with any of the following:

- advanced age

\(^5\) Eptifibatide and tirofiban are licensed for use with aspirin and unfractionated heparin. They do not have UK marketing authorisation for use with clopidogrel. This recommendation is therefore for an off-label use of these drugs. Informed consent should be obtained and documented before they are used in combination with clopidogrel.
• known bleeding complications
• renal impairment
• low body weight.

1.4.3 Consider unfractionated heparin, with dose adjustment guided by monitoring of clotting function, as an alternative to fondaparinux for patients with significant renal impairment (creatinine >265 micromoles per litre).

1.4.4 In the cardiac catheter laboratory, offer systemic unfractionated heparin (50–100 units/kg) to patients previously receiving fondaparinux who are undergoing PCI.

1.4.5 Do not use bivalirudin for the routine management of unstable angina or NSTEMI.

1.5 Management strategies

Early invasive versus conservative management

1.5.1 Offer coronary angiography within 96 hours of first admission to hospital to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality >3.0%) if they have no contraindications to angiography (such as active bleeding or comorbidity).

1.5.2 Offer conservative management without early coronary angiography to patients with a low risk of adverse cardiovascular events (predicted 6-month mortality ≤3.0%).

1.5.3 Offer coronary angiography to patients with a low risk of adverse cardiovascular events (predicted 6-month mortality ≤3.0%) if ischaemia is subsequently experienced or is demonstrated by ischaemia testing.
**Percutaneous coronary intervention versus coronary artery bypass grafting**

1.5.4 When advising patients about the choice of revascularisation strategy (PCI or CABG), take account of coronary angiographic findings, comorbidities, and the benefits and risks of each intervention.

1.5.5 When the place, or choice, of revascularisation is unclear, resolve this by discussion involving the patient, an interventional cardiologist, cardiac surgeon and other relevant healthcare professionals.

**Testing for ischaemia**

1.5.6 To detect and quantify inducible ischaemia, consider offering ischaemia testing before discharge to patients whose condition has been managed conservatively and who have not had coronary angiography.

**Assessing left ventricular function**

1.5.7 Assessment of left ventricular function is recommended in all patients who have had an MI. [This recommendation is from 'MI: secondary prevention' (NICE clinical guideline 48).]

1.5.8 Consider assessing left ventricular function in all patients with unstable angina.

1.5.9 Record measures of left ventricular function in the patient’s care record and in correspondence with the primary healthcare team and the patient.

**Rehabilitation and discharge planning**

1.5.10 Before discharge offer patients advice and information about::

- their diagnosis and arrangements for follow-up [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
- cardiac rehabilitation [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
management of cardiovascular risk factors and drug therapy for secondary prevention [in line with 'MI: secondary prevention' (NICE clinical guideline 48) and 'Lipid modification' (NICE clinical guideline 67)]

- lifestyle changes [in line with 'MI: secondary prevention' (NICE clinical guideline 48)]
- health education.

1.5.11 Cardiac rehabilitation should be equally accessible and relevant to all patients after an MI, particularly people from groups that are less likely to access this service. These include people from black and minority ethnic groups, older people, people from lower socioeconomic groups, women, people from rural communities and people with mental and physical health comorbidities. [This recommendation is from ‘MI: secondary prevention’ (NICE clinical guideline 48).]

1.5.12 All patients who smoke should be advised to quit and be offered support and advice, and referral to an intensive support service (for example, the NHS Stop Smoking Services) in line with 'Brief interventions and referral for smoking cessation in primary care and other settings' (NICE public health guidance 1). [This recommendation is adapted from ‘MI: secondary prevention’ (NICE clinical guideline 48).]

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from http://guidance.nice.org.uk/CG/Wave14/24.
How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a guideline development group (see appendix A), which reviewed the evidence and developed the recommendations. An independent guideline review panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website (www.nice.org.uk/guidelinesprocess). A booklet, ‘How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS’ (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1739).

3 Implementation

NICE has developed tools to help organisations implement this guidance (see www.nice.org.uk/CGXX).

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group’s full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Testing for ischaemia

4.1.1 What is the comparative efficacy and cost effectiveness of non-invasive tests (for example, stress ECG, echocardiography, radionuclide scanning, magnetic resonance imaging [MRI]) for the investigation of myocardial ischaemia in people suspected or known to have coronary artery disease?
Why this is important

An increasing number of non-invasive tests are now available for the investigation of suspected myocardial ischaemia. These tests need different equipment, different clinical expertise, come at different costs and may differ in their ability to detect and quantify myocardial ischaemia. Their place in the routine investigation of patients admitted with unstable angina and NSTEMI (particularly those who have not undergone angiography), compared with their selective use, is not clear. Management of unstable angina and NSTEMI would be enhanced if the relative place of these investigations was better understood and an assessment of their cost effectiveness made.

4.2 Risk assessment

4.2.1 What is the efficacy and cost effectiveness of the systematic use of risk scoring systems (in addition to clinical assessment) for ischaemic outcomes and bleeding complications in the management of unstable angina and NSTEMI (at all levels of risk) compared with clinical assessment alone?

Why this is important

Most risk scoring systems currently predict the likelihood of mortality or ischaemic cardiovascular events at various times after a patient's admission to hospital with an acute coronary syndrome. A number of interventions (such as drugs and revascularisation procedures) have been shown to reduce these adverse outcomes. This effect tends to be greatest in patients at highest risk. However, as a broad generalisation those who are at highest ischaemic risk are also those who are at higher risk of bleeding complications associated with the use of multiple antiplatelet and antithrombin agents. There are fewer scoring systems that predict bleeding risk, but we know that bleeding complications are associated with a significantly worse outcome. Use of a combination of scoring systems assessing ischaemic and bleeding risk when evaluating
data from randomised trials and registries may help to determine where the net clinical benefit (reduction in ischaemic risk minus any increase in bleeding risk) lies.

4.2.2 For patients with unstable angina and NSTEMI (at differing levels of risk), how do clinical outcome data (adverse cardiovascular events and bleeding complications) collected in cardiac registries compare with those derived from randomised clinical trials.

Why this is important
Patients recruited to participate in clinical trials are often highly selected; trials tend not to include patients who are very elderly, are at high risk, or have significant comorbidity. On the other hand, good registry data include information on all patients, but are obviously observational and not randomised. Often there is uncertainty about how the outcome data from randomised controlled trials (RCTs) can be applied to the much larger unselected population of patients admitted to UK hospitals with unstable angina and NSTEMI. A greater understanding of the differences between RCT and registry populations, and their levels of ischaemic and bleeding risk, would help inform future management. Collection of well-validated registry data is essential if conclusions from RCTs are to be applied appropriately to all patients with unstable angina and NSTEMI, and not just those patients who are comparable to trial populations.

5 Other versions of this guideline

5.1 Full guideline
The full guideline, ['Full guideline title' (in quotes, no italics)] contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for [add], and is available from [NCC website details to be added] and our website (www.nice.org.uk/CGXXfullguideline). [Note: these details will apply to the published full guideline.]

Acute coronary syndromes: NICE guideline DRAFT (July 2009) Page 16 of 23
5.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/CGXXquickrefguide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

5.3 ‘Understanding NICE guidance’

A summary for patients and carers (‘Understanding NICE guidance’) is available from www.nice.org.uk/CGXXpublicinfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about unstable angina and NSTEMI.

6 Related NICE guidance

Published


Under development
NICE is developing the following guidance (details available from www.nice.org.uk):

- Chest pain of recent onset. NICE clinical guideline. Publication expected February 2010.
- Stable angina. NICE clinical guideline. Publication expected July 2011.
- Laser transmyocardial revascularisation for refractory angina pectoris. NICE interventional procedure guidance. Publication date to be confirmed.
- Percutaneous laser revascularisation for refractory angina pectoris. NICE interventional procedure guidance. Publication date to be confirmed.

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.
Appendix A: The Guideline Development Group

Professor John Camm (Chair)
BHF Professor of Clinical Cardiology, St George’s, University of London

Dr Huon Gray (Clinical Advisor)
Clinical Advisor, National Clinical Guidelines Centre; Consultant Cardiologist, Southampton University Hospital

Mr Sotiris Antoniou
Principal Cardiac Pharmacist, Barts and the London NHS Trust; Lead Pharmacist for North East London Cardiac and Stroke Network

Ms Lina Bakhshi
Senior Information Scientist

Ms Jenny Cadman
Cardiac Rehabilitation Service Manager, Senior Nurse in Cardiology, Luton and Dunstable Hospital NHS Trust

Dr Emily Crowe
Senior Research Fellow, from May 2008

Dr Mark de Belder
Consultant Cardiologist, James Cook University Hospital, Middlesbrough

Dr Jose Diaz
Research Fellow, until May 2008

Mr David H Geldard
Patient and carer representative, Immediate Past President, Heart Care Partnership (UK)

Dr Robert Henderson
Consultant Cardiologist and Clinical Teacher, Nottingham University Hospitals
Ms Marjan Jahangiri
Professor of Cardiac Surgery, St George's University of London

Ms Taryn Krause
Senior Project Manager, from November 2008

Miss Kate Lovibond
Health Economist

Mr Gavin Maxwell
Patient and carer representative, Patient and Carer Network, Royal College of Physicians London

Dr Francis Morris
Accident and Emergency Physician, Sheffield Teaching Hospitals NHS Trust

Mr Alun Roebuck
Cardiology Nurse Consultant, Sunderland City Hospital

Ms Nicola Sloan
Research Fellow, July 2008 to March 2009

Ms Claire Turner
Senior Project Manager, until November 2008

Professor S Richard Underwood
Professor of Cardiac Imaging, Imperial College London

Mr Mark Whitbread
Clinical Practice Manager, Senior Paramedic, Cardiac Lead Medical Directorate, London Ambulance Service NHS Trust
Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

[NICE to add]

[Name; style = Unnumbered bold heading]
[job title and location; style = NICE normal]
Appendix C: The algorithms

The algorithms are in a separate file.