

Managing unstable angina and non-ST elevation MI

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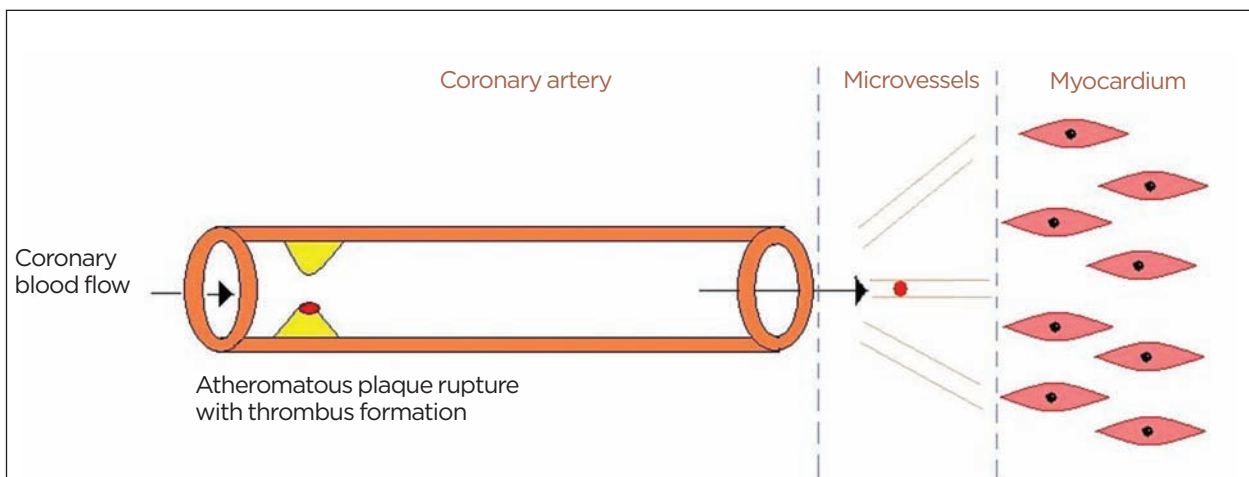


FIGURE 1

In NSTEMI, the platelet-rich thrombus may dislodge and embolise distally into the coronary vasculature, thus reducing the blood flow resulting in myocardial death and the release of cardiac troponin. In unstable angina, the thrombus is usually non occlusive and does not cause myocardial necrosis (i.e. no detectable troponin release)

How should patients be diagnosed?



ACUTE CORONARY SYNDROME (ACS), ENCOMPASSING UNSTABLE ANGINA (UA),

non-ST elevation myocardial infarction (NSTEMI), see figure 1 above, and ST-elevation myocardial infarction (STEMI), is often the result of an acute thrombotic occlusion of the coronary vessels, associated with atheromatous plaque rupture or erosion.

ACS is associated with a severely impaired prognosis and requires prompt and efficient specialist treatment.

Patients presenting with STEMI most often show a complete occlusion of one or more of the epicardial coronary arteries.¹ NSTEMI and UA - collectively known as non-ST elevation ACS (NSTEMI-ACS) - share a similar pathogenesis with acute coronary

How should risk be assessed?

thrombosis reducing the lumen of the coronary artery and severely restricting myocardial blood supply.

The thrombus in NSTEMI-ACS is often platelet rich and sub-occlusive as opposed to the fibrin-rich red clot that completely occludes the coronary artery in patients with STEMI. Distal embolisation of platelets and other components of the thrombus often takes place in NSTEMI, resulting in the occlusion of the coronary microcirculation and further myocardial ischaemia and/or necrosis.

DIAGNOSING UNSTABLE ANGINA AND NSTEMI

The clinical presentation may be identical across all three components of ACS. Establishing an accurate diagnosis without delay is of paramount importance to start

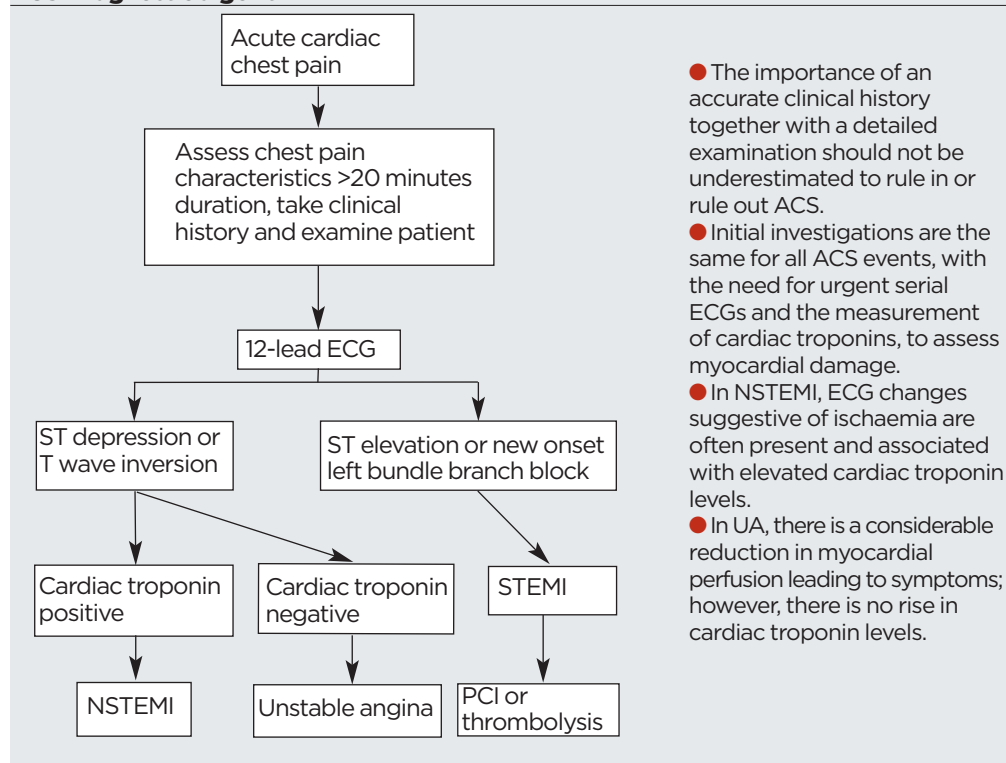
What are the treatment options?

treatment promptly, see figure 2, p26. Patients with suspected ACS need to be referred immediately to A&E. Important features pointing towards a diagnosis of ACS include:

- typical characteristics of chest pain
- presence of risk factors
- ECG changes suggestive of myocardial ischaemia, see table 1, p26.

Chest pain

Chest discomfort in patients with ACS typically occurs at rest, is anginal in character and can range from mild tightness to central crushing chest pain. This is not infrequently associated with symptoms such as nausea, dyspnoea or diaphoresis. The chest pain may radiate to the arms, back or jaw and is often >20 minutes in duration. Atypical chest pain at rest is relatively common in the elderly »

Figure 2**ACS: Diagnostic algorithm**

and in patients with diabetes mellitus.

Extra-cardiac causes of chest pain at rest mimicking angina pectoris should be identified but it should be remembered that these may coexist with ACS and not necessarily be the cause of the chest pain that brings the patient to the attention of the physician.

It is important to remember that although in most cases angina can be easily recognised, patients may occasionally present with atypical symptoms that make the diagnosis of ACS difficult; this is particularly common in patients with cognitive impairment, diabetes mellitus and the elderly.¹

ECG changes

In all patients presenting with chest pain suggestive of myocardial ischaemia a 12-lead ECG should be recorded. This is of paramount importance for the diagnosis of ACS and should be obtained as soon as possible, preferably within 10 minutes of first contact with a healthcare professional. Serial ECGs are useful to look for dynamic changes of the ST segment and to assess the ECG response to the administration of

Table 1**Clinical and ECG variables useful for assessment of patients presenting with symptoms suggestive of ACS****Characteristics of chest pain in patients with ACS^{1,3}**

- prolonged anginal pain at rest (>20 minutes)
- new-onset angina (Class III Canadian Cardiovascular Society) - marked limitations of ordinary physical activity i.e. angina on walking
- recent destabilisation of previously stable angina with at least CCS III angina characteristics (crescendo angina)
- post-MI angina with longer and more frequent episodes of pain
- chest pain associated with haemodynamic instability
- chest pain associated with nausea, vomiting, dyspnoea or diaphoresis

Risk factors for coronary artery disease**Modifiable**

- smoking
- hypertension
- diabetes mellitus
- impaired glucose tolerance
- obesity

Non-modifiable

- past history of ischaemic heart disease
- family history of ACS in first-degree relative <55 years of age
- male gender
- age
- premature menopause
- ethnicity

ECG changes associated with NSTEMI-ACS^{1,3}

- ST segment depression >0.5 mm (0.05 mV) in two or more contiguous leads, in the appropriate clinical context, is suggestive of NSTEMI-ACS and is linked to patient prognosis. (ST depression of >1 mm is associated with an 11% risk of 1-year mortality or subsequent MI.) See figure 3, p27
- deep symmetrical T wave inversion >2mm in the precordial leads, see figure 4, p27

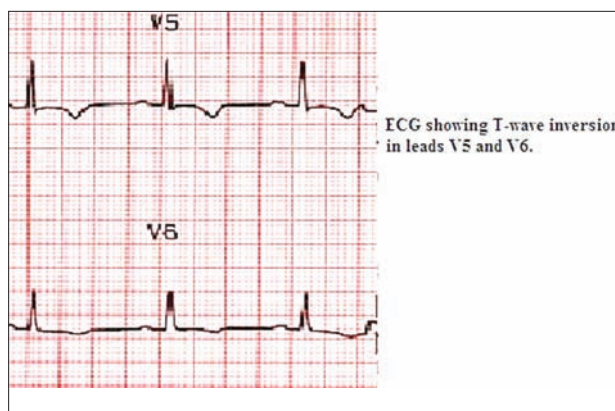
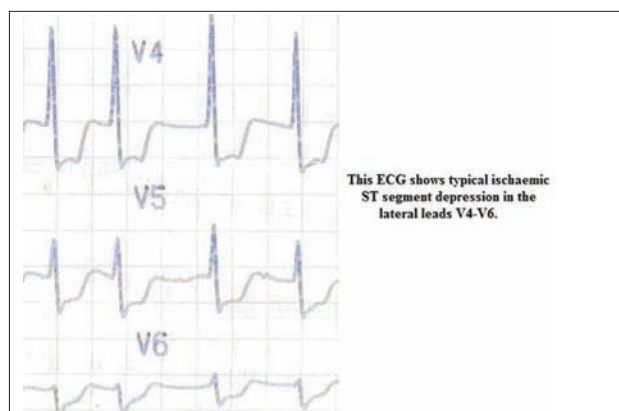


FIGURE 3 (LEFT)
ECG changes in NSTEMI-ACS:
ST depression

FIGURE 4 (RIGHT)
ECG changes in NSTEMI-ACS:
T wave inversion

treatment. Previous ECGs, if and when available, are useful for comparison. In ACS patients with persistent ST segment elevation (i.e. STEMI), primary percutaneous coronary intervention (PCI) or fibrinolytic therapy if PCI is not available should be carried out without delay. There is no need to wait for the results of blood tests, i.e. cardiac troponin levels, to proceed to intervention in these patients. Management of STEMI, however, is beyond the scope of this article.

Approximately 5% of patients with NSTEMI-ACS have normal ECGs.¹ In the presence of a history suggestive of ACS, these patients with normal or equivocal ECGs should be transferred immediately to hospital for specialist assessment and treatment.¹

In NSTEMI-ACS patients, the diagnosis of UA (typical symptoms and ECG changes, without elevation of markers of necrosis) vs NSTEMI (positive troponin results) may not be possible until troponin measurements are carried out in the hospital setting. The 12-lead ECG should be repeated on a regular basis in stable patients (i.e. every 6-24 hours) and every time

there is a recurrence of chest pain or other cardiovascular symptoms.

RISK STRATIFICATION IN ACS

Despite a relatively similar presentation, prognosis may differ in different patients. Several risk scores, involving clinical, biochemical and ECG characteristics, have been proposed, which help in the risk stratification of ACS patients and represent the basis to guide treatment; in particular, coronary intervention,² see table 2, below.

Despite the usually serious nature of ACS, some patients are at a relatively low risk of developing cardiovascular events and may be considered for inpatient or outpatient investigations to characterise their condition further. Patients in the moderate-risk group however, should have their coronary anatomy assessed within 72-96 hours, and those falling in the high-risk bracket need urgent angiographic investigation and intervention.

There are several scoring systems which may be useful for the assessment of risk of further major adverse cardiac events (MACE). The three most widely used risk

stratification systems in the clinical setting are:

- Thrombolysis In Myocardial Infarction (TIMI) risk score²
- Global Registry for Acute Cardiac Events (GRACE)³
- Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT)²

These risk stratification systems are based on findings in large population registries encompassing the full spectrum of ACS patients.¹ The GRACE score uses different variables to predict the risk of in-hospital death and 6-month mortality.¹ The GRACE risk score involves more complex calculations than some of the other risk stratification systems, as it requires the assessment of many variables, some of which may not be available in primary care. The GRACE investigators have divided patient risk into three categories i.e. low, intermediate and high. These are, as expected, associated with different mortality risk both in-hospital and post-discharge.

The TIMI risk scoring system was previously more widely used than »

Table 2

Markers of cardiovascular risk in patients with ACS (based on AHA and ESC guidelines)¹

Low risk	Intermediate risk	High risk
● Resolution of chest pain with no further recurrence ● No ECG changes on arrival ● No ECG changes 12 hours post admission ● Normal admission troponin ● Normal 12-hour troponin ● No signs of heart failure ● No haemodynamic compromise	● PMH of MI, CABG or diabetes ● Recent PCI (within 6 months suggests in-stent restenosis) ● Asymptomatic dynamic ST changes ● Renal impairment (eGFR<60) ● Moderately positive troponin T (0.01 < TnT < 0.1 ng/ml) ● Impaired LVEF (<40%) ● Intermediate GRACE risk score	● Persistent intractable chest pain unresponsive to angina therapy ● Recurrent episodes of angina with/without dynamic ECG changes ● Unresolving chest pain >20 minutes at rest ● New or worsening murmur of mitral regurgitation ● Markedly elevated troponin T > 0.1 ng/ml ● New onset or progressive heart failure ● Presence of haemodynamic compromise ● Life-threatening arrhythmias e.g. VT or VF

SYMPOSIUM CARDIOVASCULAR MEDICINE

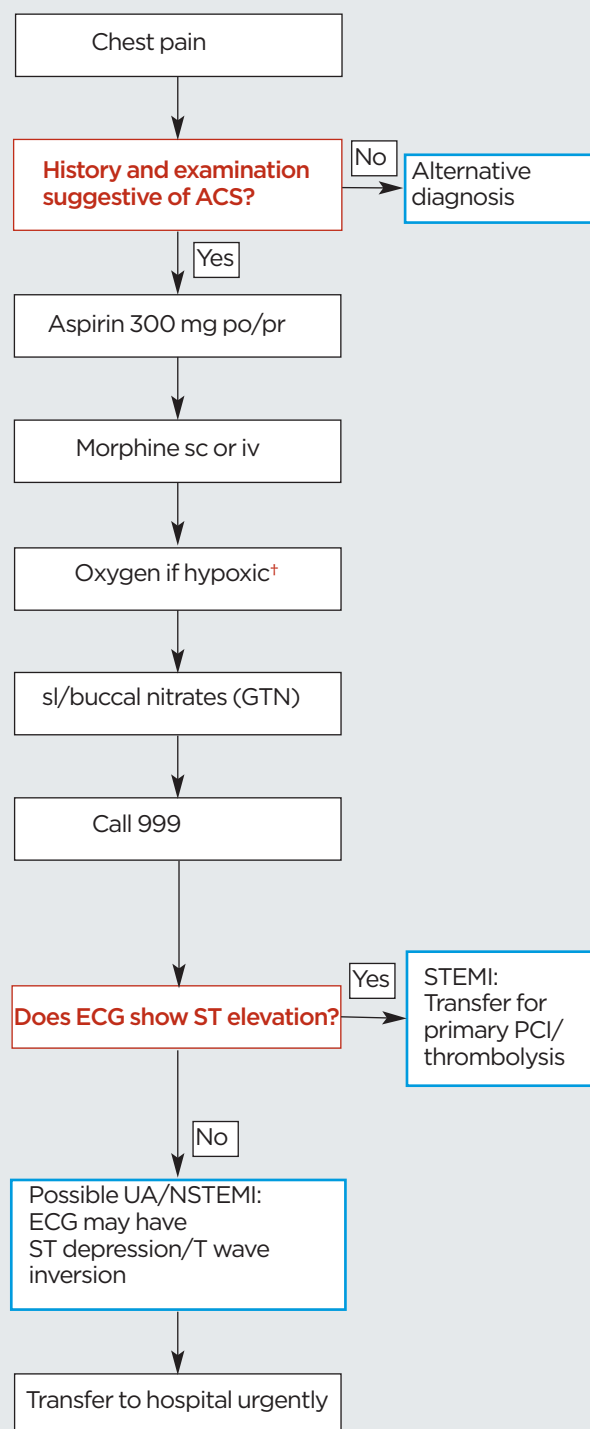
UNSTABLE ANGINA AND NON-STEMI

Table 3**Pharmacological management of ACS**

Drug/class	Dose	Indication	Mechanism	Caution note	Trials
Analgesia/stabilisers					
Morphine	4–8 mg sc or iv	ACS Heart failure	Analgesic; vasodilatation (reduces preload)	Monitor for respiratory depression. Nausea and vomiting, give anti-emetic. May develop pruritus	
Oxygen	2–15 L/min	Hypoxia Pulmonary oedema	Improves oxygenation Reduces ischaemia	Careful titration of oxygen level in COPD	
Antiplatelets					
Aspirin	Load 300 mg Regular 75–150 mg	ACS: Reduces further platelet aggregation and thrombus formation	Prevents production of thromboxane-A ₂	Peptic ulceration, bleeding	ISIS 2
Clopidogrel	Load 300 mg Regular 75 mg	ACS: Reduces further platelet aggregation and thrombus formation	Platelet ADP antagonist	Peptic ulceration, bleeding, PPIs*	CURE
Prasugrel	Load 60 mg Regular 10 mg	ACS: More effective platelet inhibition – for patients likely to undergo PCI. Given with aspirin	Platelet ADP antagonist	Increased bleeding In patients who are likely to undergo immediate PCI give prasugrel with aspirin rather than clopidogrel	TRITON-TIMI 38
GP IIb/IIIa antagonists	Depends on type used. (Eptifibatide, tirofiban, abciximab)	High-risk patients (for MI, death) with UA/NSTEMI	Inhibition of platelet bridging by antagonising the GP IIb/IIIa receptor	Bleeding and thrombocytopenia	RESTORE TARGET CAPTURE
Angina drugs					
Nitrates	Sublingual spray/tablet/iv infusion	Ischaemic cardiac chest pain	Venodilation, reducing preload and myocardial O ₂ demand	Hypotension Headache Contraindicated in patients on sildenafil	Small observational studies
Beta-blockers	Start at lowest tolerated dose and titrate upwards	ACS: myocardial ischaemia. Also used in secondary prevention	Promotes coronary perfusion through increasing diastole duration Reduced HR decreases O ₂ demand	Bradycardia, hypotension Avoid in haemodynamically unstable patients Contraindicated in: asthma, heart failure, peripheral vascular disease	CAPRICORN COMMIT GUSTO-1 HINT
Calcium channel blockers	Depending on type. Start at lowest tolerated dose	ACS: Myocardial ischaemia When beta-blockers unsuitable	Promotes coronary perfusion through increasing diastole duration	Verapamil and diltiazem can have deleterious effects in the presence of LVD	DRS DAVIT MDPIT
Antithrombotic drugs					
Heparin	Check local policy Usually LMWH†	ACS	Binds to anti- thrombin III to prevent thrombus formation by blocking factor Xa	Bleeding and thrombocytopenia Reduce dose in renal impairment	FRISC SYNERGY ESSENCE
Fondaparinux	2.5 mg sc daily	ACS	Activates anti- thrombin to block factor Xa	Do not give prior to PCI. Reduce dose in renal impairment	OASIS-5
Bivalirudin (direct thrombin inhibitor)	Initial 100 µg/kg then 250 µg/kg/h (for 72 h). Doses vary if preceding PCI	ACS	Direct blockade of thrombin IIa. Therefore prevention of further thrombus formation	Bleeding	OASIS-5 ACUITY

*PPIs with clopidogrel may reduce efficacy of its antiplatelet function.

†LMWH is usually the drug of choice in treatment of ACS. Patients who are likely to have interventional procedures will benefit from unfractionated heparin (UH)

Figure 5**Pre-hospital management of ACS**

†NICE recommends that supplemental oxygen should only be given to:

- patients with $\text{SpO}_2 < 94\%$ who are not at risk of hypercapnic respiratory failure, aiming for SpO_2 of 94–98%
- patients with COPD who are at risk of hypercapnic respiratory failure, to achieve a target SpO_2 of 88–92% until blood gas analysis is available

the GRACE scoring system due to its reliance on fewer variables to assess patient outcome. However, for this reason it is perhaps less accurate than the GRACE scoring system.¹ The TIMI risk index, however, allows clinically useful prediction of 30-day and 1-year mortality risk in ACS patients.² The PURSUIT risk stratification score is also of interest, as it allows the differentiation between NSTEMI and UA regarding 30-day mortality risk.²

The evaluation of risk in a given individual is a dynamic process that needs constant updating, as the clinical situation evolves, often very rapidly.

EVIDENCE-BASED TREATMENT OPTIONS

Prompt institution of treatment is essential in ACS and patients with suspected ACS should be transferred without delay to specialist centres or hospital emergency departments. Current treatment is based on tackling the pathophysiological mechanisms responsible for the condition and includes:

- antiplatelet drugs
- antithrombotic agents
- angina drugs
- analgesic interventions
- PCI

Initial treatment, the prehospital phase, should be initiated rapidly. It includes the use of aspirin, nitrates, morphine and oxygen (if hypoxic), see figure 5, left.

PHARMACOTHERAPY

Pharmacological treatment options are listed in table 3, p28.

Antiplatelet therapy

Aspirin is the first choice antiplatelet agent; in the absence of contraindications, an initial dose of 300 mg should be given immediately, orally (rectally or via a nasogastric tube are alternative routes) in all cases of suspected ACS. If there is a clear contraindication to aspirin, clopidogrel can be used as an alternative. In addition to aspirin, a loading dose of clopidogrel, 300 mg, should be given to optimise antiplatelet treatment, followed by 75 mg daily, standard dose, for 12 months. This is recommended especially in patients who have a 6-month mortality risk exceeding 1.5% and in those without contraindications i.e. risk of profound bleeding.⁴

Prasugrel has been recently added to the list of antiplatelet agents

recommended for use in patients with ACS. High-risk patients with UA or NSTEMI, including those with ongoing chest pain and dynamic changes on the ECG who are likely to undergo angiography within 96 hours of admission, should be considered for GP IIb/IIIa inhibitors (i.e. eptifibatide or tirofiban). The GP IIb/IIIa antagonist abciximab is used as an adjunct to PCI for patients at intermediate or high risk.

These agents are administered in the hospital setting once blood tests and accurate risk assessment have been carried out.⁴

Angina treatment

Sublingual nitrates (spray or tablets) should be given immediately. A nitrate infusion in the form of 50 mg glyceryl trinitrate (GTN) in 50 ml of saline is given at a starting rate 1–2 ml/h to provide continuous nitrate therapy. Careful blood pressure monitoring is required to prevent the development of hypotension, which could further reduce myocardial perfusion. Symptoms need to be assessed regularly to determine whether nitrate tolerance develops. This is best achieved by asking the patient to score their discomfort regularly on a scale of 1–10.

Beta-blockers are needed to achieve further control of symptoms in NSTEMI-ACS. These agents have anti-ischaemic effects, which depend on their actions on increased sympathetic tone, as well as negative chronotropic and inotropic actions that help reduce myocardial oxygen demand.³

Antithrombotic agents

Patients with UA or NSTEMI should be given a subcutaneous injection of LMWH. Fondaparinux is offered to patients without high risk of bleeding unless angiography is planned within 24 hours of admission. Unfractionated heparin is given to patients with creatinine concentrations $> 265 \mu\text{mol/L}$.

Analgesia

Relieving ischaemia and chest pain is of paramount importance. Patients who continue to experience chest pain despite initial nitrate therapy, should be offered intravenous opioids, i.e. morphine. Morphine has potent effects as an analgesic and anxiolytic and helps in providing

key points

SELECTED BY

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Acute coronary syndrome (ACS), encompassing unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), is often the result of an acute thrombotic occlusion of the coronary vessels, associated with atheromatous plaque rupture or erosion.

ACS is associated with a severely impaired prognosis and requires prompt and efficient specialist treatment. The clinical presentation may be identical across all three components of ACS. Establishing an accurate diagnosis without delay is of paramount importance to start treatment promptly. Patients with suspected ACS need to be referred immediately to A&E.

Important features pointing towards a diagnosis of ACS include: typical characteristics of chest pain, presence of risk factors, and ECG changes suggestive of myocardial ischaemia. Chest discomfort in patients with ACS typically occurs at rest, is anginal in character and can range from mild tightness to central crushing chest pain. This is not infrequently associated with symptoms such as nausea, dyspnoea or diaphoresis. The chest pain may radiate to the arms, back or jaw and is often >20 minutes in duration.

The importance of an accurate clinical history together with a detailed examination should not be underestimated to rule in or rule out ACS. Initial investigations are the same for all ACS events, with the need for urgent serial ECGs and the measurement of cardiac troponins, to assess myocardial damage. In NSTEMI, ECG changes suggestive of ischaemia are often present and associated with elevated cardiac troponin levels. In UA, there is a considerable reduction in myocardial perfusion leading to symptoms; however, there is no rise in cardiac troponin levels.

Initial treatment, the prehospital phase, should be initiated rapidly. It includes the use of aspirin, nitrates, morphine and oxygen (if hypoxic). Risk stratification is an imperative process in the assessment of ACS to allow efficient delivery of specialist care. Current treatment is based on tackling the pathophysiological mechanisms leading to myocardial ischaemia and necrosis, preventing and minimising further thrombotic occlusion of the epicardial coronary arteries and reducing myocardial damage. Treatment includes: antiplatelet drugs; antithrombotic agents; angina drugs; analgesic interventions; and PCI. GPs play a major role in ensuring optimal patient management after hospital discharge and secondary prevention of cardiovascular events.

haemodynamic stability. It also reduces systolic blood pressure and heart rate thus reducing myocardial oxygen demand.²

OPTIMAL MANAGEMENT AFTER DISCHARGE

The GP plays a major role in ensuring optimal patient management after hospital discharge and secondary prevention of cardiovascular events. Patients should be reviewed regularly in order to be offered the following:

- lifestyle advice e.g. smoking cessation, healthy diet, regular exercise
- regular assessment of cardiovascular risk e.g. Framingham Score/University of Manchester Charts
- monitoring of serum fasting lipids and assessment of beneficial effects and side effects of cholesterol- and triglyceride-lowering drugs
- monitoring of serum fasting glucose and arranging oral glucose tolerance tests if appropriate. In patients with diabetes, ensure good glycaemic control and monitoring HbA_{1c}
- monitoring blood pressure regularly and assessment of effects/side effects of antihypertensive agents

It is also important to ensure that patients are receiving the following treatment where appropriate:

- antiplatelet therapy
- angina therapy and doses are up-titrated if necessary
- heart failure medications
- post MI patients - drugs shown to improve prognosis e.g. ACE inhibitors and beta-blockers
- healthcare education

CONCLUSION

ACS is a serious condition which requires immediate attention and prompt management. Risk stratification is an imperative process in the assessment of ACS to allow efficient delivery of specialist care. The treatment options available for patients with ACS are based on addressing the pathophysiological mechanisms leading to myocardial ischaemia and necrosis, preventing and minimising further thrombotic occlusion of the epicardial coronary arteries and reducing myocardial damage.

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Useful information

NICE

www.nice.org.uk

British Heart Foundation

www.bhf.org.uk

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