Ischaemic heart disease: management of non-ST-elevation acute coronary syndrome

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Abstract

Non-ST segment elevation acute coronary syndrome (NSTE-ACS) is a clinical diagnosis based on history, electrocardiogram and serum biomarker concentration. A diagnosis of myocardial infarction requires the detection of a rise and/or fall of cardiac biomarker concentration with at least one value above the upper reference limit, and at least one feature of myocardial ischaemia such as typical symptoms or electrocardiographic abnormality. High-sensitivity assays allow earlier detection of lower concentrations of troponin but specificity has decreased and raised serum troponin is now detected in conditions other than acute coronary syndrome.

Patients with NSTE-ACS are at increased risk of adverse cardiovascular outcomes, and should be risk stratified with an established risk scoring system (e.g. GRACE) to identify those likely to benefit from evidence-based treatments. Patients with NSTE-ACS should be offered aspirin and an anticoagulant unless these are contraindicated by bleeding risk. An ADP-receptor antagonist should be offered to all patients with a predicted 6-month mortality >1.5%. Glycoprotein IIb/IIIa receptor inhibitors reduce the risk of ischaemic events but increase the risk of bleeding, and clinical judgement remains important in determining when these agents should be used. A routine invasive strategy (coronary angiography and revascularization in those with suitable coronary anatomy) improves outcome in patients at high risk and is recommended for all patients with a predicted 6-month mortality >3% and no contraindications (such as active bleeding or comorbidity). All patients with a confirmed diagnosis of NSTE-ACS should be offered high-intensity statin therapy.

Keywords Acute coronary syndrome; antiplatelet therapy; anticoagulant; coronary angiography; coronary artery bypass surgery; myocardial infarction; percutaneous coronary intervention; unstable angina

What's new?

In patients with NSTE-ACS:

- Increasingly sensitive troponin assays can detect lower concentrations of troponin earlier in the course of an acute coronary syndrome but specificity has decreased and elevated serum troponin is now detected in many conditions that mimic ACS
- The Third Universal Definition defines myocardial infarction as evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. This definition requires the detection of a rise and/or fall of cardiac biomarker concentration with at least one value above the upper reference limit, and at least one feature of myocardial ischaemia such as typical symptoms or electrocardiographic abnormality
- Risk scoring systems can identify patients at high risk who benefit most from pharmacological treatment and revascularization
- High-dosage statin is recommended for all patients with NSTE-ACS

Epidemiology

Acute coronary syndromes (ACS) include unstable angina and myocardial infarction, and present a global healthcare challenge. The age-standardized incidence of acute myocardial infarction varies geographically and has fallen over recent years but is estimated to lie between 2 and 5 per 1000 per annum.[1,2] Factors decreasing the reported incidence, including the impact of statins and anti-smoking legislation, are countered by changes in diagnostic criteria, population ageing, and the epidemic of obesity and diabetes.[2,3] The incidence rate is higher for non-ST-segment elevation ACS (NSTE-ACS) and these patients have higher longer-term mortality than patients with ST-segment elevation myocardial infarction, probably reflecting an adverse risk factor profile.[4]

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Pathophysiology

Most cases of ACS are mediated by inflammatory processes within the atherosclerotic coronary plaque that predispose to plaque disruption and coronary thrombosis. Obstruction of epicardial blood flow or downstream embolism of thrombus causes myocardial necrosis, releasing cardiac biomarkers into the circulation. Other pathogenetic mechanisms of ACS include superficial endothelial erosion and, rarely, disruptive nodular calcification.[5]

Non-atherosclerotic causes of ACS include:

- spontaneous coronary artery dissection
- coronary artery spasm
- cocaine abuse
- coronary embolism
- coronary inflammation
- coronary artery trauma (including complications of cardiac catheterization)
- congenital coronary artery anomaly.

Clinical assessment

Patients with ACS typically present with retrosternal pain or discomfort at rest (>20 minutes), which may radiate to the neck, jaw or arms. Associated symptoms may include sweating, nausea, dyspnoea or syncope. Atypical presentations are common, especially in young, elderly or female patients, or in those with diabetes, renal failure, or dementia.

Clinical examination is often normal but signs of heart failure or haemodynamic instability indicate a worse prognosis. Conditions

that exacerbate myocardial ischaemia (e.g. anaemia, fever, thyrotoxicosis) should be sought and other conditions that may mimic non-ST-segment elevation ACS should be excluded (Table 1).

Investigations

Electrocardiography

An electrocardiogram (ECG) should be recorded within 10 minutes of presentation with suspected ACS to identify patients with persistent (>20 minutes) ST-segment elevation or new left bundle branch block who are eligible for reperfusion therapy (primary angioplasty or fibrinolysis). Patients with NSTE-ACS may have ST-segment depression, transient ST-segment elevation or T-wave abnormalities, but the ECG can also be normal. Comparison with a previous ECG and right ventricular (V_4R, V_3R) or posterior leads ($V_{7–9}$) can be helpful.

Serum troponin

Serum concentrations of cardiac troponin T and I may be elevated within hours of the onset of ACS and are markers of myocardial cell necrosis. High sensitivity troponin assays with an upper reference limit <0.01 ng/mL allow early detection of low concentrations of serum troponin, and the proportion of patients with ischaemic symptoms at rest but without evidence of myocardial necrosis (unstable angina) is steadily decreasing.[6] However, as sensitivity has increased, specificity has decreased and elevated serum troponin can now be detected in patients with a range of other cardiac and non-cardiac conditions (Table 2).

Diagnosis

The diagnosis of NSTE-ACS is based on clinical assessment, ECG findings and serum cardiac biomarker concentration. The Third Universal Definition defines myocardial infarction as evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. This definition requires the detection of a rise and/or fall of cardiac biomarker concentration with at least one value above the upper reference limit, and at least one feature of myocardial ischaemia such as typical symptoms or electrocardiographic abnormality.[7]

Prognosis and risk stratification

Patients with NSTE-ACS have a high risk of recurrent myocardial ischaemia, myocardial infarction and death, especially within a few days of presentation. In a large multinational ACS registry, 6-month mortality was 12% for patients with ST elevation, 11% for patients with ST depression and 5% for patients without ST deviation.[4]

Factors associated with adverse cardiovascular outcome in patients with NSTE-ACS include:

- advanced age
- heart rate
- blood pressure
- ECG abnormality
- elevated serum cardiac biomarker
- arrhythmia
- left ventricular function
- renal function
- diabetes mellitus
- anaemia, major bleeding, and blood transfusion
- cerebrovascular and peripheral vascular disease.

Single risk factors do not reliably indicate risk in individual patients with NSTE-ACS (Figure 1) and physicians often do not assimilate the most important markers of risk into clinical assessment.[8,9] Risk scoring tools (e.g. GRACE) that combine multiple variables have therefore been developed to accurately identify patients at high risk of ischaemic or bleeding events (Table 3).[10,11] Guidelines recommend that all patients with NSTE-ACS are assessed using an established risk scoring system and in the United Kingdom the National Institute for Health and Care Excellence (NICE) recommends risk stratification according to predicted 6-month mortality.[1,12]

Management

Patients with suspected NSTE-ACS should be given sublingual glyceryl trinitrate and intravenous opioid for analgesia, and admitted to hospital for further assessment. Patients with a confirmed diagnosis of NSTE-ACS should be offered pharmacological treatment including anti-ischaemic therapy, antiplatelet therapy and anticoagulation (Table 4).

Anti-ischaemic therapy

Anti-ischaemic drugs decrease myocardial oxygen consumption (by lowering heart rate, blood pressure, myocardial contractility, or ventricular preload) and/or increase myocardial oxygen supply (by coronary vasodilatation).

Cardiac and non-cardiac conditions that can mimic non-ST-elevation acute coronary syndromes

Cardiac	Pulmonary	Haematological	Vascular	Gastrointestinal	Orthopaedic/Infectious
Myocarditis	Pulmonary embolism	Sickle cell crisis	Aortic dissection	Oesophageal spasm	Cervical discopathy
Pericarditis	Pulmonary infarction	Anaemia	Aortic aneurysm	Oesophagitis	Rib fracture
Cardiomyopathy	Pneumonia		Cerebrovascular disease	Peptic ulcer	Muscle injury/inflammation
Valvular disease	Pleuritis			Pancreatitis	Costochondritis
Takotsubo cardiomyopathy	Pneumothorax			Cholecystitis	Herpes zoster

Source: Hamm CW, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the task force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011; **32**: 2999–3054. With kind permission of the European Society of Cardiology.

Table 1