Acute coronary syndrome

Acute coronary syndrome (ACS) is a medical emergency and requires immediate hospital admission. ACS is now classified mainly on the findings on the admission ECG and the results of serial cardiac troponin levels [1]. ACS refers to a range of acute myocardial ischaemic states, which include [2]:

- ST-elevation ACS (STE-ACS): patients present with acute chest pain and persistent (>20 minutes) ST-segment elevation. Most of these patients will develop an ST-elevation myocardial infarction (STEMI).
- Non-ST-elevation ACS (NSTE-ACS): patients present with acute chest pain but without persistent ST-segment elevation. The ECG shows persistent or transient ST-segment depression or T-wave inversion, flat T waves, pseudo-normalisation of T waves, or no ECG changes at presentation. NSTE-ACS is further divided into:
    - Unstable angina: normal troponin levels.
    - Non-ST-elevation myocardial infarction (NSTEMI): a rise in troponin levels.

This article refers mainly to unstable angina and NSTEMI. STEMI is discussed in the separate Acute Myocardial Infarction, Acute Myocardial Infarction Management, Complications of Acute Myocardial Infarction and Posterior Myocardial Infarct articles. There is also a separate Stable Angina article.

Epidemiology

See also the separate Epidemiology of Coronary Heart Disease article.

- The diagnosis of NSTEMI is more difficult to establish than STEMI and therefore its prevalence is harder to estimate [2].

- In 2014/2015 the UK National Registry recorded 83,842 admissions to NHS hospitals in England and Wales, Northern Ireland and Isle of Man with acute myocardial infarction. Of these, STEMI and NSTEMI comprised 40.5% and 59.5%, respectively. These proportions had not changed in the preceding five years [3].
- Coronary heart disease is the single biggest cause of death in the UK as well as being a major cause of premature mortality [4].

Risk factors

- Non-modifiable risk factors for atherosclerosis: increasing age, male, family history of premature coronary heart disease, premature menopause.
- Modifiable risk factors for atherosclerosis: smoking, diabetes mellitus (and impaired glucose tolerance), hypertension, dyslipidaemia (raised low-density lipoprotein (LDL) cholesterol, reduced high-density lipoprotein (HDL) cholesterol), obesity, physical inactivity.
- Consider non-atherosclerotic causes in younger patients or if there is no evidence of atherosclerosis: coronary emboli from sources such as an infected cardiac valve, coronary occlusion secondary to vasculitis, coronary artery spasm, cocaine use, congenital coronary anomalies, coronary trauma, increased oxygen requirement (eg, hyperthyroidism) or decreased oxygen delivery (eg, severe anaemia).

Presentation

- The presentation of unstable angina and NSTEMI may be indistinguishable, and also indistinguishable from acute STEMI. NSTE-ACS can present in a variety of ways, including [2]:
    - Prolonged (longer than 20 minutes) anginal pain at rest.
    - New-onset angina with limitation of daily activities.
    - Recent destabilisation of previously stable angina, with moderate or severe limitation of daily activities.
    - Post-myocardial infarction angina.

- Chest pain may be associated with sweating, nausea, vomiting, fatigue, shortness of breath and palpitations.
- Some patients, particularly the elderly and patients with diabetes, may not have chest pain. Patients from some ethnic groups may also present with atypical pains.
- Physical examination is focused on the assessment of cardiac function and circulatory stability and on excluding important differential diagnoses.

Assessment for possible acute coronary syndrome[5]

See also the separate Cardiac-type Chest Pain Presenting in Primary Care article.

- Consider the history of the pain, any cardiovascular risk factors, history of coronary heart disease and any previous treatment, and previous investigations for chest pain.
- Symptoms that may indicate ACS include:
    - Pain in the chest and/or other areas (eg, the arms, back or jaw) lasting longer than 15 minutes.
    - Chest pain with nausea and vomiting, marked sweating and/or breathlessness, or haemodynamic instability.
    - New-onset chest pain, or abrupt deterioration in stable angina, with recurrent pain occurring frequently with little or no exertion and often lasting longer than 15 minutes.
- The response to glyceryl trinitrate (GTN) should not be used to make a diagnosis and symptoms should not be assessed differently in men and women or among different ethnic groups.

Differential diagnosis

See also the separate Chest Pain article.

- Cardiovascular: acute pericarditis, myocarditis, aortic stenosis, aortic dissection, pulmonary embolism.

- Respiratory: pneumonia, pneumothorax.
- Gastrointestinal: oesophageal spasm, gastro-oesophageal reflux disease, acute gastritis, cholecystitis, acute pancreatitis.
- Musculoskeletal chest pain.

Investigations

It is essential to exclude a myocardial infarction with ST elevation for which immediate thrombolysis is indicated.

- 12-lead ECG:
    - To confirm a cardiac basis for presentation and may show pre-existing structural or coronary heart disease (eg, left ventricular hypertrophy, Q waves).
    - A normal or unchanged ECG does not exclude the possibility that chest pain is ischaemic in origin.
    - Changes that may be seen during episodes of angina include transient ST-segment elevations (fixed changes suggest acute infarction).
    - In unstable angina (and non-Q wave infarction), the ECG typically shows T-wave inversion or ST-segment depression; however, the ECG may be normal if some time has elapsed since the last episode of pain.

- Cardiac enzymes:
    - Within the first six hours, the sensitivity of troponins is superior to CK-MB for the detection of myocardial infarction.
    - Troponin I and T become detectable in serum three to six hours after infarction, peak at 12-24 hours, and remain raised for up to 14 days.
    - Troponins are therefore usually tested six and 12 hours after the onset of pain.
    - In patients with unstable angina, minor troponin elevations may identify patients at risk for subsequent cardiac events and death. Elevated troponin levels indicate an increased risk of mortality in both the short term and the long term. Patients with chest pain and elevated troponin levels should remain in hospital for further assessment, including an inpatient coronary angiogram.
    - Offer immediate coronary angiography to patients with unstable angina or NSTEMI if their clinical condition is unstable.
- FBC may be useful in patients with suspected anaemia and as a baseline in view of use of anticoagulants; blood glucose, renal function and electrolytes, and TFTs. CRP as a marker of acute inflammation.
- Blood glucose: hyperglycaemia is common in people admitted to hospital with ACS. Hyperglycaemia at the time of admission with ACS is a powerful predictor of poorer survival and increased risk of complications while in hospital, regardless of whether or not the patient has diabetes [6].
- Echocardiography often demonstrates wall motion abnormalities due to ischaemia. May be useful in identifying precipitants for ischaemia - eg, ventricular hypertrophy and valvular disease.
- CXR may show complications of ischaemia (eg, pulmonary oedema), or explore alternative diagnoses - eg, pneumothorax, aortic aneurysm.

- Cardiac magnetic resonance (CMR) imaging can be useful for the assessment of function and perfusion and for the detection of scar tissue. CMR can also be useful to exclude or detect ACS, to assess myocardial viability and to detect myocarditis [2].
- Coronary angiography provides information on the presence and severity of coronary artery disease and therefore remains the gold standard [2].

Risk assessment [6]

As soon as the diagnosis of unstable angina or NSTEMI is made and aspirin and antithrombin therapy have been offered, individual risk of future adverse cardiovascular events should be assessed using an established risk scoring system that predicts six-month mortality. Risk is defined as:

- Low: up to 3%.
- Intermediate: above 3% and up to 6%.
- High: above 6%.

The National Institute for Health and Care Excellence (NICE) recommends the Global Registry of Acute Cardiac Events (GRACE) risk score [7].

The Thrombolysis in Myocardial Infarction (TIMI) risk score is another method used to assess risk in patients with ACS [8]. Other risk scores may be potentially useful [9].

Factors to use when assessing risk with an established scoring system include:

- Full clinical history, including age, previous myocardial infarction, previous percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).
- Physical examination, including blood pressure and heart rate.
- 12-lead resting ECG.
- Blood tests (such as troponin I or T, creatinine, glucose and haemoglobin).

The risk of bleeding should be assessed as well as relevant comorbidity before considering treatments and at each stage of management. Factors associated with high bleeding risk include advancing age, known bleeding complications, renal impairment and low body weight.

Management[6]

Treatment includes antithrombotic treatment, as well as coronary angiography followed by revascularisation if appropriate. The treatment of patients with NSTE-ACS is directed to alleviate pain and anxiety, prevent recurrences of ischaemia and prevent or limit progression to acute myocardial infarction[1].

- Compared to a conservative strategy, an invasive strategy (PCI or CABG surgery) is associated with reduced rates of refractory angina and rehospitalisation in the shorter term and myocardial infarction in the longer term. An invasive strategy is associated with a doubled risk of procedure-related heart attack and increased risk of bleeding and procedural biomarker leaks[10].
- Available evidence suggests that an invasive strategy may be particularly useful in those at high risk for recurrent events[10].
- In lower-risk patients, consider conservative management without early coronary angiography for people with unstable angina or NSTEMI who have a low risk of adverse cardiovascular events (predicted six-month mortality 3.0% or less).

Immediate management of a suspected ACS[5]

Important information
Arrange urgent hospital admission (phone 999/112/911). Resuscitation as required. Pain relief: GTN and/or an intravenous opioid (use an antiemetic with opioids). Single loading dose of 300 mg aspirin unless the person is allergic. A resting 12-lead ECG - but don't delay transfer to hospital. Assess oxygen saturation, using pulse oximetry before hospital admission if possible. Give oxygen if oxygen saturation (SpO_2) is less than 94% with no risk of hypercapnic respiratory failure; aim for SpO_2 of 94-98% (aim for 88-92% for people with chronic obstructive pulmonary disease).

- Antiplatelet and anticoagulant therapy:

    - In the presence of ischaemic ECG changes or elevation of cardiac troponin, patients with an ACS should be treated immediately with both aspirin (300 mg loading dose) and ticagrelor (180 mg loading dose) [4].
    - Do not offer dual antiplatelet therapy to patients with chest pain before diagnosis of unstable angina or NSTEMI is made.
    - Consider clopidogrel monotherapy for patients with aspirin hypersensitivity.
    - Consider clopidogrel for patients with unstable angina or NSTEMI as part of dual antiplatelet therapy with aspirin, if they have a separate indication for ongoing oral anticoagulation. This combination can be used for up to 12 months. Persisting with triple therapy (clopidogrel plus aspirin plus anticoagulant) beyond 12 months significantly increases the bleeding risk.
    - Prasugrel in combination with aspirin is recommended by NICE as an option for preventing atherothrombotic events in adults with ACS having primary or delayed PCI [11].
    - Ticagrelor in combination with low-dose aspirin is recommended for up to 12 months as a treatment option in adults with ACS with [4] [12]:

        - STEMI that cardiologists intend to treat with primary PCI; **or**
        - NSTEMI; **or**
        - Admission to hospital with unstable angina.

    - Glycoprotein IIb/IIIa inhibitors should be considered as an adjunct to PCI for patients at intermediate or higher risk who are not already receiving a glycoprotein inhibitor (GPI).

- Antithrombin therapy: anticoagulants are used in the treatment of NSTE-ACS to inhibit thrombin generation and/or activity, thereby reducing thrombus-related events[2]:

    - Offer fondaparinux to patients without a high bleeding risk unless angiography is planned within 24 hours of admission. Offer unfractionated heparin as an alternative to fondaparinux if angiography is likely within 24 hours of admission.
    - Carefully consider the choice and dose of antithrombin in patients with a high bleeding risk.
    - Consider unfractionated heparin, with dose adjusted to clotting function, for patients with creatinine above 265 µmol/L.
    - Offer systemic unfractionated heparin (50-100 units/kg) in the cardiac catheter laboratory to patients on fondaparinux who are undergoing PCI.
    - As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients who are at intermediate or higher risk, who are not already receiving a GPI or fondaparinux and are scheduled for angiography within 24 hours of admission.
    - As an alternative to the combination of a heparin plus a GPI, consider bivalirudin for patients undergoing PCI who are at intermediate or higher risk and are not already on a GPI or fondaparinux.

- Revascularisation:
    - Consider coronary angiography (with follow-on PCI if indicated) within 72 hours of first admission for people with unstable angina or NSTEMI who have an intermediate or higher risk of adverse cardiovascular events (predicted six-month mortality above 3.0%) and no contra-indications to angiography (such as active bleeding or comorbidity). The risks and benefits of early intervention should be taken into account. NICE offers detailed advice in this respect.
    - Coronary angiography (with follow-on PCI if indicated) should be considered for people with unstable angina or NSTEMI who are initially assessed to be at low risk of adverse cardiovascular events (predicted six-month mortality 3.0% or less) if ischaemia is subsequently experienced or is demonstrated by ischaemia testing.
    - Younger people with low risk scores for mortality at six months may still be at risk of cardiovascular events and may benefit from early angiography.
    - If stenting is considered, patients with NSTE-ACS should be offered a drug-eluting stent.
    - The proportion of patients with NSTE-ACS undergoing CABG surgery during initial hospitalisation is about 10%. The benefit from bypass surgery is greatest when patients can be operated on after several days of medical stabilisation, depending on the individual risk [2].
    - For people who have previously had a myocardial infarction but not had revascularisation, consider whether revascularisation is now appropriate, considering comorbidities.

- Other treatments:

    - Nitrates (sublingual, oral or intravenous): for ongoing pain whilst waiting for more definitive procedures, and may overcome superimposed coronary artery spasm.

    - Beta-blockers improve outcome and can reduce the severity and frequency of attacks. Unless reduced left ventricular fraction has been identified, consider continuing beta-blockers for 12 months after an MI. There is no convincing evidence to support continuation of beta-blockers beyond 12 months, and a discussion should be had with the patient at this point about risks, benefits and adverse events..

    - Calcium antagonists (eg, diltiazem, verapamil) are used for patients who cannot tolerate a beta-blocker, without pulmonary congestion or reduced left ventricular ejection fraction.

    - Calcium-channel blockers may be used for people whose condition is stable after an MI, to treat hypertension and/or angina. For people with heart failure with reduced ejection fraction, use amlodipine, and avoid verapamil, diltiazem and short-acting dihydropyridine agents.

    - Angiotensin-converting enzyme (ACE) inhibitors reduce mortality and should be started when the patient is an inpatient unless contra-indicated.

    - A Cochrane review found that initiation of statin therapy within 14 days following ACS does not reduce death, myocardial infarction, or stroke up to four months; however, it does reduce the occurrence of unstable angina at four months following ACS[13].

- Hyperglycaemia[6]:
    - Hyperglycaemia in patients admitted to hospital for an ACS should be managed by keeping blood glucose levels below 11.0 mmol/L while avoiding hypoglycaemia. A dose-adjusted insulin infusion with regular monitoring of blood glucose levels should be considered.
    - All patients with hyperglycaemia after ACS and without known diabetes should be tested for HbA1c levels before discharge and fasting blood glucose levels no earlier than four days after the onset of ACS.
- After stabilisation, secondary risk reduction measures should be implemented. These measures include stopping smoking, continued aspirin therapy, management of hypertension if present, statins, ACE inhibitors and beta-blockers[14]. If a patient was stabilised with medical treatment then it is likely they will undergo treadmill exercise testing.

Further management

- To detect and quantify inducible ischaemia, consider ischaemia testing before discharge for patients whose condition has been managed conservatively and who have not had coronary angiography.
- Assess left ventricular function in all patients who have had a myocardial infarction and consider assessing left ventricular function in all patients with unstable angina.
- Cardiac rehabilitation: rehabilitation and discharge planning.
- Secondary prevention: management of cardiovascular risk factors with lifestyle changes and drug therapy as indicated.

Complications

- Acute myocardial infarction.
- Cardiogenic shock.
- Ischaemic mitral regurgitation.

- Supraventricular arrhythmias: rare complication of ischaemia.
- Ventricular arrhythmias: simple and complex premature ventricular contractions and non-sustained ventricular tachycardia.
- Atrioventricular nodal blockade: usually transient in setting of reversible ischaemia (treatment is guided by location of block and haemodynamic stability).

Prognosis

People with NSTE-ACS have a high incidence of recurrent myocardial ischaemia, a similar long-term outcome to those with STEMI, and a worse outcome than for people with unstable angina [6].

In-hospital death and re-infarction affect 5-10%. Despite optimal treatment with anti-ischaemic and antithrombotic drugs, death and recurrent myocardial infarction occur in another 5-10% of patients in the month after an acute episode. Factors associated with a poorer prognosis include [6]:

- Advancing age.
- Presence and severity of ECG changes of ischaemia.
- Magnitude of rise in biomarkers of myocardial injury (eg, serum troponin).
- Left ventricular dysfunction, cardiogenic shock.
- Increased heart rate, arrhythmias (ventricular fibrillation, atrial fibrillation).
- Renal impairment.
- Diabetes mellitus.
- Anaemia.
- Cerebrovascular disease, peripheral arterial disease.

Any delay in arranging angiography for high-risk patients is associated with increased mortality and adverse outcomes [15].

Prevention

Primary cardiovascular disease prevention and cardiovascular risk assessment:

- Smoking cessation.
- Dietary and exercise advice.
- Blood pressure, hyperlipidaemia and diabetes control.
- Compliance with medications, particularly aspirin.
- Comprehensive risk assessment, including exercise tolerance test for those at high risk and identification of structural heart disease (eg, left ventricular hypertrophy, aortic stenosis).

Further reading

- GRACE (Global Registry of Acute Cardiac Events)
- TIMI Study Group
- Acute coronary syndromes (including myocardial infarction) in adults; NICE Quality Standard, September 2014 - last updated November 2020
- ESC/EACTS Guidelines on myocardial revascularization; European Heart Journal, 2018

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