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Early recognition vital in acute coronary syndrome

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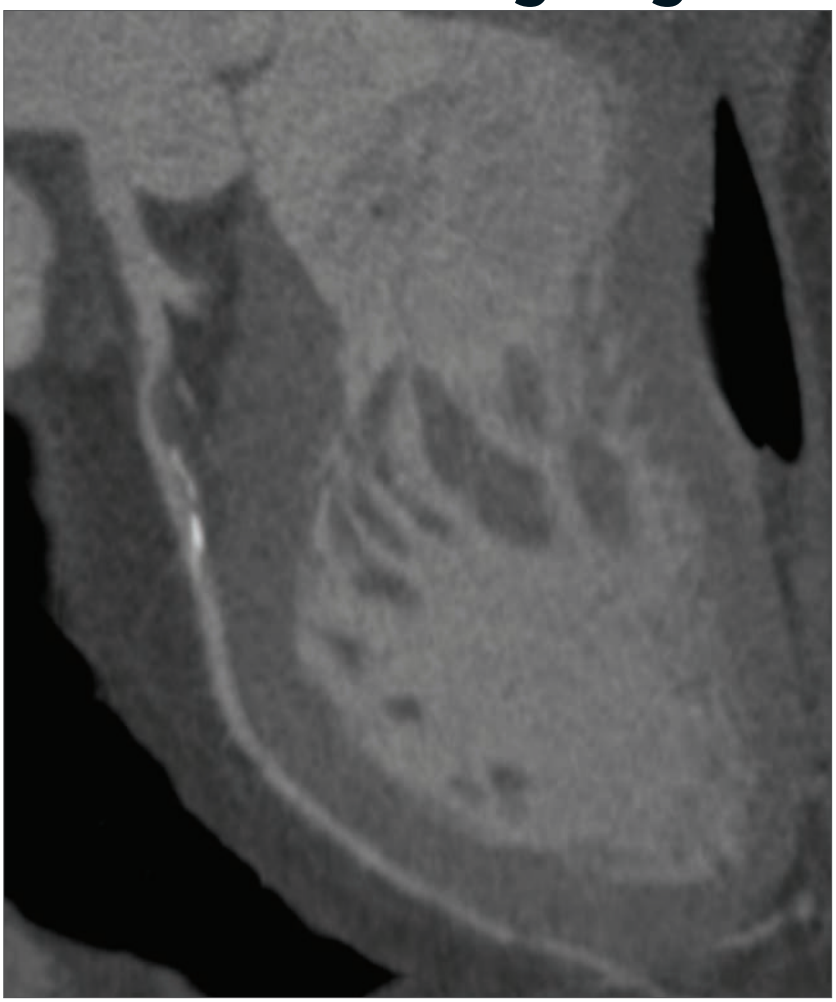

CT scan showing a diseased left anterior descending artery

What are the presenting symptoms?

How should patients be assessed?

What are the evidence-based treatment options?

ACUTE CORONARY SYNDROME (ACS) INCLUDES BOTH ST ELEVATION (STEMI) non-ST elevation (NSTEMI) myocardial infarction, and unstable angina.

The common pathological process underlying myocardial infarction (MI) involves thrombus formation on top of a complex atheromatous plaque, resulting in partial or complete occlusion of the coronary artery and myocyte necrosis. Unstable angina is defined as ischaemia at rest or on minimal exertion in the absence of myocyte necrosis.

Coronary artery disease (CAD) is the leading cause of death in the UK[1] and patients with ACS have poor outcomes.[2] Therefore early recognition, assessment and instigation of appropriate evidence-based management is essential to minimise morbidity and mortality.

PRESENTATION

Patients with ACS typically present with chest pain. This is classically central chest pain that radiates to the left arm. Additional symptoms include dyspnoea, nausea, sweating and syncope. Some individuals present atypically with gastric symptoms. These are often more common in patients with diabetes, women and the elderly. Patients may also display haemodynamic instability or present in cardiac arrest.

Clinical risk factors should also be considered when diagnosing ACS as they increase the likelihood of a positive diagnosis. Risk factors include: being older, male, a current or ex-smoker, known CAD, peripheral vascular disease, diabetes, hypercholesterolaemia, renal failure and a family history of CAD.[3]

ASSESSMENT

A full clinical history should be taken in every patient presenting with suspected ACS with elucidation of relevant risk factors. All patients should also undergo a full cardiovascular examination. This may be useful in identifying non cardiac causes of chest pain such as radioradial or radiofemoral delay, discrepancies in blood pressure between the right and the left arm, an irregular pulse, murmur, rubs and reproducible chest pain among others.

A 12-lead ECG should be performed if possible within ten minutes of »

presentation or ideally at first contact with the emergency services.[4] Patients presenting with stable angina should be referred to the rapid access chest pain clinic. Patients with angina at rest or a history suggestive of crescendo angina should be referred to secondary care for urgent assessment. Patients should have routine blood tests on admission including full blood count, urea and electrolytes, liver function tests, C-reactive protein, glucose, cholesterol and troponin.

Troponin should be measured on admission and at 12 hours. Ideally high sensitivity troponin should be measured[5] as this has higher negative predictive values for MI and enables earlier detection of acute MI. A chest x-ray should also be taken to assess for thoracic pathologies. An echocardiogram should be performed during admission in all patients with NSTEMI and STEMI. This is a helpful tool to assess regional wall motion abnormalities as well as left ventricular systolic function. It is also useful to rule out alternative diagnoses.

CONFIRMING DIAGNOSIS

The diagnosis is based on a combination of the clinical history, ECG and changes in biochemical markers of cardiovascular damage. The ECG may show ST elevation (STEMI) or in the case of NSTEMI the ECG may show transient ST elevation, ST depression, T wave inversion, T wave flattening or the ECG may be entirely normal. STEMI is defined as > 1 mm ST elevation in two or more contiguous limb leads or > 2 mm ST elevation in two or more precordial leads, or new left bundle branch block (LBBB). [6]

Table 1

Potential causes of raised troponin

- Heart failure
- Arrhythmias
- Myocarditis
- Takotsubo cardiomyopathy
- Structural heart disease
- Coronary spasm
- Trauma
- Aortic dissection
- Hypertensive emergencies
- Hypotension
- Pulmonary embolism
- Renal failure
- Acute neurological event
- Infiltrative disease (amyloidosis, haemochromatosis)
- Drugs (herceptin, doxorubicin)
- Extreme endurance
- Rhabdomyolysis

A troponin test is positive if at least one value is above the 99th centile upper reference limit. There are many conditions that can contribute to a high troponin level, see table 1, below. It is recommended that the 0/3 hour or the 0/1 hour algorithm is used for high sensitivity troponin. It is important to note that the different troponin assays vary in what is considered to be a positive result.

The diagnosis is confirmed in the presence of the following criteria: ischaemic symptoms, new ST/T wave changes or LBBB, Q waves, evidence of loss of viable myocardium or regional wall motion abnormalities on imaging and detection of thrombus on coronary angiography or at autopsy.[7]

RISK STRATIFICATION

Patients who present with crescendo symptoms or rest pain have a worse prognosis than those with stable symptoms during exertion. An ECG can also predict risk.[8] For example a patient with ST depression in two contiguous leads of ≥ 0.05 mV has a worse prognosis, compared with one with a normal ECG.[9] If there is transient ST elevation this also conveys a worse prognosis.[10]

High sensitivity troponin can also be used prognostically in that the higher the levels at presentation the higher the risk of death.[11] Risk can be calculated using the GRACE risk score. This risk score provides the most accurate assessment[12] and is based on variables such as age, heart rate, blood pressure, creatinine, Killip score, cardiac arrest on admission, elevated cardiac biomarkers and ST changes. The GRACE 2.0 calculator can be used to calculate mortality in hospital, at six months, one year and three years.

INPATIENT MANAGEMENT

Patients with ACS should be monitored on a cardiology ward.[13] Oxygen should be given when patients are in respiratory distress or oxygen levels are < 90%.[14] In patients with ongoing chest pain iv nitrates should be administered.

Beta blockers lower heart rate and myocardial contractility, thereby reducing oxygen demand. Meta-analyses have shown that they can reduce the progression to MI by 13%.[15] However, in a study looking at the risk of developing cardiogenic shock, the risk of death or becoming shocked was much higher in patients who received beta blockers within 24 hours of their admission.[16] Therefore beta blockers should be given with care in the absence of bradycardia and hypotension. It is also important to maintain good glycaemic control (7-10 mmol) in diabetes patients peri-MI as demonstrated in the DIGAMI trial.[17]

Aspirin was shown to lower MI and death rates in patients with unstable angina and to reduce mortality by a third in acute MI.[18] All patients should be given a 300 mg loading dose of aspirin with a daily maintenance dose of 75 mg thereafter.

Clopidogrel is a P2Y12 receptor inhibitor that inhibits ADP and therefore platelet aggregation. Dual therapy with aspirin and clopidogrel in NSTEMI showed a reduction in ischaemic events compared with aspirin monotherapy.[19,20] Patients should be loaded on 300 mg with a 75 mg daily maintenance dose thereafter.

Prasugrel is also a P2Y12 receptor inhibitor but has a more rapid onset and better inhibitory effect. In the TRITON-TIMI 38 trial in patients who had had a STEMI or an NSTEMI administration of prasugrel reduced the risk of recurrent cardiac events but there was a significantly increased risk of bleeding. [21] The trial however showed no benefit in patients over 75 or those with a low body weight (< 60 kg). This should be loaded in the following manner; 60 mg, followed by a daily maintenance dose of 10 mg.

'Aspirin was shown to lower MI and death rates in unstable angina and to reduce mortality by a third in acute MI'

Ticagrelor also acts on the P2Y12 receptor and has a faster onset and offset than clopidogrel.[22] In the PLATO trial[23] patients with moderate to high risk NSTEMI or STEMI were given clopidogrel or ticagrelor. Ticagrelor reduced death from cardiovascular causes, MI and cerebrovascular accident (CVA). Major bleeds were higher in the ticagrelor arm but this did not translate to rates of life-threatening or fatal bleeds.

Therefore patients with NSTEMI or STEMI should be given a combination of aspirin and ticagrelor/prasugrel if there are no contraindications. Prasugrel is only recommended in patients who are proceeding to PCI if there are no

contraindications and clopidogrel is given where the patient cannot be given ticagrelor or prasugrel because of the risk of bleeding or they require oral anticoagulation.

Patients are given glycoprotein IIb/IIIa inhibitors when there are thrombotic complications during intervention. A proton pump inhibitor should be given in patients at high risk of bleeding (previous history of gastrointestinal haemorrhage/ulceration, anticoagulant use, NSAID use, corticosteroid use) or two of more of the following: gastro-oesophageal reflux disease, *Helicobacter pylori*, chronic alcohol abuse and age.

'In patients presenting with STEMI primary percutaneous intervention has been shown to be superior to thrombolysis'

All patients should receive anticoagulation. Anticoagulants act by inhibiting thrombin generation thereby reducing thrombosis. This has been shown to reduce ischaemic events in NSTEMI and when used in combination with antiplatelets the effect is greater than when each is used alone.[24] Fondaparinux is a factor Xa inhibitor and is considered to be the most favourable option (versus unfractionated heparin, low molecular weight heparin and bivalirudin) as it has the best safety profile.[25,26] Anticoagulation should also be administered to patients with a STEMI but only if they are not undergoing immediate reperfusion therapy.

In patients presenting with STEMI primary percutaneous intervention (PPCI) has been shown to be superior to thrombolysis[27] and this benefit was greatest within 12 hours. Intervention should ideally occur within 90 minutes.[28] There is currently insufficient evidence to guide whether culprit lesion versus multivessel PCI is favourable. Where PPCI is not available thrombolytic therapy has been shown to reduce 35 day mortality[29] and should be performed unless contraindicated using fibrin-specific agents such as tissue plasminogen activator or alteplase.[1] If patients fail to respond to thrombolysis within six hours of symptom onset there is a role for rescue PCI.[30]

In patients with an NSTEMI the decision for timing regarding invasive therapy is based on risk criteria, see table 2, below.

Very high risk NSTEMIs should have coronary angiography within two hours, high risk within 24 hours and intermediate risk within 72 hours.[31, 32] The decision to proceed to CABG over PCI is dependent on having multivessel and/or left main stem disease, especially in diabetes patients who have a better prognosis following CABG compared with PCI.[33]

Importantly patients who present with cardiac arrest should undergo coronary angiography if they are conscious; those with reduced consciousness levels should be investigated for alternative causes.

'Diabetes patients have a better prognosis following CABG compared with PCI'

Patients with haemodynamic instability should be managed appropriately. In patients with pulmonary oedema with hypoxia non-invasive positive airways pressure should be considered. In patients with evidence of volume overload, hypotension and cardiogenic shock inotropes should be considered. In these patients there is evidence that early PCI (within six hours) may be beneficial.[34, 35]

Patients who have mechanical complications of MI (papillary muscle rupture, ventricular septal defects and free wall rupture) should be considered for cardiac surgery.

In patients who do not meet the criteria for intermediate risk or above, inpatient or early outpatient stress testing (stress echocardiogram, stress cardiac magnetic resonance imaging, or myocardial perfusion scan) should be performed.[36] These modalities have a much higher sensitivity compared with treadmill testing.[37]

A developing imaging modality is multidetector computed tomography which is used to assess coronary anatomy. This should be used in patients with low risk of ACS plus/minus inconclusive cardiac troponins. However, its use is limited in elderly patients who are likely to have coronary artery calcification, patients with tachycardia or an irregular heart rate.

OUTPATIENT MANAGEMENT

Patients should be referred to a cardiac rehabilitation team and must be discharged on appropriate medication. Patients should remain on dual antiplatelet therapy (DAPT) for at least six months. However, an extended duration (> 12 months) was shown to increase the risk of major bleeding and overall mortality, although it did reduce the risk of MI and thrombosis, and 12 months' therapy increased the risk of bleeding with no further beneficial effects compared with short-term therapy (six months).[38,39]

Lifelong aspirin should be continued after this point. In patients who are medically managed or undergo intervention who are on oral anticoagulation (vitamin K antagonists) »

Table 2

Risk stratification criteria in NSTEMI

Very high risk	High risk	Intermediate	Low risk
● Haemodynamic instability/cardiogenic shock ● Acute heart failure ● Refractory chest pain ● Cardiac arrest/life-threatening arrhythmias ● Recurrent dynamic ECG changes ● Mechanical complications of MI	● GRACE score > 140 ● Rise in troponin compatible with MI ● Dynamic ST changes	● GRACE score > 109 and < 140 ● Renal impairment (eGFR < 60) ● Prior PCI ● Prior CABG ● LVEF < 40% ● Early post-MI angina ● Diabetes mellitus	Anything not mentioned in the other categories

key points

SELECTED BY

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Acute coronary syndrome (ACS) includes both ST (STEMI) and non ST elevation (NSTEMI) MI, and unstable angina. The common pathological process underlying MI involves thrombus formation on top of a complex atheromatous plaque, resulting in partial or complete occlusion of the coronary artery and myocyte necrosis. Unstable angina is defined as ischaemia at rest or on minimal exertion in the absence of myocyte necrosis.

Patients with ACS typically present with chest pain; classically central chest pain that radiates to the left arm. Additional symptoms include dyspnoea, nausea, sweating and syncope. Patients can present atypically with gastric symptoms. These are often more common in patients with diabetes, women and the elderly. Clinical risk factors should also be considered when diagnosing ACS as this increases the likelihood of a positive diagnosis. Risk factors include: being older, male, a current or former smoker, known coronary artery disease (CAD), peripheral vascular disease, diabetes, hypercholesterolaemia, renal failure and a family history of CAD.

A 12-lead ECG should be performed if possible within 10 minutes of presentation or ideally at first contact with the emergency services. Troponin should be measured on admission and at 12 hours. Ideally high sensitivity troponin should be measured as this has higher negative predictive values for MI and enables earlier detection of acute MI. A chest x-ray should also be carried out to assess for thoracic pathologies. An echocardiogram should be performed during admission in all patients with NSTEMI and STEMI.

Aspirin was shown to lower MI and death rates in patients with unstable angina and to reduce mortality by a third in acute MI. All patients should be given a 300 mg loading dose of aspirin with a daily maintenance dose of 75 mg thereafter. Patients with NSTEMI or STEMI should be given a combination of aspirin and ticagrelor/prasugrel if there are no contraindications. Prasugrel is recommended in patients who are proceeding to PCI if no contraindications are present and clopidogrel is given where the patient cannot be given ticagrelor or prasugrel because of the bleeding risk or they require oral anticoagulation. All patients should receive anticoagulation.

In patients presenting with STEMI primary percutaneous intervention has been shown to be superior to thrombolysis and this benefit was greatest within 12 hours. Intervention should ideally occur within 90 minutes. Very high risk NSTEMIs should have coronary angiography within 2 hours, high risk within 24 hours and intermediate risk within 72 hours. In patients who do not meet the criteria for intermediate risk or above, inpatient or early outpatient stress testing (stress echocardiogram, stress cardiac magnetic resonance imaging or myocardial perfusion scan) should be performed. These modalities have a much higher sensitivity than treadmill testing.

the decision to continue triple or dual therapy with dual antiplatelets and an anticoagulant or a single antiplatelet and anticoagulant depends on the CHA_2DS_2-VASc score risk of stroke (see p13) and HASBLED score for bleeding risk (see p13).

As there is no data regarding prasugrel or ticagrelor as part of this, their use in triple therapy should be avoided.[7] Moreover, direct oral anticoagulants should not be used as these double the risk of clinically significant bleeds.[40]

'Patients should remain on dual antiplatelet therapy for at least six months'

The benefits of statin therapy are well established and these should be continued long term. In patients with unstable angina the data is limited regarding the benefits of beta blocker therapy but meta-analyses of the trials suggest that there is less chance of progression to MI.[15] Post-MI data have shown a 23% relative risk reduction in total mortality and 32% in sudden death.[41] Therefore beta blockers should be continued long term.

The EUROPA trial showed that ramipril reduced all-cause mortality, MI and CVA in patients with stable CAD[42] and the mortality and morbidity benefits of angiotensin converting enzyme inhibitors (ACEi) in patients with left ventricular dysfunction post MI are well established.[43] Therefore ACEi should be commenced and continued in these patient cohorts.

Eplerenone has also been shown to have a mortality benefit in patients with an ejection fraction <40% following an MI[44] and should be continued in this cohort of patients.

PERIOPERATIVE MANAGEMENT

In patients undergoing non cardiac surgery post PCI that cannot be delayed, up to three months of DAPT is recommended where bare metal stents or new drug eluting stents have been inserted. Ideally at least aspirin should be continued and if the operation has a low to moderate risk of bleeding, the operation should be performed on DAPT. If required, antiplatelets should be stopped five days prior to elective surgery but in patients on prasugrel this should be increased to seven days.[45]

CONCLUSION

Patients with suspected ACS must be assessed by a physician together with a full history, clinical examination, electrocardiogram, and chest x-ray. Ideally a high sensitivity troponin assay should be used.

The decision regarding inpatient/outpatient stress testing or progression to intervention is dependent on whether the patient presents with STEMI, NSTEMI or unstable angina.

Within the NSTEMI groups risk stratification is essential to decide on timing of invasive therapy.

Revascularisation may be performed via PCI or CABG. Patients who have had an infarct should be referred for cardiac rehabilitation and the choice and duration of medication prescribed based on the nature of the intervention, the risk of bleeding and known cardiac function with the ultimate aim of reducing future cardiovascular events.

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Useful information

For patients
SIGN
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www.sign.ac.uk/patients/publications/148/index.html

Patient
Acute coronary syndrome
http://patient.info/health/acute-coronary-syndrome-leaflet

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