



Complete Summary

GUIDELINE TITLE

Management of acute coronary syndromes in patients presenting without persistent ST- segment elevation.

BIBLIOGRAPHIC SOURCE(S)

Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2002 Dec; 23(23): 1809-40. [218 references] [PubMed](#)

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SCOPE

DISEASE/CONDITION(S)

Acute coronary syndromes without persistent ST-segment elevation

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations on the management of patients with suspected acute coronary syndromes without persistent ST-segment elevation

TARGET POPULATION

Patients with suspected acute coronary syndromes without persistent ST-segment elevation

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Physical examination, including chest examination, auscultation, heart rate and blood pressure measurements
2. Resting electrocardiogram and multilead continuous ST-segment monitoring
3. Measurement of biochemical markers of myocardial damage, such as cardiac troponin T or troponin I, creatine kinase (CK) or its isoenzyme MB (CK-MB)

Risk Stratification

1. Risk factor assessment based on clinical markers, such as age, male sex, history of prior myocardial infarction, angina, or diabetes
2. Risk assessment based on biological markers, such as troponin levels and C-reactive protein levels and interleukin-6 (IL-6)
3. Coronary angiographic assessments
4. Electrocardiographic assessments
5. Echocardiographic assessments
6. Stress testing

NOTE: Currently, haemostatic markers are not recommended for risk stratification or selection of treatment in individual patients with unstable coronary artery disease (CAD).

Treatment

1. Anti-ischaemic agents, such as beta-blockers; nitrates; and calcium channel blockers (nifedipine, diltiazem, verapamil, amlodipine)
2. Anti-thrombin drugs, such as unfractionated heparin; low-molecular-weight heparins (dalteparin, enoxaparin), and direct thrombin inhibitors (hirudin)
3. Antiplatelet agents, such as aspirin; adenosine diphosphate receptor antagonists (ticlopidine, clopidogrel); and glycoprotein IIb/IIIa receptor blockers (abciximab, eptifibatide, tirofiban)

4. Fibrinolytic treatment (considered, but not recommended)
5. Coronary revascularization procedures
 - Coronary angiography
 - Percutaneous coronary interventions, such as balloon angioplasty, stent implantation
 - Coronary artery bypass surgery
 - Percutaneous coronary interventions and surgery

Long-Term Management

1. Risk factor modification
2. Long-term treatment with aspirin
3. Long-term beta-blocker therapy
4. Smoking cessation
5. Lipid-lowering therapy, such as hydroxymethylglutaryl coenzyme A reductase (HMG-CoA) inhibitors
6. Angiotensin-converting enzyme (ACE) inhibitors

MAJOR OUTCOMES CONSIDERED

- Prognostic value of diagnostic tests
- Death (mortality) rates
- Myocardial infarction rates
- Incidence of angina
- Thrombosis formation
- Symptom relief
- Recurrent or ongoing myocardial ischaemia/infarction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Strength of Evidence

- A. Data derived from at least two randomized clinical trials or meta-analyses
- B. Data derived from a single randomized trial and/or meta-analysis from non-randomized studies
- C. Consensus opinion of the experts based on trials and clinical experience

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Usefulness or Efficacy of a Recommended Treatment

Class I = Evidence and/or general agreement that a given treatment is beneficial, useful and effective

Class II = Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment

II a: weight of evidence/opinion is in favour of usefulness/efficacy

II b: usefulness/efficacy is less well established by evidence/opinion

Class III * = Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful.

* Use of Class III is discouraged by the ESC

COST ANALYSIS

Patients with left main or three-vessel disease, especially those with associated left ventricular dysfunction, are usually managed with coronary artery bypass graft (CABG) surgery. In this situation CABG is well documented to prolong survival, improve quality of life and reduce readmissions. Furthermore it is a more cost-effective alternative than percutaneous coronary intervention (PCI) because of better symptom relief and a decreased need for repeat interventions.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline document was extensively revised and circulated to the members of the European Society of Cardiology (ESC) Committee for Practice Guidelines (S. Priori [Chair], V. Dean, M.A. Alonso Garcia, J.J. Blanc, A. Budaj, M. Cowie, J. Deckers, J. Lekakis, B. Lindahl, E.Fernandez Burgos, G. Mazzotta, J. Morais, A.Oto, O. Smiseth, K. H. McGregor, D. Jumeau, C. Després), and to the Members of the ESC Board.

After further revision, it was submitted for approval to the ESC Committee for Practice Guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations are followed by a level of evidence rating (A-C), the definitions of which are repeated at the end of the Major Recommendations field.

Diagnosis

In patients with suspected acute ischaemic heart disease:

- An electrocardiogram (ECG) should be obtained at rest and multilead continuous ST-segment monitoring initiated (or frequent ECGs recorded where monitoring is unavailable).
- Troponin T or I should be measured on admission and, if normal, repeated 6 to 12 hours later.
- Myoglobin and/or creatine kinase isoenzyme MB (CK-MB) mass should be measured in patients with recent (<6 hours) symptoms as an early marker of myocardial infarction and in patients with recurrent ischaemia after recent (<2 weeks) infarction to detect further infarction.

Level of evidence: A

Risk Assessment

Risk assessment should be precise, reliable and, preferably, easily and rapidly available at low cost. The following methods are recommended:

- Markers of thrombotic risk, i.e., acute risk:
 - Recurrence of chest pain
 - ST-segment depression
 - Dynamic ST-segment changes
 - Elevated level of cardiac troponins
 - Thrombus on angiography

- Markers of underlying disease i.e., long-term risk:
 - Clinical markers
 - Age
 - History of prior myocardial infarction (MI), prior coronary artery bypass grafting (CABG), diabetes, congestive heart failure (CHF), hypertension
 - Biological markers
 - Renal dysfunction (elevated creatinine or reduced creatinine clearance)
 - Inflammatory markers, C-reactive protein (CRP) elevation, Fibrinogen elevation, interleukin-6 (IL-6) elevation
 - Angiographical markers
 - Left ventricular (LV) dysfunction
 - Extent of coronary artery disease

Level evidence for all markers: A

Treatment

Anti-ischaemic agents

Beta-blockers

- Beta-blockers are recommended in acute coronary syndrome (ACS) in the absence of contraindications; the intravenous route should be preferred in patients at high risk.

Level of evidence: B

There is no evidence that any specific beta-blocking agent is more effective in producing beneficial effects in unstable angina. If there are concerns regarding patient tolerance, for example in patients with pre-existing pulmonary disease, or left ventricular dysfunction a short-acting agent should be preferred for initial therapy. Initiation of parenteral beta-blocker therapy requires frequent monitoring of vital signs, and preferably continuous ECG monitoring. Oral therapy should subsequently be instituted to achieve a target heart rate between 50 and 60 beats per minute. Patients with significantly impaired atrioventricular conduction, a history of asthma, or of acute LV dysfunction should not receive beta-blockers.

Nitrates

- In patients with acute coronary syndrome who require hospital admission, intravenous nitrates may be considered in the absence of contraindications.

Level of evidence: C

The dose should be titrated upwards until symptoms are relieved or side effects (notably headache or hypotension) occur. A limitation of continuous nitrate therapy is the phenomenon of tolerance, which is related both to the dose administered and to the duration of treatment. When symptoms are

controlled, intravenous nitrates should be replaced by non-parenteral alternatives with appropriate nitrate-free intervals. An alternative is to use nitrate-like drugs, such as sydnonimines or potassium channel activators.

Potassium channel activators

No specific data are available in the use of potassium channel activators or acute coronary syndromes.

Calcium channel blockers

- Calcium channel blockers provide symptom relief in patients already receiving nitrates and beta-blockers; they are useful in some patients with contraindications to beta-blockade, and in the subgroup of patients with variant angina.
- Nifedipine, or other dihydropyridines, should not be used without concomitant beta-blocker therapy. Calcium channel blockers should be avoided in patients with significantly impaired left ventricular function or atrioventricular conduction.

Anti-thrombin therapy

Heparin and low-molecular-weight heparin (LMWH)

- In a meta-analysis of the effect of heparin added to aspirin among patients with unstable angina (six randomized trials), there was 7.9% rate of death or myocardial infarction in the aspirin + heparin group and 10.3% in the aspirin alone group (absolute risk reduction = 2.4%, odds ratio: 0.74 [95% confidence interval 0.5 to 1.09], P=0.10).

Level of evidence: B

Thus, these results do not provide conclusive evidence of benefit from adding heparin to aspirin, but it must be stressed that appropriately powered large scale trials have not been conducted. Nevertheless, clinical guidelines recommend a strategy including administration of unfractionated heparin with aspirin as a pragmatic extrapolation of the available evidence.

- There is convincing evidence in aspirin-treated patients that LMWH is better than placebo.

Level of evidence: A

- Two trials have provided data in favour of LMWH (enoxaparin) over unfractionated heparin when administered as an acute regimen. Acute treatment with low-molecular-weight heparins is at least as effective as unfractionated heparin.

Level of evidence: A

- For LMWHs overall it can be concluded that acute treatment is at least as effective as unfractionated heparin.

Level of evidence: A

Direct thrombin inhibitors

- In a combined analysis of clinical trials evaluating the use of the direct thrombin inhibitor hirudin, there was a 22% relative risk reduction in cardiovascular death or myocardial infarction at 72 hours, 17% at 7 days, and 10% at 35 days.

Level of evidence: B

This combined analysis is statistically significant at 72 hours and 7 days and of borderline significance at 35 days ($P=0.057$). Hirudin has been approved for patients with heparin-induced thrombocytopenia. None of the hirudins are currently licensed for acute coronary syndromes.

Management of bleeding complications related to antithrombin treatment

- Minor bleeding is usually treated by simply stopping the treatment. Major bleedings such as haematemesis, melaena or intracranial haemorrhage may require the use of heparin antagonists. The risk of inducing a rebound thrombotic phenomenon should be assessed for such patients on an individual basis. The anticoagulant and haemorrhagic effects of unfractionated heparin are reversed by an equimolar concentration of protamine sulfate, which neutralizes the antifactor IIa activity but results in only partial neutralization of the anti-factor Xa of low-molecular-weight heparin.

Antiplatelet agents

Aspirin

- Acute treatment with aspirin is recommended in all patients with suspected acute coronary syndromes in the absence of contraindications and for long-term treatment thereafter.

Level of evidence: A (for both acute and long-term treatment)

Adenosine diphosphate (ADP) receptor antagonists: Thienopyridines

- In acute coronary syndrome patients clopidogrel is recommended for acute treatment and for longer term treatment for at least 9-12 months.

Level of evidence: B

Beyond this level of evidence, treatment will depend on the risk status of the patient and individual clinical judgement. Clopidogrel should be given to acute coronary syndrome patients scheduled for angiography unless there is a likelihood that the patient will proceed to urgent surgery (within 5 days).

- Clopidogrel may also be recommended for immediate and long-term therapy in patients who do not tolerate aspirin, and is recommended in patients receiving a stent.

Level of evidence: B

Glycoprotein IIb/IIIa receptor inhibitors

- Activated glycoprotein IIb/IIIa receptor inhibitors connect with fibrinogen to form bridges between activated platelets, leading to formation of platelet thrombi. Direct inhibitors of the glycoprotein IIb/IIIa receptors have been developed, and have been tested in various conditions where platelet activation plays a major role, in particular in patients undergoing percutaneous coronary intervention (PCI), patients admitted with acute coronary syndromes, and patients receiving thrombolytic therapy for acute myocardial infarction.

Glycoprotein IIb/IIIa receptor blockers and percutaneous coronary intervention (PCI)

- In patients undergoing percutaneous coronary intervention (PCI) concomitant administration of glycoprotein IIb/IIIa receptor blockers consistently reduces thrombotic complications, in particular periprocedural myocardial infarction.
- Treatment with a glycoprotein IIb/IIIa receptor blocker is recommended in all patients with acute coronary syndromes undergoing percutaneous coronary intervention.

Level of evidence: A

The infusion should be continued for 12 hours (abciximab) or 24 hours (eptifibatide, tirofiban) after the procedure.

Glycoprotein IIb/IIIa receptor inhibitors in acute coronary syndromes

- Overall, treatment with a glycoprotein IIb/IIIa receptor blocker in addition to aspirin and weight adjusted low dose heparin should be considered in all patients with acute coronary syndromes and an elevated troponin T or troponin I level, who are scheduled for early revascularization.

Level of evidence: A

There was no benefit for patients with negative troponins.

- Glycoprotein IIb/IIIa blockers are recommended, in particular in patients with diabetes and an acute coronary syndrome.

Glycoprotein IIb/IIIa receptor inhibitors and coronary artery bypass surgery

- Inhibition of platelet aggregation may result in bleeding complications, either spontaneously or at the time of cardiac surgery. However, surgery in patients receiving such drugs has been shown to be safe when appropriate measures

are taken to ensure adequate homeostasis. Glycoprotein IIb/IIIa receptor blockers should be discontinued before (4 hours) or at the time of cardiac surgery. Eptifibatide and tirofiban have a short half-life, so that platelet function is recovered, at least partly, at the end of the procedure when haemostasis is necessary. Abciximab has a longer effective half-life. If excessive bleeding occurs in patients previously receiving abciximab, fresh platelet transfusions may be administered.

Management of complications related to administration of glycoprotein IIb/IIIa inhibitors

- With antiplatelet drugs and particularly with glycoprotein IIb/IIIa receptor inhibitors the bleeding risk is clearly related to the dose of adjunctive heparin and specific reduced dosing schedules are recommended.
- In the setting of percutaneous coronary intervention, it is recommended to significantly restrict the doses of heparin to $70 \text{ IU} \cdot \text{kg}^{-1}$ with a target activated clotting time of 200 s. When local complications such as important haematoma or continuous bleeding at the puncture site occur, surgical intervention may be required.
- Thrombocytopenia may occur in a small percentage of patients during administration of parenteral glycoprotein IIb/IIIa receptor inhibitors. Stopping treatment usually results in a return to normal platelet levels. Re-administration might be an issue for abciximab, due to its inherent immunogenicity. In practice, the re-administration registry shows similar safety and efficacy for repeat administration as compared with first time administration.

Fibrinolytic treatment

- Thrombolytic therapy is not recommended for patients with acute coronary syndromes without persistent ST-segment elevation.

Coronary revascularization

Revascularization (either percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG] for unstable coronary artery disease) is performed to treat recurrent or ongoing myocardial ischaemia and to avoid progression to myocardial infarction or death. The indications for myocardial revascularization and the preferred approach depend on the extent and angiographic characteristics of the lesions identified by coronary angiography.

Refer to the original guideline document for a discussion of coronary angiography, percutaneous coronary interventions, and coronary artery bypass surgery as well as respective indications for percutaneous coronary intervention or surgery.

Invasive treatment strategy vs. conservative strategy

- It appears that a modern invasive strategy, preceded by modern anti-ischaemic and antithrombotic medication, in high-risk patients with unstable coronary artery disease reduces death, myocardial infarction, symptoms and readmissions compared to a conservative strategy.

Level of evidence: A

Management Strategy in Acute Coronary Syndromes

Initial assessment at presentation

In most patients only chest discomfort (chest pain) might be present and suspicion of acute coronary syndrome is only a working diagnosis. The initial assessment includes the following steps:

- It is important to obtain a careful history and a precise description of the symptoms. A physical examination with particular attention to the possible presence of valvular heart disease (aortic stenosis), hypertrophic cardiomyopathy, heart failure, and pulmonary disease is required.
- An ECG is recorded: comparison with a previous ECG, if available, is very valuable, particularly in patients with pre-existing cardiac pathology such as left ventricular hypertrophy or known coronary disease. The ECG allows differentiation of patients with a suspicion of acute coronary syndromes in two categories requiring different therapeutic approaches:
 - ST-segment elevation signifies complete occlusion of a major coronary artery and immediate reperfusion therapy is usually indicated. This represented 42% of the cases in the European Heart Survey on acute coronary syndromes. Management of these patients falls outside the scope of this guideline and is addressed in the European Society Guidelines on Acute Myocardial Infarction.
 - ST-segment changes but without persistent ST-segment elevation or a normal ECG (51% of cases).
 - In a few cases (7%), there is no definite characterization and there are undetermined ECG changes such as bundle branch block or pacemaker rhythm.
- In the latter two cases, biochemical markers are required for further characterization: Laboratory assessments should include haemoglobin (to detect anaemia) and markers of myocardial damage, preferably cardiac troponin T or cardiac troponin I. If concentrations of troponins or cardiac enzymes rise, irreversible cell damage will have occurred and these patients must be regarded as having had myocardial infarction according to the definition of the consensus conference.
- Then starts an observational period, which includes a multi-lead ECG ischaemia monitoring. If the patient experiences a new episode of chest pain, a 12-lead ECG should be obtained and compared with a tracing obtained when symptoms have resolved spontaneously or after nitrates. In addition an echocardiogram may be recorded to assess left ventricular function and to eliminate other cardiovascular causes of chest pain. Finally, a second troponin measurement should be obtained after 6 to 12 hours.
- Patients can then be classified as acute coronary syndromes, distinguishing myocardial infarction (with elevated markers of necrosis), and unstable angina (ECG changes but no signs of necrosis) with a remaining group of other disease or as yet undetermined cause of their symptoms.
- Once diagnosed, acute coronary syndromes without persistent ST-segment elevation (ST-segment depression, negative T waves, pseudonormalization of T waves or normal ECG) require an initial medical treatment including aspirin 75 to 150 mg daily, clopidogrel (once registered for this indication), low-

- molecular-weight heparin or unfractionated heparin, beta-blocker and oral or intravenous nitrates in cases of persistent or recurrent chest pain. Clopidogrel should replace aspirin in patients with hypersensitivity or major gastrointestinal intolerance to aspirin. Calcium antagonists may be preferred over beta-blockers in those patients who have contraindications to, or who are known not to tolerate, a beta-blocker. In the subsequent observation period (6 to 12 hours) specific attention should be given to recurrence of chest pain during which an ECG will be recorded. Signs of haemodynamic instability should be carefully noted (hypotension, pulmonary rales) and treated.
- Within this initial period risk assessment can be performed based on the clinical, electrocardiographic and biochemical data, and further treatment strategy can be selected (see figure 9 in the original guideline document). Risk stratification can identify two groups of patients: high-risk and low-risk patients.

Strategies according to risk stratification

High-risk patients

Patients judged to be a high risk for progression to myocardial infarction or death include those:

- with recurrent ischaemia (either recurrent chest pain or dynamic ST-segment changes, in particular ST-segment depression, or transient ST-segment elevation)
- with early post-infarction unstable angina
- with elevated troponin levels
- who develop haemodynamic instability within the observation period
- with major arrhythmias (repetitive ventricular tachycardia, ventricular fibrillation)
- with diabetes mellitus
- with an ECG pattern which precludes assessment of ST-segment changes

In these patients the following strategy is recommended:

- While waiting and preparing for angiography, treatment with low-molecular-weight heparin should be continued. Administration of glycoprotein IIb/IIIa receptor inhibitor will be started and continued for 12 (abciximab) or 24 (tirofiban, eptifibatide) hours after the procedure if angioplasty is performed.
- Coronary angiography should be planned as soon as possible, but without undue urgency. A relatively small group of patients will require a coronary angiogram within the first hour. This includes patients with severe ongoing ischaemia, major arrhythmias, haemodynamic instability. In most cases coronary angiography is performed within the 48 hours, or at least within hospitalization period. In patients with lesions suitable for myocardial revascularization, the decision regarding the most suitable procedure will be made after careful evaluation of the extent and characteristics of the lesions, where appropriate, in consultation with surgical colleagues. In general, recommendations for the choice of a revascularization procedure in unstable angina are similar to those for elective revascularization procedures. In patients with single vessel disease, percutaneous intervention of the culprit lesion is the first choice. In patients with left main- or triple-vessel disease,

coronary artery bypass grafting (CABG) is the recommended procedure, particularly in patients with left ventricular dysfunction, except in cases of serious co-morbidity, which contraindicates surgery. In double-vessel and in some cases of triple-vessel coronary disease, either percutaneous intervention or coronary bypass surgery may be appropriate. In some patients, a staged procedure may be considered, with immediate balloon angioplasty and stenting of the culprit lesion and subsequent reassessment of the need for treatment of other lesions, either by a percutaneous procedure or coronary artery bypass grafting (CABG). If percutaneous intervention is the selected procedure, it may be performed immediately after angiography in the same session.

- Patients with suitable lesions for percutaneous coronary intervention will receive clopidogrel. In patients planned for CABG clopidogrel will be stopped, except if the operation is deferred. In that case, clopidogrel should be stopped about 5 days before operation.
- If angiography reveals no options for revascularization, owing to the extent of the lesions and/or poor distal run-off, or reveals no major coronary stenosis, patients will be referred for medical therapy. The diagnosis of an acute coronary syndrome may need to be reconsidered and particular attention should be given to possible other reasons for the presenting symptoms. However, the absence of significant stenosis does not preclude the diagnosis of an acute coronary syndrome. In selected patients, an ergonovin test may detect or rule out excessive coronary vasoconstriction.

Low-risk patients

Patients considered to be at low risk for rapid progression to myocardial infarction or death include those:

- who have no recurrence of chest pain within the observational period
- without ST-segment depression or elevation but rather negative T waves, flat T waves or normal ECG
- without elevation of troponin or other biochemical markers of myocardial necrosis on the initial and repeat measurement (performed between 6 to 12 hours)

In these patients the strategy is as follows:

- Oral treatment should be recommended, including aspirin, clopidogrel (loading dose of 300 mg followed by 75 mg daily), beta-blockers and possibly nitrates or calcium antagonists.
- Secondary preventive measures should be instituted as discussed below (under Long-Term Management). Low-molecular-weight heparin may be discontinued when, after the observation period, no ECG changes are apparent and a second troponin measurement is negative.
- A stress test is recommended. The purpose of such a test is first, to confirm or establish a diagnosis of coronary artery disease and when this is yet uncertain, second, to assess the risk for future events in patients with coronary artery disease.
- In patients with significant ischaemia during the stress test, coronary angiography and subsequent revascularization, should be considered, particularly when this occurs at a low workload on the bicycle or treadmill. It

should be appreciated that a standard exercise test may be inconclusive (no abnormalities at a relatively low workload). In such patients an additional stress echocardiogram, or stress myocardial perfusion scintigram may be appropriate.

- In some patients, the diagnosis may remain uncertain, particularly in patients with a normal electrocardiogram throughout the observation period, without elevated markers of myocardial necrosis, and with a normal stress test and good exercise tolerance. The symptoms resulting in presentation to the hospital were probably not caused by myocardial ischaemia, and additional investigations of other organ systems may be appropriate. In any case, the risk for cardiac events in such patients is very low. Therefore, additional tests can usually be performed at a later time, at the outpatient clinic.

Long-Term Management

- Aggressive and extensive risk factor modification is warranted in all patients following diagnosis of acute coronary syndrome.
- It is mandatory that patients quit smoking: patients should be clearly informed that smoking is a major risk factor. Referral to smoking cessation clinics is recommended, and the use of nicotine replacement therapy should be considered.
- Blood pressure control should be optimized.
- Aspirin should be prescribed (75-150 mg).
- Clopidogrel 75 mg should be prescribed for at least 9, possibly 12 months, and the dose of aspirin should be reduced to 75-100 mg.
- Beta-blockers improve prognosis in patients after myocardial infarction and should be continued after acute coronary syndromes.
- Lipid lowering therapy should be initiated without delay.
- A role for angiotensin-converting enzyme (ACE) inhibitors in secondary prevention of coronary syndromes has been suggested.
- Since coronary atherosclerosis and its complications are multifactorial, much attention should be paid to treat all modifiable risk factors in an effort to reduce recurrence of cardiac events.

Definitions:

Strength of Evidence

- A. Data derived from at least two randomized clinical trials or meta-analyses
- B. Data derived from a single randomized trial and/or meta-analysis from non-randomized studies
- C. Consensus opinion of the experts based on trials and clinical experience

CLINICAL ALGORITHM(S)

An algorithm is provided for the recommended management strategy in acute coronary syndromes.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Acute coronary syndromes are a major healthcare problem and represent a large number of hospitalizations annually throughout Europe. The results of recent clinical trials indicate that a clinical strategy, which incorporates careful risk stratification in conjunction with novel therapeutic agents and revascularization in adequately selected patients, may help to improve both immediate and long-term outcome in patients with acute coronary syndromes.

POTENTIAL HARMS

Nitrates

- Side effects include headache and hypotension.

Calcium channel blockers

- Phenylalkylamines (such as verapamil) may induce atrioventricular block.
- Several analyses that pooled data from observational studies suggest that short-acting nifedipine might be associated with a dose-dependent detrimental effect on mortality in patients with coronary artery disease.

Antithrombin drugs

- Heparin (unfractionated or low-molecular-weight) and direct thrombin inhibitors (hirudin) can cause major bleeding, such as haematemesis, melaena, or intracranial haemorrhage.
- Heparin can induce thrombocytopenia.

Aspirin

- Gastrointestinal side effects are relatively infrequent with low doses of aspirin. Allergy is rare.

Clopidogrel

- There is a risk of both major and minor bleeding episodes during clopidogrel use.

Glycoprotein IIb/IIIa inhibitors

- Bleeding, haematoma, and thrombocytopenia can occur with this class of drugs. Bleeding risk is clearly related to the dose of adjunctive heparin and specific reduced dosing schedules are recommended.

Balloon angioplasty/Percutaneous coronary interventions

- Balloon angioplasty induces plaque disruption and can enhance the thrombogenicity of the plaque. Even with adjunctive glycoprotein IIb/IIIa inhibitors, there are about 5% of procedure-related myocardial infarctions.

Coronary artery bypass surgery

- This procedure is associated with a low risk of mortality. Perioperative mortality and morbidity are higher in patients with severe unstable angina and in patients with unstable angina after a recent (<7 days) myocardial infarction.

Subgroups Most Likely to be Harmed:

- Calcium channel blockers should be avoided in patients with significantly impaired left ventricular function or atrioventricular conduction. Nifedipine, or other dihydropyridines, should not be used without concomitant beta-blocker therapy.
- Minor bleeds were considerably more common for the elderly and females, receiving abciximab, who constitute the greatest risk.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Beta-blockers are contraindicated in patients with significantly impaired atrioventricular conduction, a history of asthma, or of acute left ventricular dysfunction.
- Aspirin is contraindicated in individuals with allergy, active peptic ulcer, local bleeding or haemorrhagic diatheses.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are based upon evidence resulting from many clinical trials. However, these trials were restricted to selected populations with different clinical characteristics which may not reflect those seen in actual clinical practice. Furthermore, it should be appreciated that this topic is a rapidly moving field; the present guidelines reflect current knowledge and were revised in the light of additional data presented in late 2000 and during 2001.
- Specific findings in individual patients may and should result in deviation from the proposed strategy. For every patient, the physician should make an individual decision taking into account the patient's history, his presentation, findings during observation or investigation in hospital, and the available treatment facilities. The guidelines should be used as guidelines, which will apply to the majority of cases, while other choices may be more appropriate in individual patients or in specific local circumstances.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation meetings are being organized, at the national level, in several European countries with the help of their specific National Society of Cardiology.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2002 Dec; 23(23):1809-40. [218 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Sep (revised 2002 Dec)

GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society

SOURCE(S) OF FUNDING

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GUIDELINE COMMITTEE

European Society of Cardiology (ESC) Task Force on the Management of Acute Coronary Syndromes

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Michel E. Bertrand, Chair; Maarten L. Simoons; Keith A. A. Fox; Lars C. Wallentin; Christian W. Hamm; Eugene McFadden; Pim J. De Feyter; Giuseppe Specchia; Witold Ruzyllo

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Albanian Society of Cardiology - Medical Specialty Society
Belgian Society of Cardiology - Medical Specialty Society
British Cardiac Society - Medical Specialty Society
Bulgarian Society of Cardiology - Medical Specialty Society
Czech Society of Cardiology - Medical Specialty Society
Danish Society of Cardiology - Medical Specialty Society
Estonian Cardiac Society - Medical Specialty Society
Finnish Cardiac Society - Medical Specialty Society
French Society of Cardiology - Medical Specialty Society
German Society of Cardiology - Medical Specialty Society
Hellenic Cardiological Society - Medical Specialty Society
Italian Federation of Cardiology - Medical Specialty Society
Latvian Society of Cardiology - Medical Specialty Society
Lebanese Society of Cardiology - Medical Specialty Society
Lithuanian Society of Cardiology - Medical Specialty Society
Macedonian Society of Cardiology - Medical Specialty Society
Polish Cardiac Society - Medical Specialty Society
Portuguese Society of Cardiology - Medical Specialty Society
San Marino Society of Cardiology - Medical Specialty Society
Slovak Society of Cardiology - Medical Specialty Society
Slovenian Society of Cardiology - Medical Specialty Society
Spanish Society of Cardiology - Medical Specialty Society
Swiss Society of Cardiology - Medical Specialty Society
Ukrainian Society of Cardiology - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, de Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes: acute coronary syndromes without persistent ST segment elevation; recommendations of the Task Force of the European Society of Cardiology. Eur Heart J 2000 Sep;21(17):1406-32.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [European Society of Cardiology \(ESC\) Web site](#).

Print copies: Available from Elsevier Science Ltd. European Heart Journal, ESC Guidelines - Reprints, 32 Jamestown Road, London, NW1 7BY, United Kingdom. Tel: +44.207.424.4422; Fax: +44 207 424 4515; Web site: www.eurheartj.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Recommendations for Task Force creation and report production. Sophia Antipolis (France): European Society of Cardiology, 2002.

Electronic copies: Available in Portable Document Format (PDF) from the [European Society of Cardiology \(ESC\) Web site](#).

- Guidelines on management of acute coronary syndromes in patients presenting without ST-segment elevation. Pocket guidelines. Sophia Antipolis (France): European Society of Cardiology, 2002.

Electronic copies: An order form for ESC pocket guidelines is available in Portable Document Format (PDF) from the [European Society of Cardiology \(ESC\) Web site](#).

- Guidelines on management of acute coronary syndromes in patients presenting without ST-segment elevation. Educational slides. Sophia Antipolis (France): European Society of Cardiology, 2001.

Electronic copies: Available in Microsoft PowerPoint from the [European Society of Cardiology \(ESC\) Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 17, 2001. The information was verified by the guideline developer on September 27, 2001. This summary was updated by ECRI on April 16, 2003.

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