The Practitioner®

CPD study pack

October 2019;262(1819)

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- Tracking down and treating the cause of syncope
- Managing stable angina in primary care
- Early recognition and prompt referral key in acute pancreatitis

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- Prescribing review
- Educational meetings
- Significant event audit
- Practice meeting
- Implement a new service
- Take on new role
- Significant event audits
- Change with feedback from patients and/or colleagues

Further options for sessional GPs
- Self audit of own practice:
  - Record-keeping
  - Referrals for investigations
  - Prospective condition based reviews
  - Random case analysis with colleagues
  - Review of telephone triage outcomes
- Update drugs in emergency bag

CPD Framework

Online all articles are associated with CPD prompts to written reflection in the form of three PDF fillable templates:
- Article review framework
- Case review framework
- Audit framework

SYNCOPE

1 Which of the statements are true?

A Reflex syncope is the most common cause of syncope
True ☐ **False** ☐

B Vasovagal syncope is likely if syncope is precipitated by pain, fear or standing
True ☐ **False** ☐

C Pacemakers are often indicated in reflex syncope
True ☐ **False** ☐

D Carotid sinus massage should be carried out to reproduce symptoms in suspected carotid sinus syncope
True ☐ **False** ☐

E Orthostatic hypotensive syncopal episodes are rare in patients under the age of 50
True ☐ **False** ☐

2 Match the statistic to the statement.

A The proportion of the general population who will have at least one episode of syncope in their lifetime

B The percentage of patients presenting to the emergency department with syncope who are admitted

C The proportion of cases in which clinical history alone is sufficient to differentiate syncope from other causes of transient loss of consciousness

D The combination of clinical history, physical examination and 12-lead ECG can provide a certain or suspected aetiology of syncope in up to what percentage of cases?

1 45%
2 50%
3 60%
4 70%

3 List four other causes of transient loss of consciousness that syncope needs to be differentiated from.

4 List any changes to your clinical practice that you may make having read this article.

STABLE ANGINA

5 List the three features that are characteristic of typical angina.

6 Which of the statements are true?

A A resting 12-lead ECG is recommended in all patients with suspected angina
True ☐ **False** ☐

B A normal exercise tolerance test excludes a diagnosis of underlying coronary artery disease
True ☐ **False** ☐

C In patients with refractory angina attendance at angina management programmes has been shown to improve symptom control and exercise tolerance
True ☐ **False** ☐

D Around a third of patients diagnosed with ischaemic heart disease present with stable angina
True ☐ **False** ☐

E CT coronary angiography is recommended as a first-line investigation in patients with a new diagnosis of suspected stable angina
True ☐ **False** ☐

»

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7 List the six major drug classes for the treatment of stable angina.

8 List any changes to your clinical practice that you may make having read this article.

ACUTE PANCREATITIS

9 Which of the statements are true?

A All patients with clinical findings suggestive of acute pancreatitis should be referred to hospital for urgent evaluation
True ☐ False ☐

B The incidence of acute pancreatitis is increasing in young women who drink excessive amounts of alcohol
True ☐ False ☐

C The diagnosis of acute pancreatitis should be considered in any patient presenting with abdominal pain
True ☐ False ☐

D Many patients who develop severe disease seem well on admission but deteriorate over subsequent days
True ☐ False ☐

E An elevated ALT at presentation ≥ 150 IU/L has a positive predictive value of 85% in predicting a gallstone aetiology
True ☐ False ☐

10 History and examination can be indicative of the diagnosis. However, two out of three diagnostic criteria should be met. List the three criteria.

11 Complete the statement:
The most common pattern of pain is

pain that radiates to the

is exacerbated by

and is alleviated by

12 List any changes to your clinical practice that you may make having read this article.

Answers

SYNCOPE
1 **A** True **B** True **C** False **D** True **E** False (under 40)

2 **A** 2 **B** 2 **C** C3 **D** 2

3 Seizures; hypoglycaemia; trauma and psychogenic causes

STABLE ANGINA
5 A constricting discomfort in the front of the chest, or in the neck, shoulders, jaw or arms; precipitated by physical exertion; relieved by rest or GTN within about 5 minutes

6 **A** True **B** False **C** True **D** False (half) **E** True

7 Beta-blockers; calcium channel blockers; nitrates, potassium channel activators; sinus node inhibitors; and late sodium current inhibitors

ACUTE PANCREATITIS
9 **A** True **B** True **C** True **D** True **E** False (95%)

10 Typical history; elevated serum amylase or lipase (>3 ULN); imaging (ultrasound, CT or MRI) consistent with acute pancreatitis

11 Severe epigastric; back; movement; sitting forwards

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Tracking down and treating the cause of syncope

Leo M, Betts T. Tracking down and treating the cause of syncope.
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Tracking down and treating the cause of syncope

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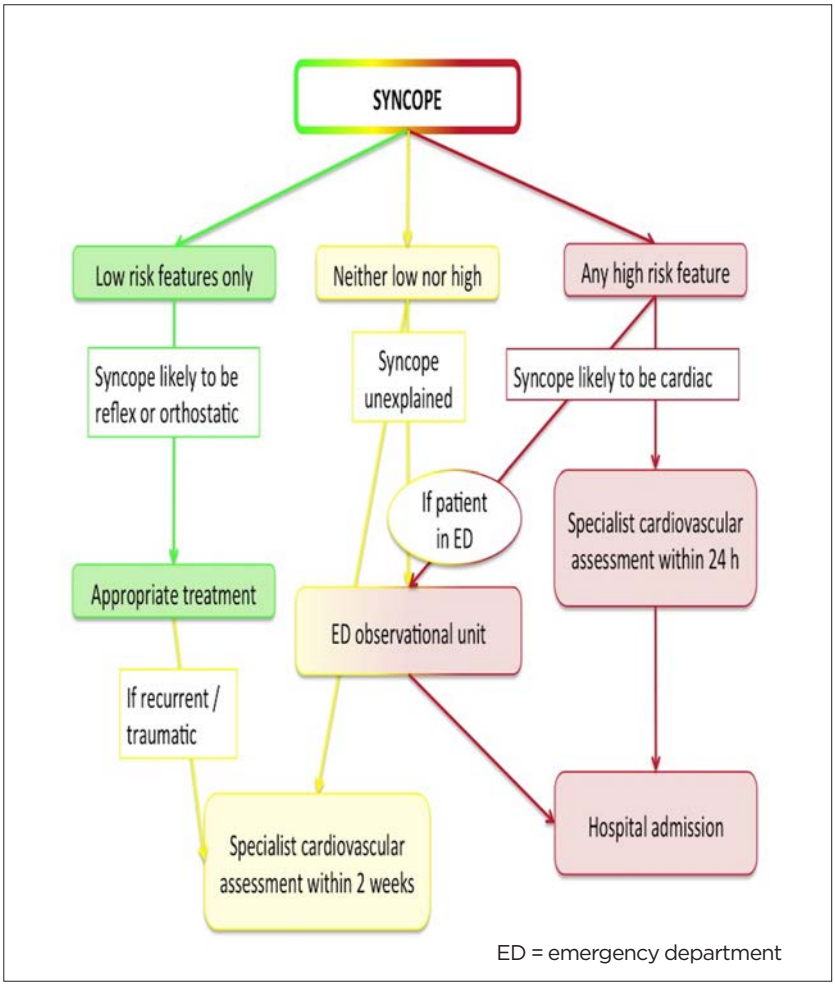


FIGURE 1
Risk stratification flow chart for management of patients with syncope after initial evaluation (modified from the 2018 ESC guidelines on syncope[2])

What are the mechanisms involved?

How should risk stratification be carried out?

What are the management strategies?

EVENTS OF A SUSPECTED SYNCOPAL NATURE ARE EXTREMELY FREQUENT IN THE GENERAL POPULATION, with 50% of people having at least one episode in their lifetime. The incidence is similar in men and women and increases with age, with two peaks of prevalence at 10-30 years and > 65 years.[1]

Syncope is a transient loss of consciousness (T-LOC) caused by cerebral hypoperfusion, characterised by a rapid onset, short duration and spontaneous complete recovery. It needs to be differentiated from other conditions that can cause T-LOC such as seizures, hypoglycaemia, trauma and psychogenic causes.[2,3]

From a pathophysiological viewpoint, three principal types of syncope can be identified: reflex or neurally mediated, orthostatic hypotensive and cardiac.[2,3] The common denominator of all these conditions is low systemic blood pressure (BP) causing global cerebral hypoperfusion and hence syncope.

Reflex syncopal episodes are caused by inappropriate functioning of normal cardiovascular reflexes in response to specific triggers, resulting in vasodilatation (vasopressor response), bradycardia (cardioinhibitory response) or a combination of both (mixed response). According to the trigger, reflex syncope can be classified as vasovagal (orthostatic or emotional), situational (triggered by micturition, gastrointestinal stimulation, coughing, sneezing, exercise, etc), carotid sinus syncope (caused by carotid sinus hypersensitivity), or atypical forms (without prodromes and/or without apparent triggers and/or atypical presentation).

Orthostatic hypotensive syncopal episodes are caused by hypotension in the setting of postural changes, i.e. going from a lying or sitting position to standing. They can be drug-induced (e.g. by vasodilators, diuretics, phenothiazines, antidepressants), result from volume depletion (haemorrhage, diarrhoea, vomiting) or caused by chronic impairment of the sympathetic tone resulting in insufficient peripheral vasoconstriction in response to orthostatic stress (Parkinson's disease, dementia, diabetes, kidney failure etc). Of note, a possible causal effect of orthostatic hypotension in dementia has also been recently suggested.[4]

Cardiac forms of syncope result from reduced cardiac output caused by »

cardiac arrhythmias (bradyarrhythmias or tachyarrhythmias) or structural cardiovascular conditions (aortic stenosis, acute myocardial infarction/ischaemia, hypertrophic cardiomyopathy, cardiac masses, pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valve dysfunction, pulmonary embolism, acute aortic dissection, pulmonary hypertension).

Reflex syncope is the most frequent cause of syncope in any setting and at all ages, followed by cardiac syncope and orthostatic hypotension. In individuals under 40 years of age, orthostatic hypotensive syncopal episodes are extremely rare.[5-7] The prognosis of syncope is dependent on the cause and the presence of underlying disease.

Table 1

Clinical history in a patient with suspected syncope

Patient's posture immediately before the event
- Upright
- Supine
- Seated

Precipitating factors
- Fatigue, sleep, food deprivation
- Ambient temperature
- Alcohol consumption
- Pain, strong emotions such as fear or apprehension
- Physical exercise

Prodromal symptoms
- Dizziness, lightheadedness
- Vertigo, sweating, epigastric discomfort, nausea, blurred vision, paraesthesia, chest pain, palpitations, headache, focal neurological deficits, déjà vu, confusion

Appearance during event
- Pallor, tongue biting, any body movements

Recovery
- Rapid
- Persisting somnolence, fatigue for minutes/hours
- Headache, neurological deficits
- Chest pain, palpitations

Medications
- Cardiac and antihypertensive medications, Parkinson's drug therapy, alpha-blockers for prostatism

Personal history
- Cardiac disease
- Parkinson's disease, dementia, diabetes

Family history
- Sudden cardiac death in young relatives
- Syncope, arrhythmias, cardiomyopathy, inherited cardiac conditions and channelopathies

There is also the consequential risk of syncope i.e. the impact that the syncope has on a patient's life through physical trauma and frequency of episodes. Cardiac syncope is often associated with high morbidity and considerable mortality, while reflex syncope has a more favourable, benign prognosis.

EXAMINATION

The initial assessment of patients with suspected syncope should aim to:
- Determine if the T-LOC event was due to syncope or to non-syncopal causes
- Identify the underlying cause of syncope
- Stratify the patient's risk of a serious outcome, and determine the urgency of any additional investigations and/or treatment required and the need for hospital admission (see figure 1, p11).[2,3]

It should include taking a clinical history, physical examination and a 12-lead ECG. The clinical history should be focused on: a detailed recollection of the T-LOC event (by the patient and any witnesses), the patient's medical history and drug history, and any family history of cardiac disease, see table 1, left.

The physical examination should include general inspection, cardiovascular examination with repeated systemic BP measurements, basic neurological examinations, see table 2, below.

A stepwise approach should be applied to the analysis of the ECG to identify abnormalities suggestive of cardiac syncope, see figure 2, opposite.

Table 2

Physical examination in a patient with suspected syncope

General inspection
- Head injury, lacerations, extremity fractures or other signs of trauma
- Tongue biting

Cardiopulmonary examination
- Heart rhythm abnormalities
- Heart murmurs
- Carotid bruits
- Peripheral oedema, raised jugular venous pressure, bilateral crackles or other signs of heart failure
- Peripheral SaO_2

Repeated blood pressure measurements
- While lying
- During active standing (after 3 min)

Neurological examination
- Focal neurological deficits

The initial assessment should also be used to stratify the patient's risk of serious cardiovascular events or sudden arrhythmic death through the identification of low- and high-risk features, see figure 3, opposite.[1]

Recent data show that approximately 50% of patients who present to emergency departments with syncope are currently admitted. Of these, 0.8% will die in the next 7-30 days, 6.9% will have a non-fatal severe outcome in the emergency department, and 3.6% will have a non-fatal severe outcome after discharge. Almost 90% will not come to serious harm and with hindsight did not require urgent admission and could have been managed with outpatient investigations.[2]

The 2014 NICE guideline on loss of consciousness and the 2018 ESC guidelines on syncope both stress that an accurate risk stratification of patients with syncope could potentially avoid unnecessary admissions of low-risk patients while ensuring early and comprehensive investigation and treatment in high-risk patients.[2,3]

CONFIRMING DIAGNOSIS

In approximately 60% of cases the clinical history alone is sufficient to differentiate syncope from other causes of T-LOC.[8] The combination of clinical history, physical examination and 12-lead ECG can provide a certain or suspected aetiology of syncope in up to 50% of cases.[9]

The 2018 ESC guidelines suggest diagnostic criteria for nearly certain or highly probable aetiological diagnosis after first evaluation.[2]
- Vasovagal syncope can be considered highly probable if syncope is precipitated by pain, fear or standing and is associated with a typical progressive prodrome (pallor, sweating and/or nausea).
- Situational syncope can be considered highly probable or confirmed if syncope occurs during or immediately after specific triggers.
- Syncope due to classical orthostatic hypotension can be considered confirmed if spontaneous symptoms are reproduced by a fall in systolic BP of at least 20 mmHg, a fall in diastolic BP of at least 10 mmHg or a decrease in systolic BP to < 90 mmHg within three minutes of standing.
- Cardiac syncope should be suspected in the presence of concomitant sustained cardiac arrhythmias, myocardial infarction, pulmonary embolism or aortic dissection; it can be

considered highly probable in the presence of known structural or electrical cardiac diseases (severe aortic stenosis, hypertrophic cardiomyopathy, Long QT syndrome, Brugada syndrome, etc) or in the presence of abnormal ECG findings, as indicated in figure 2, right.

The 2018 ESC guidelines on syncope continue to favour tilt testing in patients with suspected reflex or orthostatic syncope,[2] although the strength of recommendation has changed from I in the 2009 guidelines to IIa in the most recent version. Because of its low specificity, the test is not suggested in cases of unexplained syncope. False positives occur in up to 47% of patients with cardiac syncope.[10] The new concept of hypotensive susceptibility, i.e. susceptibility to orthostatic stress, has been introduced in the 2018 ESC guidelines to explain the positivity of tilt testing in most patients with unexplained syncope regardless of the cause.[2]

Of note, the 2014 NICE guideline[3] suggests no additional investigations in uncomplicated cases of vasovagal, situational or orthostatic hypotensive syncope with no high-risk features. In particular, tilt testing is only suggested in patients with recurrent severe episodes of reflex syncope to assess if the syncope is accompanied by a severe cardioinhibitory response which may then influence subsequent treatment.

As stated in both guidelines,[2,3] carotid sinus massage should be performed to reproduce symptoms in cases of suspected carotid sinus syncope. This test can be performed in the primary care setting if ECG monitoring and BP recording is available. With the patient lying supine, after checking there are no carotid bruits, the right carotid pulse is firmly massaged for 3-5 seconds while recording BP and a rhythm strip on the ECG. A ventricular pause lasting >3 seconds and/or a fall in systolic BP of > 50 mmHg is known as carotid sinus hypersensitivity.

However, carotid sinus syncope can only be confirmed in the case of symptoms during carotid sinus massage, usually occurring in the presence of ventricular pauses > 6 seconds, and clinical features of reflex syncope. Carotid sinus hypersensitivity is a common incidental finding in older men without syncope.[10] A potential complication of carotid sinus massage is TIA/stroke in 0.24% of cases.[2] Therefore, it should be undertaken with caution in patients with previous TIA, stroke, or known carotid stenosis >70%. The carotids should be ausculated for bruits before performing massage. »

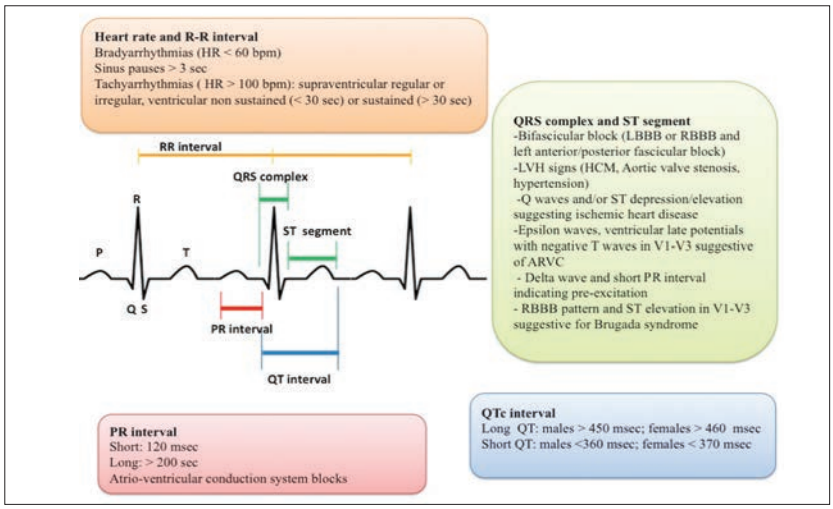


FIGURE 2
ECG features suggesting cardiac syncope

FIGURE 3
Low- and high-risk features at initial evaluation in patients with syncope[2]

	LOW-RISK FEATURES	HIGH-RISK FEATURES
CLINICAL HISTORY	- Prodrome and precipitating factors typical of reflex syncope - Long history of recurrent syncopal episodes with same characteristics - No history of previous cardiac disease	- New chest discomfort, breathlessness, abdominal pain, headache - Palpitations preceding syncope - History of severe structural or coronary artery disease - No warning or short prodrome * - Syncope while sitting * - Family history of SCD at young age *
PHYSICAL EXAMINATION	Normal physical examination	- Persistent bradycardia < 40 bpm - Heart murmur - Unexplained systolic BP< 90 mmHg - Serious injury
ECG	Normal ECG	- ST Elevation Myocardial Infarction - Brugada/ARVC pattern - Persistent sinus bradycardia or AF < 40 bpm or sinus pauses > 3 sec in awake state - Mobitz II type second degree AV block - Third degree AV block - BBB, ventricular hypertrophy, Q waves - Sustained/non sustained VT - PPM/ICD dysfunction - Short/Long QT interval - Paroxysmal AF/SVT ** - Mobitz I second degree AV block ** - First degree AV block with marked prolongation of PR interval ** - Asymptomatic inappropriate mild sinus bradycardia or AF (40-50 bpm) **

Key: AF = atrial fibrillation; ARVC = arrhythmogenic right ventricular cardiomyopathy; AV = atrioventricular; BBB = bundle branch block; PPM = permanent pacemaker; ICD = implantable cardioverter defibrillator; SCD = sudden cardiac death; SVT= supraventricular tachycardia; VT = ventricular tachycardia.
* High-risk feature only in association with abnormal ECG or structural heart disease
** High-risk feature only if history consistent with arrhythmic syncope

key points

SELECTED BY

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Events of a suspected syncopal nature are extremely frequent in the general population, with 50% of people having at least one episode in their lifetime. Syncope is a transient loss of consciousness (T-LOC) caused by cerebral hypoperfusion, characterised by a rapid onset, short duration and spontaneous complete recovery. It needs to be differentiated from other conditions that can cause T-LOC such as seizures, hypoglycaemia, trauma and psychogenic causes.

Three principal types of syncope can be identified: reflex or neurally mediated, orthostatic hypotensive and cardiac. The common denominator of all these conditions is low systemic BP causing global cerebral hypoperfusion. Reflex syncope is the most frequent cause of syncope in any setting and at all ages, followed by cardiac syncope and orthostatic hypotension. In individuals under 40 years of age, orthostatic hypotensive syncopal episodes are extremely rare. Cardiac syncope is often associated with high morbidity and considerable mortality, while reflex syncope has a more favourable, benign prognosis.

Recent data show that around 50% of patients who present to emergency departments with syncope are admitted. Of these, 0.8% will die in the next 7-30 days, 6.9% will have a non-fatal severe outcome in the emergency department, and 3.6% will have a non-fatal severe outcome after discharge. Almost 90% will not come to serious harm and with hindsight did not require urgent admission and could have been managed with outpatient investigations.

In around 60% of cases the clinical history alone is sufficient to differentiate syncope from other causes of T-LOC. The combination of clinical history, physical examination and 12-lead ECG can provide a certain or suspected aetiology of syncope in up to 50% of cases. NICE guidance suggests no additional investigations in uncomplicated cases of vasovagal, situational or orthostatic hypotensive syncope with no high-risk features. In particular, tilt testing is only suggested in patients with recurrent severe episodes of reflex syncope. Additional investigations are usually required in cases of suspected cardiac syncope to confirm the diagnosis and/or stratify the patient's risk of serious outcomes.

In patients with reflex syncope and with orthostatic hypotension lifestyle modifications are recommended as first-line therapy. The treatment of cardiac syncope is mainly directed at the underlying cardiac disease. Patients with infrequent episodes and low-risk features (and who are likely to have reflex, situational or orthostatic syncope), should be reassured about the benign nature of the event and treated appropriately. All other patients need an expert syncope review within two weeks and can be safely managed in an outpatient setting.

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Additional investigations are usually required in cases of suspected cardiac syncope to confirm the diagnosis and/or stratify the risk of serious outcomes.[2,3]

- Echocardiography is indicated in the case of suspected structural heart disease.
- Exercise testing should be performed in patients who experience syncope during or shortly after exertion.
- Prolonged ECG monitoring is indicated in the case of suspected arrhythmic syncope. Different ECG monitoring systems with different duration and features are currently available. The choice should be based on frequency of symptoms and on the ability of the patient or the bystander to activate a recorder before or during a syncopal episode.

Continuous ECG monitors can record the ECG continuously for up to 14 days. The 24-48 hr ECG Holter monitoring has a very low diagnostic yield (1.8-4% in patients with syncope);[12,13] it should be used only in patients with daily episodes. Apart from the traditional ECG Holter devices that use leads, leadless devices consisting of single-use patch electrodes, are currently available (ZIO,[14] Carnation) and they can record continuously for up to 7 or 14 days.

Event monitors make patient-activated recordings when the patient either places the device against their chest or presses their thumbs on two electrodes. They can record symptoms during prodromes or associated palpitations, but the device will not be activated when the patient is unconscious.

External loop recorders are event monitors with a loop memory. The ECG is continuously recorded and deleted, unless activated by the patient. Devices will also make automated recordings if the heart rate drops below or exceeds predefined rates. They are useful when symptoms occur every few weeks.

Implantable loop recorders (ILRs) are small devices that are inserted subcutaneously under local anaesthesia. They have a battery life of up to five years and a loop memory that stores retrospective ECG recordings automatically in the case of predefined arrhythmia recurring or if activated by the patient. The recordings can be downloaded wirelessly for analysis.[15] ILRs are ideally suited to individuals with very infrequent, potentially high-risk syncope.

- An electrophysiological study is suggested in selected cases of unexplained syncope despite non-invasive evaluation in patients with previous myocardial infarction (to identify patients who could benefit from an ICD), in patients with bifascicular block (to diagnose high degree AV block requiring permanent pacing) and in patients with palpitations during syncope (to diagnose a treatable cause such as supraventricular tachycardia).

In cases of unexplained T-LOC events or recurrent syncopal episodes of unknown cause, patients and their relatives should be encouraged to record videos during the event.

MANAGEMENT

In patients with reflex syncope and with orthostatic hypotension lifestyle modifications are recommended as first-line therapy. Lifestyle changes such as increasing dietary salt and water intake, avoiding triggers and hot crowded environments, reducing alcohol consumption, plus moderate exercise training can have a huge impact in reducing the frequency of syncopal episodes. Any hypotensive and psychotropic drugs should be reduced or discontinued, if possible.[16] Compression stockings should be considered to reduce the venous pooling in patients with orthostatic hypotension. In the case of prodromal symptoms, physical counterpressure manoeuvres (sitting or lying down in order to avoid injury, leg crossing, squatting), should be performed at the onset of symptoms to increase BP in the hope of averting syncope.

Tilt training, consisting of progressively longer periods of prescribed upright posture, seems to have only little efficacy in reducing syncope by increasing the peripheral vascular compliance to orthostatic stress.

Midodrine, an alpha-agonist, and fludrocortisone[17] have shown contrasting results in reducing syncopal recurrences in patients with vasovagal syncope and therefore they are not currently recommended other than in cases of severe recurrent forms of reflex or orthostatic syncope not responsive to lifestyle measures. They seem to be most beneficial as adjunctive therapy in patients with orthostatic hypotension.

A pacemaker is only rarely indicated in reflex syncope. It could be considered in order to reduce the recurrence of syncope in patients older than 40 years with recurrent, severe and unpredictable episodes that have a predominant cardioinhibitory component, i.e. pauses of > 10 seconds. Of note, recent data show a high spontaneous remission rate in patients with frequent vasovagal syncope. It might be worth following the

patient up for a brief period before starting a specific therapy.[18]

The treatment of cardiac syncope is mainly directed at the underlying cardiac disease. Potential reversible causes of arrhythmias (drugs, electrolyte imbalances) should be investigated in the first instance and treated if present. Critical obstruction such as severe aortic stenosis or hypertrophic cardiomyopathy may be amenable to surgical intervention. Cardiac pacing is recommended for treatment of bradycardia-induced syncope resulting from significant conduction disease. Catheter ablation and drugs are potential treatment options for tachycardia-induced syncope.

ICD therapy might be indicated in the case of ventricular tachycardia with structural or electrical heart disease and in the case of unexplained syncope (suspected as arrhythmic) in patients with high-risk conditions including severely depressed left ventricular systolic function (LVEF < 35%), hypertrophic cardiomyopathy, Brugada syndrome and long QT syndrome.

The goal of treatment of syncope secondary to structural heart disease is treatment of the underlying disease with reduction of the associated risk of death.

Patients with syncope may be subject to driving restrictions, see DVLA guidance for medical professionals, Useful information box, below right.

REFERRAL

Patients with infrequent episodes and low-risk features (and who are likely to have reflex, situational or orthostatic syncope), should be reassured about the benign nature of the event and treated appropriately. Specialist cardiovascular assessment is not required.

Patients with any high-risk features and thus likely to have cardiac syncope, or those with recurrent traumatic syncopal episodes should be admitted to hospital (or to an emergency department observational unit) and/or referred for urgent specialist cardiovascular assessment within 24 hours.

All other patients need an expert syncope review within two weeks and can be safely managed in an outpatient setting or, if initially evaluated in an emergency department, they could be managed in the observational unit.

Competing interests: None

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Useful information

Arrhythmia Alliance
www.heartrhythmcharity.org.uk

STARS (Syncope Trust And Reflex anoxic Seizures)
www.stars.org.uk

DVLA guidance for medical professionals
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/736938/assessing-fitness-to-drive-a-guide-for-medical-professionals.pdf

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Tracking down and treating the cause of syncope

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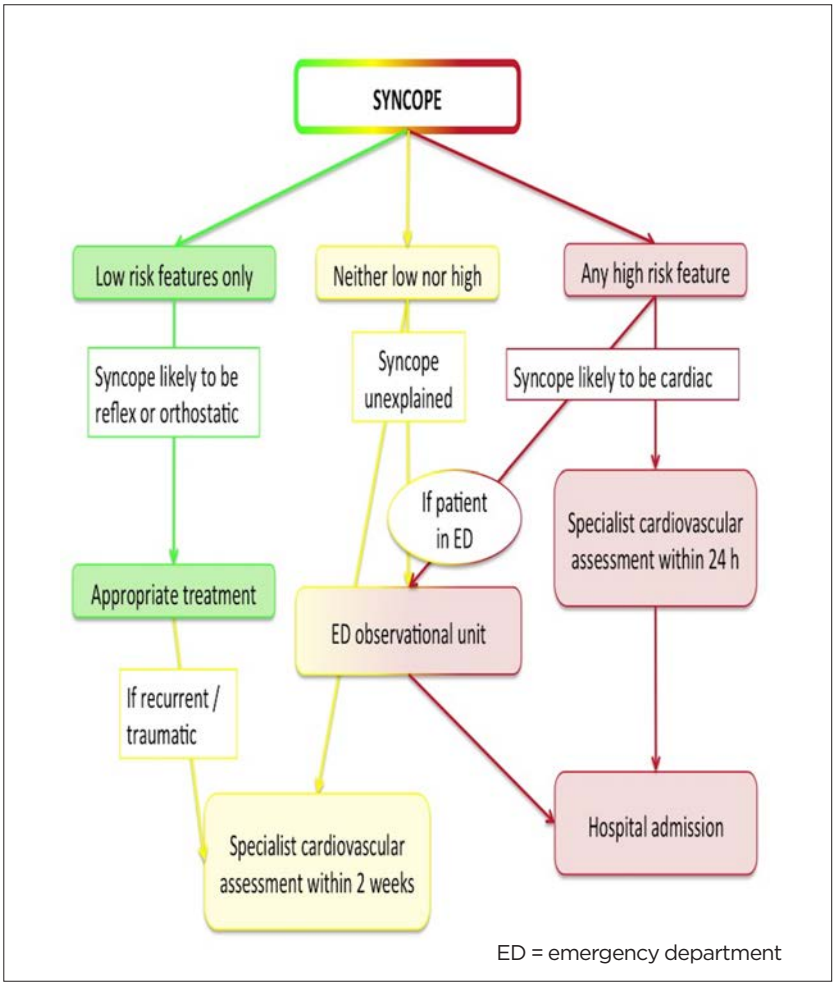


FIGURE 1
Risk stratification flow chart for management of patients with syncope after initial evaluation (modified from the 2018 ESC guidelines on syncope[2])

What are the mechanisms involved?

How should risk stratification be carried out?

What are the management strategies?

EVENTS OF A SUSPECTED SYNCOPAL NATURE ARE EXTREMELY FREQUENT IN THE GENERAL POPULATION, with 50% of people having at least one episode in their lifetime. The incidence is similar in men and women and increases with age, with two peaks of prevalence at 10-30 years and > 65 years.[1]

Syncope is a transient loss of consciousness (T-LOC) caused by cerebral hypoperfusion, characterised by a rapid onset, short duration and spontaneous complete recovery. It needs to be differentiated from other conditions that can cause T-LOC such as seizures, hypoglycaemia, trauma and psychogenic causes.[2,3]

From a pathophysiological viewpoint, three principal types of syncope can be identified: reflex or neurally mediated, orthostatic hypotensive and cardiac.[2,3] The common denominator of all these conditions is low systemic blood pressure (BP) causing global cerebral hypoperfusion and hence syncope.

Reflex syncopal episodes are caused by inappropriate functioning of normal cardiovascular reflexes in response to specific triggers, resulting in vasodilatation (vasopressor response), bradycardia (cardioinhibitory response) or a combination of both (mixed response). According to the trigger, reflex syncope can be classified as vasovagal (orthostatic or emotional), situational (triggered by micturition, gastrointestinal stimulation, coughing, sneezing, exercise, etc), carotid sinus syncope (caused by carotid sinus hypersensitivity), or atypical forms (without prodromes and/or without apparent triggers and/or atypical presentation).

Orthostatic hypotensive syncopal episodes are caused by hypotension in the setting of postural changes, i.e. going from a lying or sitting position to standing. They can be drug-induced (e.g. by vasodilators, diuretics, phenothiazines, antidepressants), result from volume depletion (haemorrhage, diarrhoea, vomiting) or caused by chronic impairment of the sympathetic tone resulting in insufficient peripheral vasoconstriction in response to orthostatic stress (Parkinson's disease, dementia, diabetes, kidney failure etc). Of note, a possible causal effect of orthostatic hypotension in dementia has also been recently suggested.[4]

Cardiac forms of syncope result from reduced cardiac output caused by »

cardiac arrhythmias (bradyarrhythmias or tachyarrhythmias) or structural cardiovascular conditions (aortic stenosis, acute myocardial infarction/ischaemia, hypertrophic cardiomyopathy, cardiac masses, pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valve dysfunction, pulmonary embolism, acute aortic dissection, pulmonary hypertension).

Reflex syncope is the most frequent cause of syncope in any setting and at all ages, followed by cardiac syncope and orthostatic hypotension. In individuals under 40 years of age, orthostatic hypotensive syncopal episodes are extremely rare.[5-7] The prognosis of syncope is dependent on the cause and the presence of underlying disease.

Table 1

Clinical history in a patient with suspected syncope

Patient's posture immediately before the event
- Upright
- Supine
- Seated

Precipitating factors
- Fatigue, sleep, food deprivation
- Ambient temperature
- Alcohol consumption
- Pain, strong emotions such as fear or apprehension
- Physical exercise

Prodromal symptoms
- Dizziness, lightheadedness
- Vertigo, sweating, epigastric discomfort, nausea, blurred vision, paraesthesia, chest pain, palpitations, headache, focal neurological deficits, déjà vu, confusion

Appearance during event
- Pallor, tongue biting, any body movements

Recovery
- Rapid
- Persisting somnolence, fatigue for minutes/hours
- Headache, neurological deficits
- Chest pain, palpitations

Medications
- Cardiac and antihypertensive medications, Parkinson's drug therapy, alpha-blockers for prostatism

Personal history
- Cardiac disease
- Parkinson's disease, dementia, diabetes

Family history
- Sudden cardiac death in young relatives
- Syncope, arrhythmias, cardiomyopathy, inherited cardiac conditions and channelopathies

There is also the consequential risk of syncope i.e. the impact that the syncope has on a patient's life through physical trauma and frequency of episodes. Cardiac syncope is often associated with high morbidity and considerable mortality, while reflex syncope has a more favourable, benign prognosis.

EXAMINATION

The initial assessment of patients with suspected syncope should aim to:
- Determine if the T-LOC event was due to syncope or to non-syncopal causes
- Identify the underlying cause of syncope
- Stratify the patient's risk of a serious outcome, and determine the urgency of any additional investigations and/or treatment required and the need for hospital admission (see figure 1, p11).[2,3]

It should include taking a clinical history, physical examination and a 12-lead ECG. The clinical history should be focused on: a detailed recollection of the T-LOC event (by the patient and any witnesses), the patient's medical history and drug history, and any family history of cardiac disease, see table 1, left.

The physical examination should include general inspection, cardiovascular examination with repeated systemic BP measurements, basic neurological examinations, see table 2, below.

A stepwise approach should be applied to the analysis of the ECG to identify abnormalities suggestive of cardiac syncope, see figure 2, opposite.

Table 2

Physical examination in a patient with suspected syncope

General inspection
- Head injury, lacerations, extremity fractures or other signs of trauma
- Tongue biting

Cardiopulmonary examination
- Heart rhythm abnormalities
- Heart murmurs
- Carotid bruits
- Peripheral oedema, raised jugular venous pressure, bilateral crackles or other signs of heart failure
- Peripheral SaO_2

Repeated blood pressure measurements
- While lying
- During active standing (after 3 min)

Neurological examination
- Focal neurological deficits

The initial assessment should also be used to stratify the patient's risk of serious cardiovascular events or sudden arrhythmic death through the identification of low- and high-risk features, see figure 3, opposite.[1]

Recent data show that approximately 50% of patients who present to emergency departments with syncope are currently admitted. Of these, 0.8% will die in the next 7-30 days, 6.9% will have a non-fatal severe outcome in the emergency department, and 3.6% will have a non-fatal severe outcome after discharge. Almost 90% will not come to serious harm and with hindsight did not require urgent admission and could have been managed with outpatient investigations.[2]

The 2014 NICE guideline on loss of consciousness and the 2018 ESC guidelines on syncope both stress that an accurate risk stratification of patients with syncope could potentially avoid unnecessary admissions of low-risk patients while ensuring early and comprehensive investigation and treatment in high-risk patients.[2,3]

CONFIRMING DIAGNOSIS

In approximately 60% of cases the clinical history alone is sufficient to differentiate syncope from other causes of T-LOC.[8] The combination of clinical history, physical examination and 12-lead ECG can provide a certain or suspected aetiology of syncope in up to 50% of cases.[9]

The 2018 ESC guidelines suggest diagnostic criteria for nearly certain or highly probable aetiological diagnosis after first evaluation.[2]
- Vasovagal syncope can be considered highly probable if syncope is precipitated by pain, fear or standing and is associated with a typical progressive prodrome (pallor, sweating and/or nausea).
- Situational syncope can be considered highly probable or confirmed if syncope occurs during or immediately after specific triggers.
- Syncope due to classical orthostatic hypotension can be considered confirmed if spontaneous symptoms are reproduced by a fall in systolic BP of at least 20 mmHg, a fall in diastolic BP of at least 10 mmHg or a decrease in systolic BP to < 90 mmHg within three minutes of standing.
- Cardiac syncope should be suspected in the presence of concomitant sustained cardiac arrhythmias, myocardial infarction, pulmonary embolism or aortic dissection; it can be

considered highly probable in the presence of known structural or electrical cardiac diseases (severe aortic stenosis, hypertrophic cardiomyopathy, Long QT syndrome, Brugada syndrome, etc) or in the presence of abnormal ECG findings, as indicated in figure 2, right.

The 2018 ESC guidelines on syncope continue to favour tilt testing in patients with suspected reflex or orthostatic syncope,[2] although the strength of recommendation has changed from I in the 2009 guidelines to IIa in the most recent version. Because of its low specificity, the test is not suggested in cases of unexplained syncope. False positives occur in up to 47% of patients with cardiac syncope.[10] The new concept of hypotensive susceptibility, i.e. susceptibility to orthostatic stress, has been introduced in the 2018 ESC guidelines to explain the positivity of tilt testing in most patients with unexplained syncope regardless of the cause.[2]

Of note, the 2014 NICE guideline[3] suggests no additional investigations in uncomplicated cases of vasovagal, situational or orthostatic hypotensive syncope with no high-risk features. In particular, tilt testing is only suggested in patients with recurrent severe episodes of reflex syncope to assess if the syncope is accompanied by a severe cardioinhibitory response which may then influence subsequent treatment.

As stated in both guidelines,[2,3] carotid sinus massage should be performed to reproduce symptoms in cases of suspected carotid sinus syncope. This test can be performed in the primary care setting if ECG monitoring and BP recording is available. With the patient lying supine, after checking there are no carotid bruits, the right carotid pulse is firmly massaged for 3-5 seconds while recording BP and a rhythm strip on the ECG. A ventricular pause lasting >3 seconds and/or a fall in systolic BP of > 50 mmHg is known as carotid sinus hypersensitivity.

However, carotid sinus syncope can only be confirmed in the case of symptoms during carotid sinus massage, usually occurring in the presence of ventricular pauses > 6 seconds, and clinical features of reflex syncope. Carotid sinus hypersensitivity is a common incidental finding in older men without syncope.[10] A potential complication of carotid sinus massage is TIA/stroke in 0.24% of cases.[2] Therefore, it should be undertaken with caution in patients with previous TIA, stroke, or known carotid stenosis >70%. The carotids should be ausculated for bruits before performing massage. »

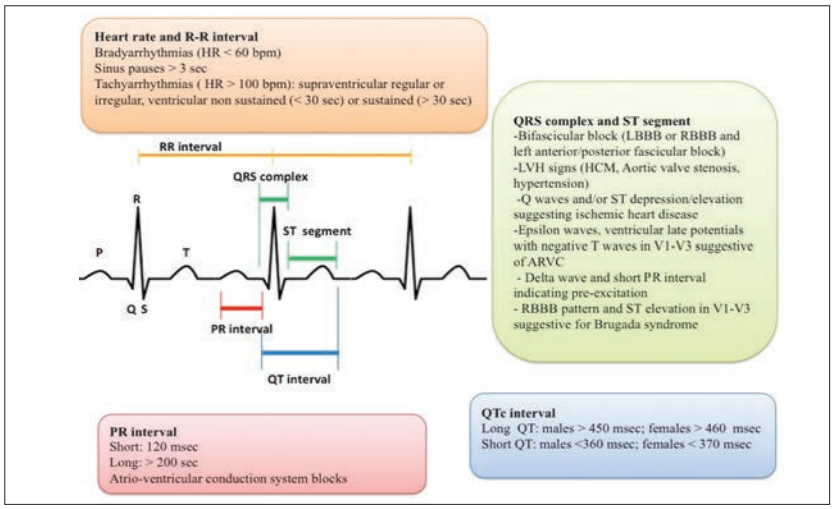


FIGURE 2
ECG features suggesting cardiac syncope

FIGURE 3
Low- and high-risk features at initial evaluation in patients with syncope[2]

	LOW-RISK FEATURES	HIGH-RISK FEATURES
CLINICAL HISTORY	- Prodrome and precipitating factors typical of reflex syncope - Long history of recurrent syncopal episodes with same characteristics - No history of previous cardiac disease	- New chest discomfort, breathlessness, abdominal pain, headache - Palpitations preceding syncope - History of severe structural or coronary artery disease - No warning or short prodrome * - Syncope while sitting * - Family history of SCD at young age *
PHYSICAL EXAMINATION	Normal physical examination	- Persistent bradycardia < 40 bpm - Heart murmur - Unexplained systolic BP< 90 mmHg - Serious injury
ECG	Normal ECG	- ST Elevation Myocardial Infarction - Brugada/ARVC pattern - Persistent sinus bradycardia or AF < 40 bpm or sinus pauses > 3 sec in awake state - Mobitz II type second degree AV block - Third degree AV block - BBB, ventricular hypertrophy, Q waves - Sustained/non sustained VT - PPM/ICD dysfunction - Short/Long QT interval - Paroxysmal AF/SVT ** - Mobitz I second degree AV block ** - First degree AV block with marked prolongation of PR interval ** - Asymptomatic inappropriate mild sinus bradycardia or AF (40-50 bpm) **

Key: AF = atrial fibrillation; ARVC = arrhythmogenic right ventricular cardiomyopathy; AV = atrioventricular; BBB = bundle branch block; PPM = permanent pacemaker; ICD = implantable cardioverter defibrillator; SCD = sudden cardiac death; SVT= supraventricular tachycardia; VT = ventricular tachycardia.
* High-risk feature only in association with abnormal ECG or structural heart disease
** High-risk feature only if history consistent with arrhythmic syncope

key points

SELECTED BY

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Events of a suspected syncopal nature are extremely frequent in the general population, with 50% of people having at least one episode in their lifetime. Syncope is a transient loss of consciousness (T-LOC) caused by cerebral hypoperfusion, characterised by a rapid onset, short duration and spontaneous complete recovery. It needs to be differentiated from other conditions that can cause T-LOC such as seizures, hypoglycaemia, trauma and psychogenic causes.

Three principal types of syncope can be identified: reflex or neurally mediated, orthostatic hypotensive and cardiac. The common denominator of all these conditions is low systemic BP causing global cerebral hypoperfusion. Reflex syncope is the most frequent cause of syncope in any setting and at all ages, followed by cardiac syncope and orthostatic hypotension. In individuals under 40 years of age, orthostatic hypotensive syncopal episodes are extremely rare. Cardiac syncope is often associated with high morbidity and considerable mortality, while reflex syncope has a more favourable, benign prognosis.

Recent data show that around 50% of patients who present to emergency departments with syncope are admitted. Of these, 0.8% will die in the next 7-30 days, 6.9% will have a non-fatal severe outcome in the emergency department, and 3.6% will have a non-fatal severe outcome after discharge. Almost 90% will not come to serious harm and with hindsight did not require urgent admission and could have been managed with outpatient investigations.

In around 60% of cases the clinical history alone is sufficient to differentiate syncope from other causes of T-LOC. The combination of clinical history, physical examination and 12-lead ECG can provide a certain or suspected aetiology of syncope in up to 50% of cases. NICE guidance suggests no additional investigations in uncomplicated cases of vasovagal, situational or orthostatic hypotensive syncope with no high-risk features. In particular, tilt testing is only suggested in patients with recurrent severe episodes of reflex syncope. Additional investigations are usually required in cases of suspected cardiac syncope to confirm the diagnosis and/or stratify the patient's risk of serious outcomes.

In patients with reflex syncope and with orthostatic hypotension lifestyle modifications are recommended as first-line therapy. The treatment of cardiac syncope is mainly directed at the underlying cardiac disease. Patients with infrequent episodes and low-risk features (and who are likely to have reflex, situational or orthostatic syncope), should be reassured about the benign nature of the event and treated appropriately. All other patients need an expert syncope review within two weeks and can be safely managed in an outpatient setting.

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Additional investigations are usually required in cases of suspected cardiac syncope to confirm the diagnosis and/or stratify the risk of serious outcomes.[2,3]

- Echocardiography is indicated in the case of suspected structural heart disease.
- Exercise testing should be performed in patients who experience syncope during or shortly after exertion.
- Prolonged ECG monitoring is indicated in the case of suspected arrhythmic syncope. Different ECG monitoring systems with different duration and features are currently available. The choice should be based on frequency of symptoms and on the ability of the patient or the bystander to activate a recorder before or during a syncopal episode.

Continuous ECG monitors can record the ECG continuously for up to 14 days. The 24-48 hr ECG Holter monitoring has a very low diagnostic yield (1.8-4% in patients with syncope);[12,13] it should be used only in patients with daily episodes. Apart from the traditional ECG Holter devices that use leads, leadless devices consisting of single-use patch electrodes, are currently available (ZIO,[14] Carnation) and they can record continuously for up to 7 or 14 days.

Event monitors make patient-activated recordings when the patient either places the device against their chest or presses their thumbs on two electrodes. They can record symptoms during prodromes or associated palpitations, but the device will not be activated when the patient is unconscious.

External loop recorders are event monitors with a loop memory. The ECG is continuously recorded and deleted, unless activated by the patient. Devices will also make automated recordings if the heart rate drops below or exceeds predefined rates. They are useful when symptoms occur every few weeks.

Implantable loop recorders (ILRs) are small devices that are inserted subcutaneously under local anaesthesia. They have a battery life of up to five years and a loop memory that stores retrospective ECG recordings automatically in the case of predefined arrhythmia recurring or if activated by the patient. The recordings can be downloaded wirelessly for analysis.[15] ILRs are ideally suited to individuals with very infrequent, potentially high-risk syncope.

- An electrophysiological study is suggested in selected cases of unexplained syncope despite non-invasive evaluation in patients with previous myocardial infarction (to identify patients who could benefit from an ICD), in patients with bifascicular block (to diagnose high degree AV block requiring permanent pacing) and in patients with palpitations during syncope (to diagnose a treatable cause such as supraventricular tachycardia).

In cases of unexplained T-LOC events or recurrent syncopal episodes of unknown cause, patients and their relatives should be encouraged to record videos during the event.

MANAGEMENT

In patients with reflex syncope and with orthostatic hypotension lifestyle modifications are recommended as first-line therapy. Lifestyle changes such as increasing dietary salt and water intake, avoiding triggers and hot crowded environments, reducing alcohol consumption, plus moderate exercise training can have a huge impact in reducing the frequency of syncopal episodes. Any hypotensive and psychotropic drugs should be reduced or discontinued, if possible.[16] Compression stockings should be considered to reduce the venous pooling in patients with orthostatic hypotension. In the case of prodromal symptoms, physical counterpressure manoeuvres (sitting or lying down in order to avoid injury, leg crossing, squatting), should be performed at the onset of symptoms to increase BP in the hope of averting syncope.

Tilt training, consisting of progressively longer periods of prescribed upright posture, seems to have only little efficacy in reducing syncope by increasing the peripheral vascular compliance to orthostatic stress.

Midodrine, an alpha-agonist, and fludrocortisone[17] have shown contrasting results in reducing syncopal recurrences in patients with vasovagal syncope and therefore they are not currently recommended other than in cases of severe recurrent forms of reflex or orthostatic syncope not responsive to lifestyle measures. They seem to be most beneficial as adjunctive therapy in patients with orthostatic hypotension.

A pacemaker is only rarely indicated in reflex syncope. It could be considered in order to reduce the recurrence of syncope in patients older than 40 years with recurrent, severe and unpredictable episodes that have a predominant cardioinhibitory component, i.e. pauses of > 10 seconds. Of note, recent data show a high spontaneous remission rate in patients with frequent vasovagal syncope. It might be worth following the

patient up for a brief period before starting a specific therapy.[18]

The treatment of cardiac syncope is mainly directed at the underlying cardiac disease. Potential reversible causes of arrhythmias (drugs, electrolyte imbalances) should be investigated in the first instance and treated if present. Critical obstruction such as severe aortic stenosis or hypertrophic cardiomyopathy may be amenable to surgical intervention. Cardiac pacing is recommended for treatment of bradycardia-induced syncope resulting from significant conduction disease. Catheter ablation and drugs are potential treatment options for tachycardia-induced syncope.

ICD therapy might be indicated in the case of ventricular tachycardia with structural or electrical heart disease and in the case of unexplained syncope (suspected as arrhythmic) in patients with high-risk conditions including severely depressed left ventricular systolic function (LVEF < 35%), hypertrophic cardiomyopathy, Brugada syndrome and long QT syndrome.

The goal of treatment of syncope secondary to structural heart disease is treatment of the underlying disease with reduction of the associated risk of death.

Patients with syncope may be subject to driving restrictions, see DVLA guidance for medical professionals, Useful information box, below right.

REFERRAL

Patients with infrequent episodes and low-risk features (and who are likely to have reflex, situational or orthostatic syncope), should be reassured about the benign nature of the event and treated appropriately. Specialist cardiovascular assessment is not required.

Patients with any high-risk features and thus likely to have cardiac syncope, or those with recurrent traumatic syncopal episodes should be admitted to hospital (or to an emergency department observational unit) and/or referred for urgent specialist cardiovascular assessment within 24 hours.

All other patients need an expert syncope review within two weeks and can be safely managed in an outpatient setting or, if initially evaluated in an emergency department, they could be managed in the observational unit.

Competing interests: None

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Useful information

Arrhythmia Alliance
www.heartrhythmcharity.org.uk

STARS (Syncope Trust And Reflex anoxic Seizures)
www.stars.org.uk

DVLA guidance for medical professionals
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/736938/assessing-fitness-to-drive-a-guide-for-medical-professionals.pdf

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Managing stable angina in primary care

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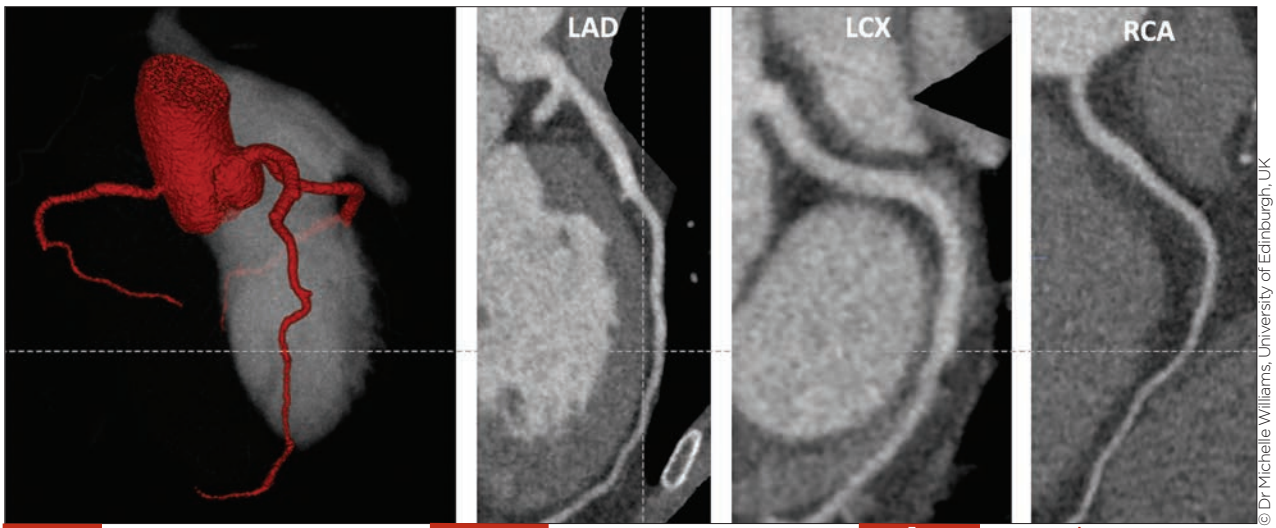
Managing stable angina in primary care

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FIGURE 1
CTCA images showing normal coronary arteries in a 70-year-old man referred with suspected stable angina

LAD = left anterior descending artery; Lcx = left circumflex artery; RCA = right coronary artery

How should patients be assessed?

STABLE ANGINA IS ESTIMATED TO AFFECT MORE THAN 1.3 MILLION PEOPLE IN THE UK WITH almost 100,000 new cases diagnosed each year.[1] The prevalence of angina increases sharply with age. Around 50% of people diagnosed with ischaemic heart disease (IHD) present with stable angina as the first symptom.[1]

Patients with stable angina typically describe a predictable tightness or constriction of the chest brought on by physical exertion or emotional stress that may radiate to the neck and jaw, upper limbs, or less commonly to the back. It occurs as a result of myocardial ischaemia, most commonly due to atherosclerotic coronary artery disease (CAD). Although angina may also occur where there is an imbalance between myocardial oxygen supply and demand, e.g. hypertrophic cardiomyopathy or severe aortic stenosis, this article will focus mainly on the diagnosis and management of stable angina due to CAD.

Table 1

Chest pain characteristics to guide diagnosis of angina[2]

- A constricting discomfort in the front of the chest, or in the neck, shoulders, jaw, or arms
- Precipitated by physical exertion
- Relieved by rest or GTN within about five minutes

The presence of all three features is defined as typical angina, two of the three features as atypical angina and one or none of the features as non-anginal chest pain

What investigations should be carried out?

INITIAL ASSESSMENT

In many cases the history alone is sufficient to reach a diagnosis of stable angina.[2,3,4] NICE recommends the classification of chest pain into typical angina, atypical angina or non-anginal chest pain based on the presence of key features of the pain, to aid diagnosis and guide investigation and management, see table 1, left.[2]

The presence of all three features suggests a diagnosis of typical angina. The presence of two features is considered atypical angina and where one or none of the features are present the pain may be defined as non-anginal.[2] Stable angina is unlikely if the chest pain is continuous or prolonged, unrelated to exertion, is brought on by movement or inspiration, or is associated with other symptoms such as palpitations, dizziness, tingling or difficulty swallowing. Angina symptoms may be influenced by a number of factors including comorbidity (e.g. diabetes mellitus) and gender.

Cardiovascular risk factors

Along with a detailed assessment of the presenting symptoms and prior history of cardiovascular disease, risk factors which predispose to CAD should be evaluated, see table 2, p18. The likelihood of a diagnosis of angina increases with the number of cardiovascular risk factors present.

Patients with angina who smoke should be strongly advised to stop. Education, self-help materials, counselling and pharmacological support may be offered where appropriate to patients wishing to cease smoking. Blood pressure should be recorded and hypertension, if present, managed according to current UK guidelines.[5] Patients should be offered healthy eating advice, undertake an appropriate aerobic exercise regimen and, if obese, lose weight with a target BMI < 25 kg/m^2.

Baseline investigations

Patients presenting with a new diagnosis of suspected stable angina should have a number of blood tests performed at baseline, see table 3, p18, »

What are the management options?

and be considered for referral to secondary care. Specialist referral should also be considered for patients with known stable angina and a deterioration in symptoms, or those with limiting symptoms despite optimal drug therapy.

A resting 12-lead ECG is recommended in all patients with suspected angina. A normal result does not exclude the presence of CAD. An abnormal resting ECG increases the likelihood that the patient has underlying CAD and may also identify other conditions such as atrial fibrillation or structural heart disease.

Patients deemed to have non-cardiac chest pain should be reassured of this at an early stage and alternative diagnoses considered.[2,4] This reduces anxiety and distress, and prevents unnecessary hospital admissions and consultations.

FURTHER INVESTIGATION

Further investigation may be undertaken to confirm the presence of CAD, evaluate the burden of myocardial ischaemia, stratify future cardiac risk and identify those who may benefit from coronary revascularisation.

The choice of investigation will be determined by clinical presentation, pre-test probability, prior history of CAD, and local availability of these investigations, see table 4, p19.[2,3,4]

In general, anatomical investigations determine the presence of underlying CAD and identify individuals with a pattern of CAD that may benefit from revascularisation, while functional tests evaluate the burden of myocardial ischaemia and facilitate risk stratification.

Traditionally the exercise tolerance test (ETT) has played a key role in the investigation of patients with suspected stable angina. However, the sensitivity and specificity of the ETT in patients with stable angina is dependent on the pretest probability and limits its utility as a diagnostic tool.[2,4] A normal ETT may reassure many patients but it does not exclude a diagnosis of underlying CAD. In patients with an established diagnosis of CAD, the ETT remains a useful tool to assess ischaemic burden and prognosis.[4]

CT coronary angiography (CTCA) is a non-invasive procedure that evaluates the presence, location and severity of underlying CAD and has emerged as a valuable tool for the investigation of suspected angina, see figure 1, p17.

In a recent meta-analysis performed by NICE, the diagnostic accuracy of CTCA (sensitivity 96% and specificity 79%) was superior to contemporary functional or invasive testing in the detection of significant CAD. Taken together with limited cost-effectiveness data, NICE currently recommends CTCA as a first-line investigation in patients with a new diagnosis of suspected stable angina.[2] CTCA is particularly useful as a rule-out test where the index of suspicion of underlying CAD is low. The diagnostic accuracy of CTCA is reduced in patients with a high pretest probability, largely due to the presence of coronary calcification. In Scotland, SIGN recommends CTCA as a first-line investigation where a diagnosis of stable angina is suspected but not clear from the history alone.[4]

Importantly, there is now evidence that the use of CTCA to evaluate patients with suspected angina improves clinical outcomes. In a randomised trial of more than 4,000 patients referred to hospital with a suspected diagnosis of angina, the addition of CTCA to standard care increased diagnostic accuracy and permitted targeting of treatments and interventions to those patients who gained most benefit.[6] The use of CTCA reduced the need for further stress testing.[6] Although a short-term increase in the use of invasive coronary angiography was observed with CTCA, after five years' follow-up rates were similar between both cohorts.[7] Ultimately, this led to a 40% reduction in the risk of death from coronary heart disease or nonfatal myocardial infarction (MI) at 5 years; 2.3% vs. 3.9%, HR 0.59 (95% CI: 0.41-0.84; P = 0.004).[7]

Table 2

Common cardiovascular risk factors

- Age
- Male sex
- Ethnicity
- Family history of premature cardiovascular disease
- Hypertension
- Diabetes mellitus
- Hyperlipidaemia
- Presence of atherosclerotic disease in another vascular bed
- Previous history of ischaemic heart disease
- Chronic kidney disease
- Cigarette smoking
- Abdominal obesity
- Increased alcohol intake
- Sedentary lifestyle

Table 3

Baseline investigations in suspected angina

- Haemoglobin
- Creatinine or estimated glomerular filtration rate (eGFR)
- Fasting plasma glucose or HbA_{1C}
- Lipid profile
- Thyroid function

DRUG THERAPY

The objectives of pharmacological therapy in patients with stable angina are to prevent future vascular events and to alleviate symptoms of angina. It is important to explain to patients the diagnosis, why their medications have been prescribed and how to take them, as well as possible adverse effects and how to manage them.

Preventative therapy

Antiplatelet agents: There is clear evidence that aspirin reduces the risk of ischaemic events in patients with established CAD.[8] Aspirin should be prescribed, where possible, at a daily dose of 75-150 mg in all patients with stable angina. A recent meta-analysis has suggested that, at least for primary prevention, adjusting the daily aspirin dose according to the patient's bodyweight may be more effective at preventing cardiovascular events and avoiding unwanted side effects.[9] This hypothesis remains to be tested in a prospective randomised controlled trial in patients with stable CAD.

Clopidogrel may be considered as an alternative for patients with stable angina who are unable to take aspirin. In large-scale randomised trials in patients with stable atherosclerotic vascular disease, clopidogrel was marginally more effective than aspirin at reducing the combined endpoint of MI, ischaemic stroke or vascular death, while the addition of clopidogrel to long-term aspirin therapy did not reduce recurrent cardiac events.

Antiplatelet agents should be avoided in patients with active peptic ulceration or bleeding and used with caution in patients with bleeding disorders or a history of peptic ulcer disease.

Lipid-lowering therapy: There are robust data demonstrating that statins reduce the relative risk of death and MI in patients with IHD by as much as 40%, the derived clinical benefit being related to the reduction in LDL cholesterol.

NICE currently recommends initiating treatment with atorvastatin 80 mg once daily for the prevention of cardiovascular events in patients with stable angina.[10] A lower initial dose should be considered if there are potential drug interactions, a high risk of adverse effects or in light of patient preference.[10] The target for treatment is a 40% reduction in non HDL cholesterol.[10] If this is not achieved with initial treatment, review adherence to medication and lifestyle measures, and consider increasing the dose or switching to a more potent statin.

Although marked reductions in LDL cholesterol level may also be achieved by combining statin therapy and ezetimibe, a drug which reduces intestinal resorption of cholesterol, evidence of a clinical benefit for this combination in patients with stable CAD is still awaited.

Statins are contraindicated in active liver disease. A rare but significant side effect of statin therapy is reversible myositis, which is more common when a statin is used in combination with a fibrate or drugs that inhibit the hepatic enzyme cytochrome P450.

For patients intolerant of statin therapy, fibrates may offer a less effective alternative. Fibrates have a side-effect profile similar to that of statins, share a similar risk of myositis and should be avoided in moderate to severe renal impairment.

ACE inhibitors: The anti-ischaemic and mortality benefits of chronic ACE inhibition have been well documented in patients following MI with significant left ventricular dysfunction and in patients with diabetes mellitus.

Treatment with an ACE inhibitor should be considered for patients with stable angina where left ventricular dysfunction or diabetes mellitus are present.[3]

Anti-anginal therapy

There are currently six major drug classes available in the UK for the treatment of stable angina: beta-blockers, calcium channel blockers (CCBs), nitrates, potassium channel activators, sinus node inhibitors and late sodium current inhibitors. Ideally, the dose of a single anti-anginal agent should be optimised before introducing combined therapy. There is little evidence to support the use of three anti-anginal drugs in combination. Patients with angina that is not adequately controlled with two agents should be considered for specialist referral. The major contraindications »

Table 4

Investigations in patients with suspected stable angina

Anatomical	Imaging modality	Advantages	Disadvantages
CT coronary angiography	Ionising radiation	● High sensitivity and specificity for diagnosis of CAD ● Rapid ● Well tolerated ● Feasible on most contemporary CT scanners	● Radiation ● Incidental findings ● Limited functional information outside a research setting ● Image quality dependent on patient factors
Invasive coronary angiography	Ionising radiation	● Considered gold standard for diagnosis of CAD ● Can be combined with invasive FFR assessment to obtain accurate functional information	● Radiation ● Invasive (small risk of CVA, MI and bleeding)
Functional			
Exercise tolerance test	Surface ECG	● Inexpensive ● Readily available ● Well validated for prognosis ● No radiation	● Poor sensitivity and specificity for diagnosis of CAD ● Dependent on the patient's exercise ability
Stress echocardiography	Ultrasound	● Uses existing resources ● Readily available ● Well validated ● Permits assessment of cardiac function, viability, valves and extra-cardiac structures	● Imaging quality dependent on patient factors ● Dependent on the patient's exercise ability (dobutamine can be used) ● Modest sensitivity and specificity for diagnosis of CAD
Myocardial perfusion scintigraphy	Ionising radiation	● Well validated for prognosis	● Radiation ● Modest sensitivity and specificity for diagnosis of CAD ● Dependent on the patient's exercise ability (adenosine or dobutamine can be used) ● High false-negative rate in balanced ischaemia
Stress perfusion CMR	Nonionising (magnetic field and radio waves)	● High sensitivity and specificity for diagnosis of CAD ● Provides detailed assessment of cardiac structure and function	● Expensive and resource dependent ● Time consuming ● Some patients have poor tolerance

Key: CAD = coronary artery disease; CMR = cardiac magnetic resonance; CT = computerised tomography; CVA = cerebrovascular accident; FFR = fractional flow reserve; MI = myocardial infarction

and cautions to anti-anginal therapy can be found in table 5, below.

Beta-blockers: There are substantial data to recommend that beta-blockers be considered as first-line therapy for symptomatic relief in patients with stable angina.[2,3,4] Evidence of a prognostic benefit in stable angina is limited, with only a single observational study reporting a mortality benefit in patients with stable CAD without previous MI or heart failure. Beta-blocker therapy should be titrated on an individual basis to the maximum tolerated dose required to control symptoms or a target resting heart rate of 55-60 beats per minute, whichever occurs first. Sudden withdrawal of beta blockade may cause a rebound tachycardia and hypertension, exacerbating angina, and should be avoided.

Absolute contraindications to beta-blocker use include severe bradycardia, second- or third-degree atrioventricular block, sick sinus syndrome, decompensated heart failure and severe asthma. Diabetes mellitus, chronic obstructive pulmonary disease and peripheral vascular disease are not contraindications.

Calcium channel blockers: The dihydropyridines (nifedipine, amlodipine and felodipine) act primarily on vascular smooth muscle to cause vasodilatation, while verapamil and diltiazem act preferentially on cardiac tissue to reduce

Table 5

Contraindications and cautions with antianginal therapy

Drug class	Specific agent	Contraindication	Caution
Antiplatelet agents	Aspirin Clopidogrel	Active peptic ulcer disease (PUD) Active bleeding	Bleeding disorders; previous PUD Bleeding disorders; liver disease
Lipid-lowering therapy	Statins Fibrates	Acute or severe liver disease* Severe liver disease	Previous liver disease Renal impairment
ACE inhibitors		ACE inhibitor hypersensitivity; aortic stenosis; LV outflow tract obstruction; severe renal impairment; renal artery stenosis	Mild-moderate renal impairment; previous angioedema
Beta-blockers		Asthma; severe bradycardia; preexisting high-degree AV block; sick sinus syndrome; severe uncontrolled heart failure	First-degree AV block; severe peripheral vascular disease; coronary artery spasm
Calcium channel blockers	Cardiac specific (e.g. diltiazem/verapamil) Vasodilators (e.g. amlodipine)	Severe bradycardia; preexisting high-degree AV block; sick sinus syndrome; heart failure LV outflow tract obstruction	First-degree AV block; concomitant beta-blocker use (verapamil); severe aortic stenosis (verapamil)
Nitrates		Aortic or mitral stenosis; LV outflow tract obstruction; PDE-5 inhibitor use ≤ 24hr	
Potassium channel activator	Nicorandil	Cardiogenic shock; PDE-5 inhibitor use ≤ 24hr	Acute left ventricular failure
Sinus node inhibitor	Ivabradine	Heart rate < 70 bpm (heart rate on treatment < 50 bpm); sick sinus syndrome; preexisting high-degree AV block; acute myocardial infarction; severe hepatic insufficiency	Poorly controlled, severely limiting angina
Late sodium current inhibitor	Ranolazine	Concomitant use with potent inhibitors of cytochrome P450 3A4; moderate to severe hepatic impairment; severe renal impairment	Concomitant use with drugs that prolong QT interval; concomitant use with weak or moderate inhibitors or inducers of cytochrome P450 3A4; mild hepatic impairment; moderate renal impairment; congestive cardiac failure

*Serum concentrations of liver enzymes should be checked before, and within 1–3 months of, commencing statin therapy; treatment should be discontinued if serum transaminases rise to greater than 3 times the upper limit of the reference range

heart rate and myocardial contractility.

CCBs relieve symptoms of angina and improve exercise time as effectively as beta-blockers without conferring any prognostic benefit.[4] The choice of CCB will depend on comorbidity and drug interactions.

Rate-limiting CCBs (verapamil and diltiazem) are recommended as first line for symptomatic relief in patients with stable angina in whom beta-blockade is contraindicated or not tolerated.[3,4] Dihydropyridine CCBs should be considered for second-line therapy where breakthrough symptoms occur despite optimal beta-blockade.[3,4]

The dihydropyridine CCBs may also be effective in patients with Prinzmetal angina, a rare form of angina caused by coronary artery spasm that typically occurs at rest.

Rate-limiting CCBs are contraindicated in patients with heart failure, severe bradycardia or second- or third-degree atrioventricular block and should be used with extreme caution in combination with beta-blocker therapy. The dihydropyridine CCBs, amlodipine or felodipine, may be used safely in patients with angina and heart failure.

There are concerns about the safety of short-acting preparations of nifedipine in the treatment of angina, particularly in the setting of unstable coronary syndromes, and these should be avoided. Long-acting preparations of nifedipine may be used safely in the treatment of angina.

Nitrate therapy: In patients with stable angina, nitrates improve exercise tolerance and time to onset of ST depression during exercise testing.

Sublingual nitrates provide rapid relief of anginal symptoms, can be used prophylactically to prevent ischaemic symptoms during planned exercise, and should be offered to all patients.[3,4]

A meta-analysis comparing long-acting nitrates, beta-blockers and CCBs found no significant difference in efficacy in patients with stable angina. Long-acting nitrates should be considered as first-line therapy for patients in whom beta-blockers or CCBs are contraindicated, or as second-line therapy for breakthrough symptoms.

Tolerance is the major limitation to the use of nitrates and can be avoided by ensuring a daily 'nitrate-free period' of six to eight hours, either through twice daily eccentric (less than 12 hours apart) dosing or a long-acting, once daily preparation. Patients should be aware that they may experience an increase in symptoms of angina during the nitrate-free period and the timing of dosing should be chosen accordingly. The predominant side effect of nitrate preparations is self-liming headache which usually eases with regular use. Nitrates and phosphodiesterase inhibitors such as sildenafil should not be used within 24 hours of each other because of the risk of severe hypotension.

Potassium channel activators: Nicorandil acts primarily on vascular smooth muscle to induce coronary vasodilatation. Clinical data suggest that nicorandil and CCBs are equally effective at relieving angina. In a randomised trial of more than 5,000 patients with stable angina, nicorandil significantly reduced the primary composite endpoint of combined all cause mortality, cardiovascular events and unplanned hospitalisation.[11]

Nicorandil is contraindicated in cardiogenic shock and its major limiting side effects are hypotension and gastrointestinal (GI) ulceration that can occur at any point in the GI tract. In light of this side effect, the MHRA has recommended that nicorandil use be restricted to second-line therapy, behind beta-blocker and CCB therapy.[12]

Sinus node inhibitors: Ivabradine at recommended doses leads to a reduction in heart rate by around 10 beats per minute. The actions of ivabradine are restricted to sinus node tissue with no effects on cardiac conducting tissue in other areas, myocardial contractility or ventricular repolarisation. Patients must be in sinus rhythm for ivabradine to be effective.

In randomised, controlled trials in patients with chronic stable angina, ivabradine increased time to angina onset during exercise compared with placebo and demonstrated comparable efficacy to atenolol or amlodipine at improving exercise duration and reducing frequency of angina attacks. When used in addition to amlodipine in patients with angina, ivabradine improved exercise parameters compared with placebo.

In contrast to patients with heart failure, the use of ivabradine in stable angina does not confer any cardioprotective benefit and concerns have been raised about its use in poorly controlled angina. In a randomised trial enrolling more than 19,000 patients with stable CAD without heart failure, the addition of ivabradine to contemporary medical therapy had no effect on all cause mortality, cardiac death or non-fatal MI.[13] A prespecified subgroup analysis of patients with limiting angina, reported a small but significant increase in the combined risk of cardiovascular death or non-fatal MI with ivabradine use.[13]

Ivabradine is currently recommended as second-line treatment for patients with stable angina who are either intolerant of beta-blockade or in whom a rate-limiting CCB fails to achieve adequate heart rate control, and in combination with a beta-blocker in patients whose heart rate is inadequately controlled with an optimal beta-blocker dose.[3,4]

Ivabradine should not be initiated in patients with stable angina if the resting heart rate is < 70 beats per minute and should be withdrawn or the dose reduced if the heart rate on treatment falls below 50 beats per minute. Additional contraindications include evidence of significant conducting system disease (sick sinus syndrome, second- or third-degree heart block), severe hepatic insufficiency and acute MI. The major side effects include transient headache, dizziness and luminous phenomena. Patients with luminous phenomena typically describe a transient enhanced brightness in a limited area of the visual field. Fewer than 1 per cent of patients discontinue therapy as a result.

Late sodium current inhibitors:[3,4] Ranolazine inhibits the late inward sodium current in cardiac myocytes. When used in combination with existing antianginal therapy, ranolazine increased exercise time and reduced the frequency of anginal attacks but did not affect cardiovascular outcomes (all cause mortality, cardiac death, non-fatal MI).[14] Evidence of symptomatic benefit with ranolazine monotherapy is lacking.

Although currently licensed in the UK as adjunctive therapy in patients with stable angina, the Scottish Medicines Consortium has advised that ranolazine is not recommended for use in Scotland.

The major side effects with ranolazine are dizziness and GI, including nausea and constipation. It is metabolised predominantly through the cytochrome P450 system (3A4 and 2D6 enzymes) and is contraindicated in combination with other potent CYP3A4 inhibitors such as clarithromycin and grapefruit juice. In addition, ranolazine is known to increase the QT interval and care should be taken when used in combination with drugs known to prolong the QT interval. Ranolazine should be avoided in patients with moderate or severe hepatic impairment, severe renal impairment and in older people. »

key points

SELECTED BY

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Stable angina is estimated to affect more than 1.3 million people in the UK with almost 100,000 new cases diagnosed each year. The prevalence of angina increases sharply with age. Around 50% of people diagnosed with ischaemic heart disease (IHD) present with stable angina as the first symptom.

NICE recommends the classification of chest pain into typical angina, atypical angina or non-anginal chest pain based on the presence of key features: a constricting discomfort in the front of the chest, or in the neck, shoulders, jaw or arms; precipitated by physical exertion; relieved by rest or GTN within about 5 minutes. The presence of all three features suggests a diagnosis of typical angina, two features is considered atypical angina and where one or none of the features are present the pain is defined as non-anginal. The likelihood of a diagnosis of angina increases with the number of cardiovascular risk factors present.

A resting 12-lead ECG is recommended for all patients with suspected angina. However, a normal result does not exclude the presence of underlying coronary artery disease (CAD). An abnormal resting ECG increases the likelihood that the patient has underlying CAD and may also identify other conditions such as atrial fibrillation or structural heart disease. In general, anatomical investigations, e.g. computerised tomography coronary angiography (CTCA), determine the presence of underlying CAD and identify individuals with a pattern of CAD that may benefit from revascularisation, while functional tests, e.g. exercise tolerance testing, evaluate the burden of myocardial ischaemia and facilitate risk stratification. In a randomised trial of more than 4,000 patients with a suspected diagnosis of angina, the addition of CTCA to standard care increased diagnostic accuracy and permitted targeting of therapy and interventions to those patients who gained most benefit.

There is clear evidence that aspirin reduces the risk of ischaemic events in patients with established CAD and it should be prescribed, where possible, for all patients with stable angina. There are robust data demonstrating that statins reduce the risk of death and MI in patients with IHD by 40%, and NICE currently recommends initiating treatment with atorvastatin 80 mg once daily. Treatment with an ACE inhibitor should be considered for patients with stable angina who have left ventricular dysfunction or diabetes mellitus.

There are currently six major drug classes available in the UK for the treatment of stable angina: beta-blockers, calcium channel blockers, nitrates, potassium channel activators, sinus node inhibitors and late sodium current inhibitors. Ideally, the dose of a single anti-anginal agent should be optimised before introducing combined therapy. There is little evidence to support the use of three anti-anginal drugs in combination. Beta-blockers should be used as first-line therapy, although evidence of a prognostic benefit in stable angina is limited.

CORONARY REVASCULARISATION

Coronary revascularisation can improve symptoms of angina and may offer prognostic benefit in those patients found to have high-risk coronary anatomy (left main stem stenosis or three vessel CAD). Revascularisation may be achieved by coronary artery bypass surgery or percutaneous coronary intervention usually with stent insertion. Patients with stable angina should be considered for coronary revascularisation where symptoms persist despite optimal medical therapy, where high risk coronary anatomy is identified, or in light of patient preference.

The recent ORBITA study confirmed existing evidence that in patients with a low burden of CAD, good exercise tolerance and minimal symptoms on optimal medical therapy, revascularisation with coronary stents confers no additional benefit.[15]

Factors influencing the choice of revascularisation technique include the burden and location of underlying CAD, the presence of left ventricular dysfunction or valvular heart disease, comorbidity including diabetes mellitus or renal dysfunction, and patient age.

Decision making should be patient-centred and informed by a multidisciplinary 'heart team' review involving cardiac surgeons and cardiologists.

REFRACTORY ANGINA

A small number of patients experience severe, limiting angina that is unresponsive to medical therapy and in whom revascularisation fails or is not available. Attendance at angina management programmes has been shown to improve both symptom control and exercise tolerance.

A number of therapeutic approaches have been developed to address refractory angina including enhanced external counter pulsation therapy, techniques such as nerve block, stellate ganglion block and sympathectomy, acupuncture and a stent to restrict coronary sinus blood flow.[16] The clinical data available for these techniques is currently insufficient to recommend their routine use in patients with stable, refractory angina.

CONCLUSION

Angina pectoris is a commonly encountered condition that is associated with significant morbidity and mortality. The clinical history plays a key role in diagnosis, aided by anatomical and functional testing where appropriate.

Treatment should focus on the prevention of ischaemic cardiac events and the satisfactory control of symptoms. Management should include patient education, risk factor identification and modification, drug therapy and, where appropriate, coronary revascularisation.

Competing interests

Dr Nicholas Cruden was chair of the guideline development group for *SIGN 151. Management of stable angina*, published in April 2018

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Early recognition and prompt referral key in acute pancreatitis

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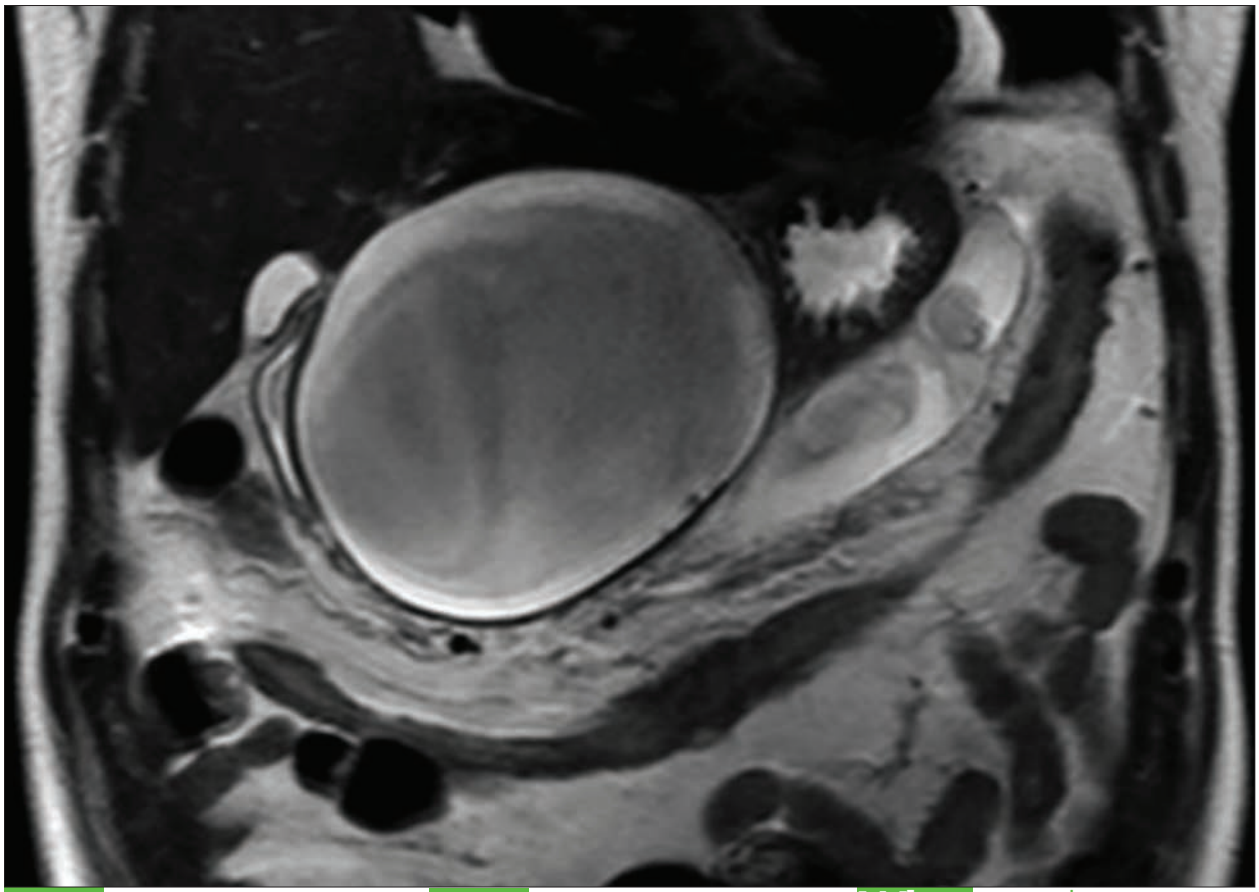


FIGURE 1
T2 weighted coronal MRI scan demonstrating an 11 cm fluid filled pancreatic pseudocyst within the head of the pancreas.
The cyst is causing compression of the gastric antrum

How should diagnosis be confirmed?

ACUTE PANCREATITIS IS CHARACTERISED BY INFLAMMATION OF THE EXOCRINE PANCREAS IN association with a local and systemic inflammatory response. It can range in severity from self-limiting, characterised by mild pancreatic oedema, to severe systemic inflammation with pancreatic necrosis, organ failure and death.

The estimated UK incidence of acute pancreatitis is up to 40 cases/100,000 per year, and appears to be increasing, particularly among young women who drink excessive amounts of alcohol.[1] The mortality rate is up to 7%, increasing to 20% in patients with pancreatic necrosis.[2] Early recognition, prompt referral to secondary care and close monitoring for complications is important in improving outcomes in acute pancreatitis. This review gives an overview of current evidence-based management strategies, incorporating recommendations from both international guidelines and those recently published by NICE.

How should patients be assessed?

CAUSES

There are many causes of acute pancreatitis. However, gallstones followed by excessive alcohol consumption account for around 75% of cases in the UK.[3] Other possible triggers are outlined in table 1, p24.

In around 20% of cases the aetiology is not readily found; this is termed idiopathic pancreatitis.[3] The presence of microlithiasis is thought to account for up to 70% of cases of idiopathic pancreatitis.[4]

What are the treatment approaches?

DIAGNOSIS

The diagnosis of acute pancreatitis should be considered in any patient presenting with abdominal pain. History and examination can be indicative of the diagnosis (this is paramount in primary care); however, two out of the following three diagnostic criteria should be met:

- Typical history
- Elevated serum amylase or lipase (> 3 ULN)
- Imaging (ultrasound, CT or MRI)

»

consistent with acute pancreatitis

The most common pattern of pain is severe epigastric pain that radiates to the back, is exacerbated by movement, and is alleviated by sitting forwards. Patients may appear agitated, distressed or confused. They may give a history of anorexia, nausea, vomiting and reduced oral intake. This history may be difficult to differentiate from peptic ulcer disease, particularly perforation, and rupture of an abdominal aortic aneurysm. Both these diagnoses are life threatening, therefore it is critical that they are considered in any patient with severe abdominal pain.

Once acute pancreatitis is suspected, a detailed history should identify risk factors for pancreatic disease. Age and sex are important demographics. Gallstone pancreatitis is seen most commonly in patients with gallbladder disease, typically women over the age of 60, while alcoholic pancreatitis is seen more frequently in men, and generally at a younger age than those with gallstone pancreatitis.[1] Metabolic, medication-related, and post-procedural causes should be considered. A family history is important to exclude hereditary pancreatitis and familial cancer syndromes. All medication, and in particular new drugs, should be reviewed.

CLINICAL EXAMINATION AND ASSESSMENT

Patients may appear hypovolaemic and may be diaphoretic, tachycardic, and tachypnoeic. Pyrexia may occur early as part of the normal inflammatory response or may be due to associated infection e.g. ascending cholangitis. Abdominal examination may reveal tenderness and distension with voluntary guarding, and with reduced bowel sounds in the presence of an associated ileus.

Haemorrhagic pancreatitis is very rare but may cause ecchymoses of the periumbilical skin (Cullen's sign), within the flanks (Grey-Turner's sign) or over the inguinal ligament (Fox's sign). Other important differentials of retroperitoneal haemorrhage include ruptured abdominal aneurysm and ruptured ectopic pregnancy.

Table 1

Pathogenesis and aetiology of acute pancreatitis

Pathogenesis	Aetiology
Ductal obstruction	Gallstones Post ERCP Malignancy Mucinous tumours Pancreas divisum Sphincter of Oddi dysfunction
Acinar cell injury	Alcohol Trauma Ischaemia Drugs (e.g. corticosteroids, azathioprine and thiazides) Infection (e.g. mumps)
Defective intracellular transport	Genetic Hypercalcaemia Hypertriglyceridaemia Autoimmune

Key: ERCP = endoscopic retrograde cholangiopancreatography

'All patients with clinical findings suggestive of acute pancreatitis should be referred to hospital for urgent evaluation'

All patients with clinical findings suggestive of acute pancreatitis should be referred to hospital for urgent evaluation. As always, good clinical acumen and experience are key when assessing borderline patients for onward referral to hospital. Certainly, any objective abnormality such as persistent tachycardia, low-grade fever or tachypnoea should alert GPs to the possibility of acute pancreatitis. Any patients with severe upper abdominal pain and risk factors for acute pancreatitis should have the condition excluded by blood tests and/or imaging.

Blood tests

A number of investigations may be performed as part of the diagnostic work up. Routine blood tests including liver enzymes, triglycerides and calcium should be carried out. In the absence of choledocholithiasis, liver function tests are usually relatively normal.

An elevated ALT at presentation suggests a likely biliary origin, with a level ≥ 150 IU/L having a positive predictive value of 95% in predicting a gallstone aetiology.[5] Raised creatinine and urea suggest acute kidney injury secondary to intravascular depletion. Amylase remains the traditional test of choice for diagnosing acute pancreatitis. Elevated levels of serum amylase or lipase (> 3 ULN) support, but are not pathognomic for, a diagnosis of acute pancreatitis. Hyperamylasaemia is also associated with severe cholecystitis, peritonitis, intestinal obstruction, mesenteric infarction, ruptured aortic aneurysm and perforated peptic ulcer.

Conversely, amylase and lipase may not reach the diagnostic threshold in cases of acute pancreatitis (e.g. in those with chronic pancreatitis); it is therefore necessary to have a low threshold for initiating treatment in suspected cases.

The diagnostic performance of these tests decreases in the hours and days after the onset of acute pancreatitis, and so additional investigations should be performed if there is suspicion of missed or established acute pancreatitis. Early and serial C-reactive protein (CRP) testing is used in acute pancreatitis as an indicator of severity and progression of inflammation.

Imaging

Radiographic studies are not used for diagnosis of acute pancreatitis, but may determine aetiology and exclude alternative diagnoses. Trans-abdominal ultrasound is the preferred initial study in suspected gallstone pancreatitis, with a sensitivity of up to 75% in detecting pancreatic inflammation.[6] CT scanning has a role in patients who become systemically unwell, septic or who do not improve, when it may indicate an alternative diagnosis e.g. perforation or local complications e.g. pancreatic necrosis.

For serial examinations, MRI is gaining favour with the use of MR cholangiopancreatography (MRCP) offering several advantages including improved depiction of pancreatic and peripancreatic collections, see figure 1, p23.

In patients considered to have idiopathic acute pancreatitis, after negative work up for biliary aetiology, endoscopic ultrasound (EUS) should be considered to detect microlithiasis and cross sectional imaging should be reviewed to exclude pancreatic neoplasm, particularly relevant in patients over 50 years old.

INITIAL TREATMENT

Although the majority of patients with acute pancreatitis have a mild clinical course, in order to detect those that may develop severe disease, close observation of all patients and early intervention is required. Many patients that develop severe disease seem well on admission yet deteriorate over subsequent days.

Initial treatment should begin even before the diagnosis is confirmed, and is

focused on fluid resuscitation and symptom control with analgesia and antiemetics. Goal-directed rehydration with Ringer's lactate solution (or Hartmann's) is the fluid of choice.[7] Adequate early fluid resuscitation is the single most important aspect of medical management, reducing organ failure and mortality rates.[8]

Effective pain control is important in order to prevent diaphragmatic splinting and thereby reduce the risk of respiratory complications. The most commonly used drugs are opiates either for breakthrough pain or as patient-controlled analgesia. Severity scoring (CRP, Atlanta or APACHE II scores are commonly used). It is also important at this stage to identify high-risk patients, in whom prompt referral to critical care for organ support, tight control of blood sugar and early correction of electrolyte abnormalities, is often pivotal.

'Early fluid resuscitation is the most important aspect of medical management, reducing organ failure and mortality rates'

Patients with severe acute pancreatitis who also have ultrasound-proven bile duct stones or patients with cholangitis or jaundice should undergo urgent endoscopic retrograde cholangio-pancreatography (ERCP) to relieve biliary obstruction. Antibiotics are not recommended for non-infected pancreatitis, as there is no clear evidence of benefit.[9] Prophylactic antibiotics have not been shown to reduce mortality, extra-pancreatic infections, or the need for surgical intervention.[10]

Severe acute pancreatitis is a catabolic state that is aggravated by inherent difficulties in delivering and utilising nutrition. Patients should eat as tolerated unless they have severe abdominal pain, in which case they are kept nil by mouth until the abdominal pain has subsided.[11]

If pain persists, or they cannot meet nutritional requirements, enteral tube feeding should be commenced.[12] Parenteral nutrition should be reserved for patients who are unable to reach nutritional goals with nasojejunal feeding.[12]

COMPLICATIONS

Local complications include pancreatic necrosis and pancreatic collections. These complications may present both during the acute episode and to GPs after an episode of 'missed' pancreatitis, or following hospital discharge. Upper abdominal pain, bloating, early satiety, nausea, vomiting and signs of infection including pyrexia, sweats and tachycardia are common presentations of these complications. Indications to drain pancreatic collections include infection and symptomatic sterile necrosis.[12]

The choice and progression of intervention depends on individual patient factors including the anatomy of the collection and may involve an endoscopic (see figure 2, below) or radiological approach.

Open (surgical) necrosectomy is no longer recommended in necrotising pancreatitis.[13] In general, many patients are suitable for a step-up approach, starting with conservative management and then either percutaneous drainage, or endoscopic transluminal drainage in selected patients within specialist centres.

Pseudocysts are sterile fluid collections occurring > 4 weeks after the initial episode.[14] They may resolve spontaneously however do require drainage in the case of complications (infection, biliary or duodenal obstruction) or if the patient is symptomatic with pain. Endoscopic cystgastrostomy is the preferred drainage option although percutaneous drainage may be considered in unfavourable anatomy.[12]

GALLSTONE PANCREATITIS

All patients presenting with gallstone pancreatitis should be considered for cholecystectomy when they are well enough to undergo surgery. In cases of mild biliary pancreatitis cholecystectomy should ideally be performed during the index admission or within two weeks of discharge, as interval cholecystectomy is associated with a significant risk of readmission for recurrent biliary events.[15]

In cases of severe gallstone pancreatitis cholecystectomy may need to be delayed until collections have improved, unless the patient is well enough for surgery and the gallbladder is some distance from the collection.[12]

In surgically unfit or frail patients, ERCP with biliary sphincterotomy may be considered as definitive treatment although the risks of sphincterotomy should be weighed against the risk of recurrent biliary events.[16]

PROGNOSIS

Most patients with mild acute pancreatitis will improve within one week of conservative management and be well enough for discharge. Long-term prognosis depends on the aetiological factors and patient compliance with lifestyle modifications. Mild acute pancreatitis generally resolves and leaves pancreatic function intact, although many patients progress to recurrent acute pancreatitis or chronic pancreatitis.

In cases of severe acute pancreatitis, patients often require input from rehabilitation teams after discharge. Late complications are often »

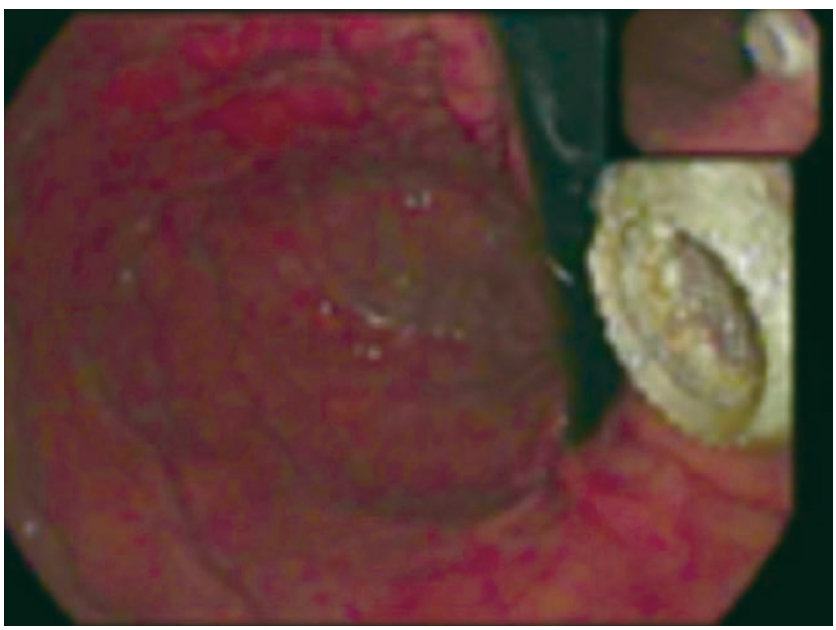


FIGURE 2
Endoscopic view of a cystgastrostomy. In this case a lumen-apposing metal stent has been used for the endoscopic drainage of infected pancreatic necrosis

key points

SELECTED BY

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Acute pancreatitis is characterised by inflammation of the exocrine pancreas in association with a local and systemic inflammatory response. Early recognition, prompt referral to secondary care and close monitoring for complications is important in improving outcomes in acute pancreatitis. Gallstones followed by excessive alcohol consumption account for around 75% of cases in the UK.

The diagnosis of acute pancreatitis should be considered in any patient presenting with abdominal pain. History and examination can be indicative of the diagnosis; however, two out of the following three diagnostic criteria should be met: typical history; elevated serum amylase or lipase (> 3 ULN); imaging (ultrasound, CT or MRI) consistent with acute pancreatitis. The most common pattern of pain is severe epigastric pain that radiates to the back, is exacerbated by movement, and is alleviated by sitting forwards. Patients may appear agitated, distressed or confused. They may give a history of anorexia, nausea, vomiting and reduced oral intake. All patients with clinical findings suggestive of acute pancreatitis should be referred for urgent evaluation.

Gallstone pancreatitis is seen most commonly in patients with gallbladder disease, typically women over the age of 60, while alcoholic pancreatitis is seen more frequently in men, and generally at a younger age than those with gallstone pancreatitis. Elevated ALT at presentation suggests a likely biliary origin, with a level ≥ 150 IU/L having a positive predictive value of 85% in predicting a gallstone aetiology.

Amylase remains the test of choice for acute pancreatitis. Elevated levels of serum amylase or lipase (> 3 ULN) support, but are not pathognomic for, a diagnosis of acute pancreatitis. The diagnostic performance of these tests decreases in the hours and days after the onset of acute pancreatitis, and so additional investigations should be performed if there is suspicion of missed or established acute pancreatitis. Early and serial CRP testing is used as an indicator of severity and progression of inflammation.

Local complications include pancreatic necrosis and pancreatic collections. These complications may present both during the acute episode and to GPs after an episode of 'missed' pancreatitis, or following hospital discharge. Upper abdominal pain, bloating, early satiety, nausea, vomiting and signs of infection including pyrexia, sweats and tachycardia are common presentations of these complications. Mild acute pancreatitis generally resolves and leaves pancreatic function intact, although many patients progress to recurrent acute pancreatitis or chronic pancreatitis. Late complications are often permanent and classically relate to pancreatic destruction. Exocrine insufficiency is a common consequence of severe disease that will result in severe nutritional deficiencies if not addressed by an experienced multidisciplinary team. NICE recommends six monthly HbA_{1c} measurement and bone mineral density assessments every two years, in order to monitor for the development of diabetes and osteopenia/osteoporosis.

permanent and classically relate to pancreatic destruction. Exocrine insufficiency is a common consequence of severe disease that will result in severe nutritional deficiencies if not addressed by an experienced multidisciplinary team. Patients should be counselled on how to take pancreatic enzyme replacement and on dose escalation.

'Post-pancreatitis diabetes is seen in those patients that survive severe acute pancreatitis'

The endocrine pancreas is more resistant to insult, but post-pancreatitis diabetes is seen in those patients that survive severe acute pancreatitis. The loss of the moderating effect of glucagon on hypoglycaemia makes glucose control very difficult to achieve in many patients and specialist diabetic input is often required. Strictures of the common bile duct may present with jaundice while strictures of the pancreatic duct may present with recurrent pain or pancreatitis.

'All patients with pancreatitis, irrespective of the cause, should be advised that alcohol might exacerbate their symptoms'

SECONDARY PREVENTION

The aetiology should be identified, and a plan to prevent recurrence should be initiated before hospital discharge. Those with alcohol-induced pancreatitis should receive alcohol cessation advice both during and following their hospital admission and may need onward referral to alcohol support services.

All patients with pancreatitis, irrespective of the cause, should be advised that alcohol might exacerbate their symptoms.

As discussed, cholecystectomy should be performed promptly in those with biliary pancreatitis.

Reviewing medications and stopping those associated with acute pancreatitis should be performed during the hospital admission, but it is important that GPs bear this in mind before restarting medications. The most recent NICE guideline recommends six monthly HbA_{1c} measurement and bone mineral density assessments every two years, in order to monitor for the development of diabetes and osteopenia/osteoporosis, respectively.[17] Effective communication between primary and secondary care is crucial to assist both teams in providing the extensive support that these patients often require.

Competing interests: None

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CPD prompt and framework
Journal article

The Practitioner

Show impact
- Collection of data
- Practice audit to show improved care

- Case studies
- Implement a protocol
- Prescribing review
- Educational meetings
- Significant event audit
- Practice meeting
- Implement a new service
- Take on new role
- Significant event audits
- Change with feedback from patients and/or colleagues

Further options for sessional GPs
- Self audit of own practice:
  - Record-keeping
  - Referrals for investigations
  - Prospective condition based reviews
  - Random case analysis with colleagues
  - Review of telephone triage outcomes
- Update drugs in emergency bag

Time credits

Impact credits
Quick impact

Later impact

Later impact=

Total credits

Title and reference

Date

What have you learned?

How will this change your practice?

What research/actions will you take that will have further impact on practice?

Draft of your action plan

CPD prompt and framework
Case review

The Practitioner

Clinical case for review

Reason for selection of the case for reflection

Evidence base used to reflect on your practice

What went well?

What could have been done better?

What were the causes of the condition/event?

What learning needs arise from this case for (a) you and (b) for the practice?

Summary of any discussion of the case with peers

What changes/actions have resulted to your personal practice?

What changes/actions have resulted to the practice?

How/when will you review these changes?

Time credits	Impact credits	Total credits

CPD prompt and framework
Audit

The Practitioner

Title

Reason for the audit (target to improve or implement)

Define criterion (or criteria) to be met

Set the standard and its basis

Plan the audit process and any involvement of peers

Time credits **Impact credits** **Total credits**

Reflection on Table 1 results

What changes were implemented to improve results?

Reflection on Table 2 results and review with peers

Table 1

Results of data 1 analysis **Date of data collection:**

Criterion	Number sampled	Achievement (%)	Standard (%)
A			
B			
C			

Table 2

Results of data 1 and data 2 analyses **Date of data collection:**

Criterion	Number sampled Data 1	Achievement (%) Data 1	Number sampled Data 2	Achievement (%) Data 2	Standard (%)
A					
B					
C					