



The investigation of syncope

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Electrocardiograph;
Carotid sinus massage;
Echocardiography;
EP studies

Summary Patients with syncope are usually referred to either neurology or cardiology clinics, yet the facilities for detailed syncope investigation are mostly in cardiac units. The diagnosis rests principally upon the history, but investigations may be required to support the clinical diagnosis. Close collaboration between the epilepsy clinician and a cardiologist is essential for effective investigation and safe management of syncope. It is frequently misdiagnosed and often erroneously treated as epilepsy. Furthermore, it is potentially a marker of sudden death when associated with certain cardiac disorders. Here we review the main syncope types and explore diagnostic approaches.

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Introduction

Syncope is an abrupt and transient loss of consciousness associated with loss of postural tone that follows a sudden fall in cerebral perfusion. Recurrent syncope is commoner than epilepsy (syncope prevalence 3–37%;^{1,2} epilepsy prevalence 0.5%³) and accounts for 3% of emergency department visits and 1% of hospital admissions.⁴ Recent work has shown that syncope is often misdiagnosed and erroneously treated as epilepsy.⁵ The diagnosis rests principally upon the history, but investigations may be required to support the clinical diagnosis. Because the range of underlying causes of syncope is wide, the physician's first task is to distinguish between the usually benign, e.g. vasovagal syncope, and the potentially life threatening, e.g. cardiac syncope.

Neurologists may have limited access to the range of cardiac investigations that may be necessary to

clarify the cause and treatment of syncope. Close collaboration between the epilepsy clinician and a cardiologist is essential for safe management of these patients.

Syncope types

The main causes of syncope are shown in [Table 1](#). In approximately one-third of cases, a presumptive diagnosis can be made on the basis of the clinical history, physical examination and 12 lead electrocardiogram (ECG). The diagnosis is undetermined in two-thirds of cases, termed syncope of undetermined origin (SUO). Even after detailed investigation, the cause remains unexplained in a one-third of all patients.⁶

Neurally-mediated (reflex) syncope

Neurally-mediated syncope describes loss of consciousness associated with reflex vasodilation and bradycardia occurring as a response to certain

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Table 1 Causes and classification of syncope.

Neurally-mediated reflex syncope <ul style="list-style-type: none"> • Vasovagal syncope • Reflex syncope with specific precipitants <ul style="list-style-type: none"> Carotid sinus syndrome Other situational, e.g. cough, micturition, swallowing
Orthostatic syncope (autonomic failure) <ul style="list-style-type: none"> • Primary (e.g. multiple system atrophy) • Secondary (diabetes, amyloid, drugs)
Cardiac syncope <ul style="list-style-type: none"> • Tachyarrhythmias <ul style="list-style-type: none"> Sustained monomorphic ventricular tachycardia Polymorphic ventricular tachycardia SVT with rapid ventricular rate • Bradyarrhythmias <ul style="list-style-type: none"> Impulse generation (e.g. sinus node diseases) Impulse conduction (e.g. complete heart block) • Mechanical obstruction <ul style="list-style-type: none"> Aortic stenosis Hypertrophic cardiomyopathy Mitral stenosis Atrial myxoma
Central nervous system syncope <ul style="list-style-type: none"> • Ictal arrhythmia • Intermittent obstructive hydrocephalus • Transient ischaemic attacks • Migraine
Metabolic syncope <ul style="list-style-type: none"> • Hypoglycaemia • Hypocalcaemia
Psychogenic syncope <ul style="list-style-type: none"> • Panic disorder • Conversion
Syncope of undetermined origin (SUO)

triggers. Most neurally-mediated reflex syncope can be categorised as vasovagal syncope, but there are subgroups where syncope is provoked only by specific triggers, e.g. coughing or swallowing.

Vasovagal syncope

Reflex (vasovagal) syncope is the commonest cause of syncope. It is generally benign and is the usual explanation for fainting in otherwise healthy individuals of all ages, but especially children and young adults. A patient's vasovagal tendency also influences the likelihood and severity of syncope developing from seemingly unrelated causes, e.g. aortic stenosis and hypertrophic cardiomyopathy. In vasovagal syncope, the blood pressure (BP) and heart rate are typically maintained until a sudden haemodynamic collapse.

Clinical features. The main clinical features that distinguish vasovagal syncope from seizures⁷ are shown in Table 2.

- **Situations and triggers.** Patients may report certain precipitants that suggest the diagnosis. Vasovagal syncope might occur in the bathroom, at night or in a hot restaurant; specific triggers include prolonged standing, hot crowded environments, emotional trauma and pain. In susceptible individuals, coughing, swallowing or micturition may provoke vasovagal syncope. Exercise-induced vasovagal syncope must be investigated in detail to distinguish it from cardiac syncope.⁸
- **Prodrome.** Warning symptoms (presyncope) that develop over 1–5 min include lightheadness, nausea, sweating, greying or blacking of vision, muffled hearing, and feeling distant.
- **Index event.** During the period of unconsciousness, a witness may describe pallor, sweating, cold skin, and brief convulsive jerks.⁹ Incontinence and injury are uncommon, and lateral tongue biting rare.
- **Recovery.** Any post-ictal confusion is typically brief, usually a few seconds, unless there had been associated head trauma. Although patients with neurally-mediated syncope are orientated soon after recovery, they are typically fatigued for minutes to hours afterwards, in contrast to patients with cardiac syncope who recover completely almost immediately on regaining consciousness.

Vasovagal syncope with specific triggers

Cough syncope, micturition syncope, swallow syncope, etc. are variants of vasovagal syncope where certain specific situations act as powerful triggers to vagal-mediated haemodynamic collapse.

Carotid sinus syndrome

Patients with carotid sinus syndrome have exaggerated baroreceptor-mediated reflexes, leading to symptomatic bradycardia and hypotension. It is rare below aged 50 years, but is an important yet frequently overlooked cause of syncope in the elderly. If specifically sought, carotid sinus syndrome is diagnosed in about 14% of elderly patients presenting with suspected presyncope or syncope.¹⁰ Carotid sinus hypersensitivity (carotid sinus massage resulting in 3 s asystole) is a common finding in elderly individuals and, in general, more malignant causes of syncope (e.g. scar-related ventricular tachycardia) should be considered before a diagnosis of carotid sinus syndrome is made.

Table 2 Clinical distinction of neurally-mediated reflex (vasovagal) syncope seizures and cardiac syncope.

	Vasovagal syncope	Seizure	Cardiac syncope
Trigger	Common (upright, bathroom, blood, needles)	Rare (flashing lights, hyperventilation)	Rare, exertional (consider left ventricular outflow obstruction)
Prodrome	Almost always (presyncope)	Common (aura)	Uncommon or brief
Onset	Gradual (often minutes)	Usually sudden	Usually sudden
Duration	1–30 s	1–3 min	Variable
Convulsive jerks	Common (brief)	Common (prolonged)	Common (brief)
Incontinence	Uncommon	Common	Uncommon
Lateral tongue bite	Very rare	Common	Very rare
Colour	Very pale, cold skin	Pale or flushed (partial seizure); blue (tonic-clonic seizure)	Very pale, cold skin
Post-ictal confusion	Rare (wakes on floor)	Common (wakes in ambulance)	Rare (wakes on the floor)
Recovery	Quickly orientated Fatigue (minutes-hours)	Slow (confused) Fatigue (minutes-hours)	Quickly orientated No fatigue

Clinical features. Carotid sinus syndrome presents, usually in the elderly, with dizziness, syncope or falls, often with injury. Important precipitating factors include head movements (especially with tight neckwear or neck pathology), prolonged standing, heavy meals, or straining on micturition, defecation and coughing.

Cardiac syncope

Cardiac syncope results from disorders of either cardiac rhythm or cardiac structure (Table 1). Disorders of cardiac rhythm are the second most common cause of syncope. Tachyarrhythmias or bradyarrhythmias can result in a sudden precipitous reduction in cardiac output resulting in loss of consciousness with little warning. Tachyarrhythmias can occur in a heterogeneous group of individuals. Patients with significant structural heart disease (e.g. history of prior myocardial infarction) and scar-related ventricular tachycardia are at high risk of sudden cardiac death due to a cardiac arrest (10–20% annual risk). Patients with genetic disorders such as congenital long QT syndrome (Fig. 1) or Brugada syndrome (Fig. 2) can present with syncope and apparently normal hearts and be at risk of sudden and unexpected death. At the other end of the spectrum are patients with structurally normal hearts and regular forms of supraventricular tachycardia (e.g. AV node-dependent tachycardia)

who may present with syncope rather than palpitations. Bradyarrhythmias occur mainly in the elderly due to degenerative changes (fibrosis) of the sinus node or the specialised conducting tissue (AV node or His-Purkinje tissue). Evidence of conduction system disease such as complete left bundle branch block, trifascicular heart block or evidence of sinus node dysfunction such as pauses alternating with atrial tachyarrhythmias (tachy-brady syndrome) increase the possibility that syncope is due to a bradyarrhythmias. Less commonly cardiac syncope can be caused by mechanical obstruction to either left ventricular outflow (hypertrophic cardiomyopathy, aortic stenosis) or left ventricular inflow (mitral stenosis, atrial myxoma).

Clinical features

Cardiac syncope can occur from any posture. There is usually little warning and recovery is rapid. Frequently syncope due to tachyarrhythmias occurs with no perception of palpitations. Syncope should always be considered due to a life-threatening ventricular tachyarrhythmia in any patient with prior history of myocardial infarction, history of heart failure, or a family history of sudden, unexpected death at a young age (<40 years). Such cases require urgent cardiological assessment. Mechanical obstruction should always be excluded in patients with exertional syncope; however, the majority of patients with conditions such as aortic stenosis or hypertrophic cardiomyopathy experience syncope

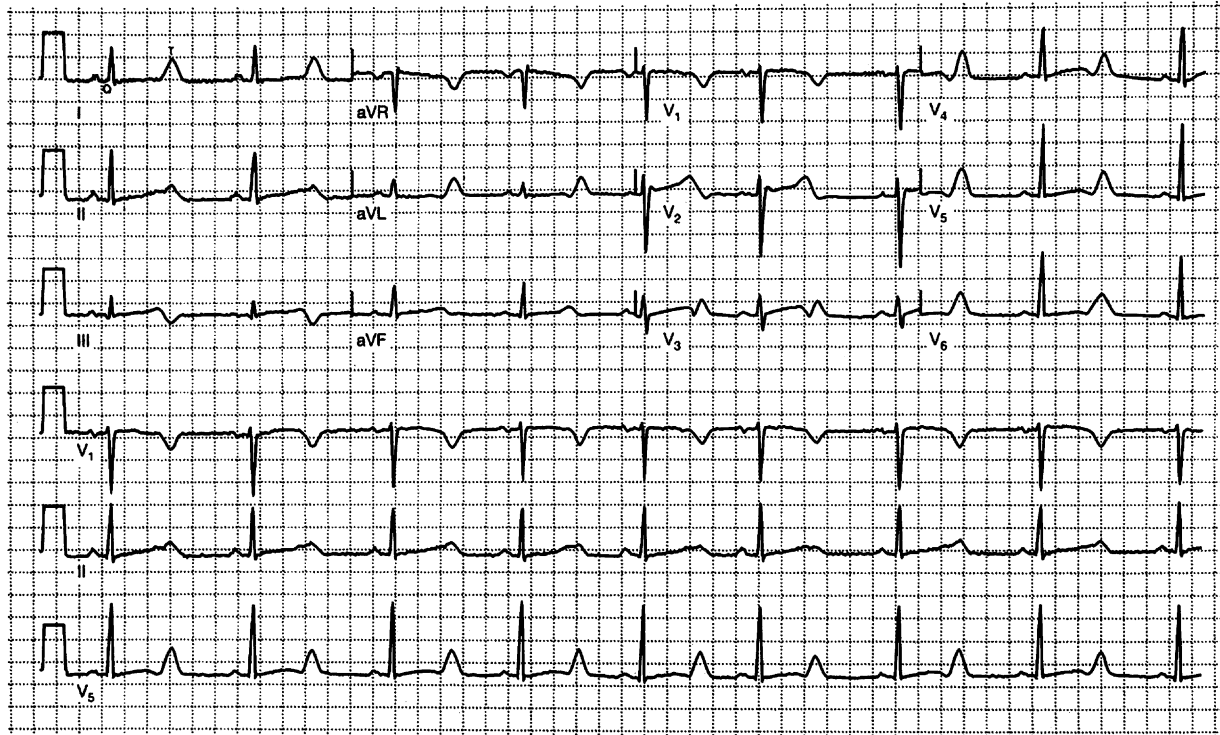


Figure 1 ECG demonstrating long QT syndrome. Note that the QT interval extends from the start of the QRS complex to the end of the T wave, and normally shortens with increased heart rates. The corrected QT interval (QTc) can be derived from the equation $QTc = QT / \sqrt{RR}$ interval (normal = 0.46 s in males and 0.47 s in females). This is the ECG from a patient with inherited long QT syndrome. The corrected QT interval is 0.61 s. Reproduced with permission from: *JAMA* 2003;289(16):2042.

either at rest or during low-level activity. Finally, a detailed drug history should be obtained to assess if the patient is on any drug associated with acquired form of long QT syndrome.

Orthostatic syncope

Orthostatic hypotension is where autonomic dysfunction impairs the normal vasoconstriction responses to a postural BP fall, allowing a postural fall in systolic BP exceeding 20 mmHg within seconds or a few minutes of standing. Orthostatic syncope occurs most often in the elderly but may accompany any autonomic peripheral neuropathy (diabetes, alcohol, amyloidosis) or complex autonomic failure (e.g. multiple system atrophy). Associated dysautonomic symptoms include impotence, urinary incontinence, nocturnal diarrhoea and constipation. Certain medications may exacerbate the problem, especially antihypertensives, diuretics, tricyclic antidepressants and anti-Parkinsonian treatment.

Clinical features

Orthostatic syncope occurs within seconds or minutes of becoming upright, typically on rising and after meals. Unlike in vasovagal syncope, the skin

stays warm, the heart rate is unchanged despite the BP fall, and sweating is absent. Measurements of BP and heart rate both lying and standing are usually sufficient to confirm the diagnosis.

Central nervous system (CNS) syncope

These are rare causes of syncope.

Clinical features

- Seizure-induced arrhythmogenic syncope results from heart rate and rhythm changes during seizures.¹¹ Tachycardias commonly accompany seizures, though rarely lead to symptoms.¹² Bradyarrhythmias are rarer, usually associated with left sided partial seizure onset,¹³ and lead to loss of consciousness which is syncopal rather than primarily due to the seizure.^{14,15} Such cases are often initially diagnosed as cardiac arrhythmogenic syncope, but partial seizures continue without collapse following cardiac pacing.
- Intermittent obstructive hydrocephalus, e.g. third ventricular cyst or Chiari malformation, typically, though not invariably, present as occipital "pressure" headaches building over seconds

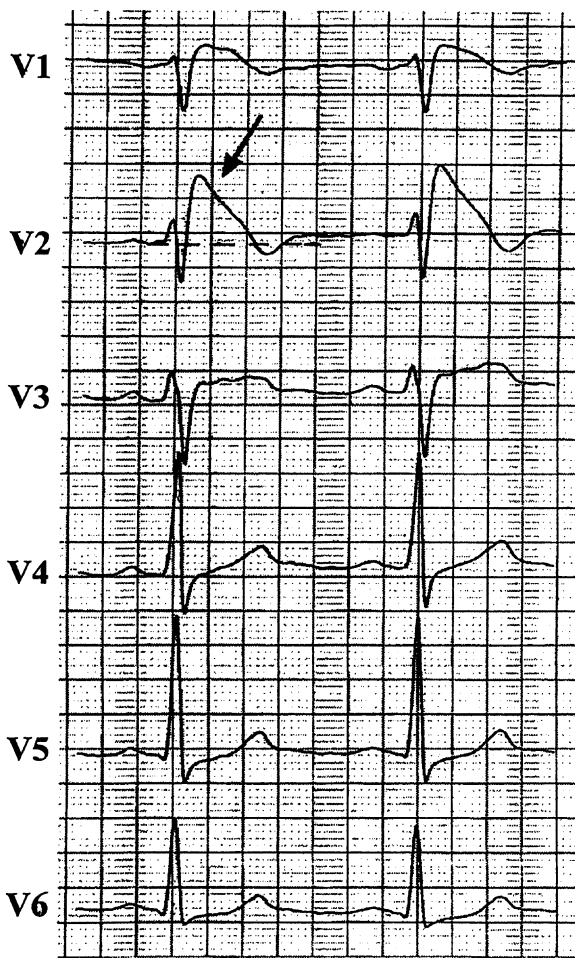


Figure 2 Precordial leads of an ECG demonstrating the Brugada pattern: persistent ST elevation in the right ventricular precordial leads (V1–V3), more evident on V2 (arrow). Reproduced with permission from: *JACC* 2003;41(10):1666.

before loss of consciousness. Colloid cysts of the third ventricle may present as “drop attacks” (without loss of consciousness) owing to stretching of the corticospinal fibres supplying the lower limbs. Intermittent elevation of intracranial pressure is a potential cause of sudden death.

- Transient ischaemic attacks rarely lead to loss of consciousness, and then only with involvement of the posterior circulation; there are usually associated brainstem symptoms including vertigo, ataxia, diplopia, and parasthesiae. A history of hypertension and vascular disease is usual.
- Migraine syncope usually manifests as a gradual onset loss of consciousness in the context of other migraine symptoms and is typically associated with familial hemiplegic migraine. Basilar artery migraine presents with syncope (commonly prolonged), typically preceded by visual blackening, vertigo, or diplopia.

Psychogenic syncope

Psychological disorders may present as syncope. The two main causes are panic (especially with hyperventilation) and dissociative (conversion) disorders. Non-epileptic attacks and syncope may also coexist in the same patient, sometimes prompting aggressive treatment of apparently resistant syncope.

Clinical features

- Panic disorder may cause attacks that culminate in true syncope through hyperventilation-induced hypocapnia with cerebral vasoconstriction. Facial and limb tingling are typical, and may be lateralised. Accompanying symptoms include anxiety, light-headedness, breathlessness, palpitation, chest and throat tightness, blurred vision and carpedal spasms.
- Dissociative non-epileptic attack disorder (pseudoseizures) may mimic recurrent syncope. The condition is notoriously difficult to diagnose and carries significant resource implications and potential unnecessary morbidity if overlooked. Major features distinguishing pseudoseizures from epileptic seizures include prolonged duration, normal colour and breathing (or hyperventilation) during attacks, erratic movements, fighting, pelvic thrusting, back arching, crying, and the absence of tongue biting, self-injury or post-ictal confusion.

Metabolic syncope

Syncope sometimes results from metabolic disturbances. Hypoglycaemia, easily diagnosed and readily reversed, should be considered in all patients with undiagnosed altered consciousness. Insulin-treated diabetes mellitus is the obvious cause. Insulinoma is rare and frequently missed. Other metabolic disorders, e.g. hypocalcaemia, may present as pre-syncope and rarely syncope.

Clinical features

Hypoglycaemic syncope presents as recurrent blackouts, often with behaviour disturbance, confusion and convulsions. Insulinoma-related neuroglycopenia occurs especially in sleep and in the early morning, and are associated with weight gain from frequent sweet drinks. Hypocalcaemia (e.g. from hypoparathyroidism) may present as recurrent episodes of tingling, carpedal spasm and syncope.

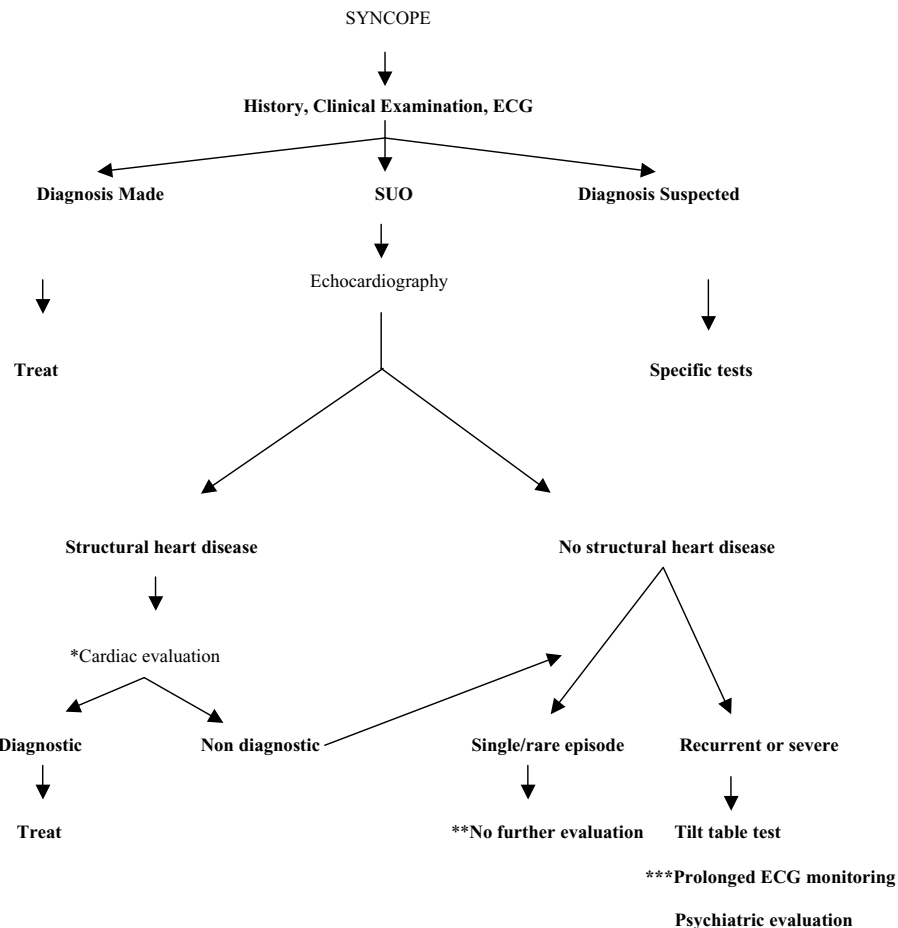


Figure 3 Algorithm for diagnosing syncope (modified from American College of Cardiologists, 1999). *In selective patients should include invasive EP studies. **Unless syncope occurred in a high-risk setting, e.g. while driving, or caused significant injury. ***Including implantable loop recorder; SUO: syncope of undetermined origin.

Investigations

The clinical history, physical examination, and electrocardiography (ECG) are essential in the initial evaluation of a patient with syncope. After these are completed, about 45% of patients have a definite diagnosis, and a further 8% have a presumptive diagnosis that can be confirmed by directed testing.² Such is the diversity of underlying causes of syncope, however, that the investigations must be selected from a broad range of possible tests. Fig. 3 gives an algorithm outlining suggested investigation pathways (modified from the American College of Cardiology, 1999^{16,17}).

Clinical history

A history taken by an appropriately experienced clinician, and including a witness account, is usually sufficient to secure a diagnosis without the need

for detailed investigations. The history should focus on precipitants of the episode (situation and triggers), the premonitory symptoms (prodrome), the characteristics of the episode itself, and the symptoms that follow it (recovery). This must be set against details of previous episodes, past and family history of neurological, cardiac and psychiatric disorders, details of medications, alcohol and illicit drugs, social situation, occupation and driving. Certain points in the history may be used to score the likelihood of syncope or seizure.¹⁸ Patients with a history of prior myocardial infarction, symptoms of congestive cardiac failure or a family history of sudden unexpected death before the age of 40 years should be carefully assessed in view of the real possibility of life-threatening ventricular tachyarrhythmias.

Indication

A full and detailed history with witness account is clearly the essential first approach to a patient presenting with blackouts.

Table 3 ECG markers predicting sudden cardiac death (after Brugada and Geelen²⁰).

Syndrome	ECG pattern
Long QT syndrome	Prolonged QT interval
Wolff-Parkinson-White syndrome	Short PR interval, delta wave, wide QRS complex
Arrhythmogenic right ventricular cardiomyopathy	Negative T waves in the right precordial leads, abnormal deflection after the QRS complex ('epsilon' wave), incomplete right bundle branch block
Anterior wall myocardial infarction with right bundle branch block	Q waves in the precordial leads, and right bundle branch block
Dilated cardiomyopathy	Low voltage in the limb and standard leads, with preservation of the voltage in the precordial leads
Hypertrophic cardiomyopathy	High QRS voltage, prominent septal Q waves in the lateral leads, and giant negative T waves in the precordial leads
Brugada syndrome	ST elevation in V1-V3 and right bundle branch block

Physical examination

The pulse rate and rhythm and the BP require particular attention. The supine and standing BP and heart rate is sometimes suggested for all patients with syncope. However, its main value is in patients (usually elderly) with possible orthostatic hypotension. In those with suspected vasovagal syncope, the BP typically remains unchanged or even rises a little on first standing. Blood pressure measured in both arms may help to diagnose brainstem transient ischaemic attacks due to subclavian steal syndrome. Cardiac auscultation is important to identify structural, particularly valvular, heart disease. Carotid sinus massage would not usually be undertaken in a neurology clinic without special arrangements.

Indication

In patients presenting with probable syncope, the physical examination should focus on the cardiovascular system; conventional neurological examination is likely to be normal. Positive physical signs consistent with underlying structural heart disease such as a murmur or evidence of heart failure significantly increase the possibility that syncope is due to a cardiac arrhythmia.

Electrocardiogram (ECG)

Its main value in syncope is to identify a possible underlying cardiac cause. It identifies the definite cause of syncope in less than 5% of cases.^{16,19} Important abnormalities to recognise in a syncope clinic are obvious rhythm disturbances, varying degrees of conduction block (e.g. first degree heart block, bi-fascicular or trifascicular block), and patterns suggesting a predisposition to serious arrhythmias

(especially Wolff-Parkinson-White and long QT syndrome). It is particularly important that clinicians investigating syncope recognise the ECG patterns associated with syncope preceding sudden cardiac death (Table 3).^{16,20} Pathological Q waves signify prior transmural myocardial infarction and imply that the patient has the substrate for scar-related ventricular tachycardia, the commonest cause of sudden cardiac death, frequently preceded by recurrent syncope.

Indication

ECG is cheap, risk free and identifies significant abnormalities in about 5% of people presenting with syncope. It is therefore recommended in almost all patients presenting with syncope, with the possible exception of young, healthy patients with obvious vasovagal symptoms.

Echocardiography

Transthoracic echocardiography in a non-invasive, outpatient test, which should be considered early in the investigation of syncope. Patients with syncope of undetermined origin can, in general, be divided into those with structural heart disease at high risk of sudden cardiac death and those with entirely normal echocardiograms who are usually at low risk of sudden death. Evidence of prior myocardial infarction, valvular heart disease and cardiomyopathies greatly increase the possibility that syncope is due to life-threatening ventricular tachyarrhythmia. SUO in patients with structural heart disease constitute between 3 and 10% of syncope patients. In one-third of these cases syncope is due to ventricular tachycardia; untreated these patients have a 10–20% annual risk of sudden death due to a cardiac arrest.^{21–23} Therefore, patients

with SUO and structural heart disease should be referred for urgent cardiological/electrophysiological assessment. The majority of patients with SUO and apparently normal hearts will have a benign condition such as neurally-mediated syncope. However, if the clinical features are atypical for neurally-mediated syncope and especially if there is family history of sudden premature death, consideration should be given to the possibility of a primary arrhythmia disorder (e.g. congenital LQTS, Brugada syndrome) or conditions which may be difficult to diagnose echocardiographically (e.g. hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy).

Indication

Echocardiography is indicated in all patients with syncope of undetermined origin based on a detailed history, physical examination and ECG analysis. In certain circumstances, it should be obtained as a matter of urgency:

- Structural heart disease, e.g. abnormal cardiovascular examination, abnormal ECG, exercise-induced symptoms, or major cardiac risk factors including age >60 years, smoker, diabetic, hypertensive, hyperlipidaemic patients.
- Cardiac syncope, e.g. brief syncope with onset from seated or lying posture, absence of prodrome, and rapid recovery. Also cardiac syncope should be considered in older patients or in those with concomitant history of palpitations.

Echocardiography is also essential before an exercise test, undertaken for exertional syncope.

Exercise test

Exercise testing is used routinely in evaluating patients with known or suspected coronary artery disease. The role of exercise testing in investigating syncope is not well studied, and the direct yield of identifying an exercise-induced arrhythmia among unselected syncope cases, is probably less than 1%.⁴ Targeted use of exercise testing aims to confirm and quantify coronary artery disease in those suspected of having it, and in ruling out coronary disease and exercise-induced arrhythmias in patients presenting with exertional syncope.

An echocardiogram must precede an exercise test in patients with exertional syncope, to exclude left ventricular obstruction, e.g. aortic stenosis, HCM.

Indication

An exercise test is indicated in patients with syncope where

- the symptoms are associated with exertion, or
- there is suspected coronary disease.

Prolonged ECG monitoring

The gold standard diagnostic test for cardiac syncope is an electrocardiographic recording during a spontaneous syncopal attack. Non-invasive ambulatory monitoring can be prescribed for 24–48 h (Holter monitoring) or for a few weeks (continuous loop recorders). Continuous loop recorder can be patient activated on restoration of consciousness and also may be programmed to autocapture events above or below a programmable heart rate. Certain arrhythmias such as ventricular tachycardia, if captured on an ambulatory recording, would strongly suggest the cause of a patient's syncope, even if unaccompanied by typical symptoms during the recording. In general, however, rhythm abnormalities must correlate exactly with symptoms to be considered diagnostic. Healthy asymptomatic individuals may demonstrate periods of second-degree heart block or sinus bradycardia especially while sleeping. Patients with significant structural heart disease and syncope secondary to scar-related ventricular tachycardia may demonstrate asymptomatic episodes of second or third degree heart block, which is a manifestation of widespread myocardial destruction. These patients need careful assessment, as they require not only back-up bradycardia pacing support but also implantable defibrillator therapy. Gibson and Heitzman²⁴ found that 19% of syncope patients showed diagnostic changes on Holter monitoring: 4% had typical symptoms with an arrhythmia (true positive: arrhythmogenic syncope diagnosed), and 15% had symptoms without arrhythmia (true negative: arrhythmogenic syncope excluded). One study²⁵ found that continuing the monitoring from 24 to 48 or 72 h identified major arrhythmias in an additional 11 and 15% of patients, respectively; however, these arrhythmias all occurred without typical symptoms.

For patients with infrequent undiagnosed syncope, a solid-state implantable loop recorder, e.g. Medtronic "Reveal" device, can record a single lead ECG continuously up to 18 months until a symptomatic event is captured. This unit (approximately 5 cm × 1 cm) is implanted subcutaneously using local anaesthesia. It can be both patient activated and programmed to autocapture events above or below a programmable heart rate. Patients are reviewed every 3 months or after each syncopal event until a definite diagnosis is made regarding the cardiac rhythm.

Indication

Cardiac arrhythmias causing syncope are rare in structurally normal hearts. Thus, ambulatory ECG monitoring (including longer term monitoring) is usually only indicated where

- syncope occurs with suspected structural heart disease, e.g. abnormal ECG or age over 60 years; or
- in suspected arrhythmogenic syncope (brief loss of consciousness, palpitation with syncope, absence of prodrome, prompt recovery);
- syncope in individuals with a family history of premature sudden unexpected death.

Cardiac electrophysiological (EP) study

Diagnostic EP studies involve percutaneous placement of electrodes into the heart to assess the cardiac rhythm in response to atrial and ventricular stimulation protocols.

The procedure is performed under local anaesthesia. Over 90% of patients with re-entrant tachycardia are inducible in the EP lab. In patients with syncope of undetermined origin and structural heart disease such as prior myocardial infarction EP testing plays a useful role in risk stratification. Patients with inducible ventricular tachycardia have a poor prognosis (30% mortality at 3 years) due to a high incidence of cardiac arrest and are usually protected with an implantable defibrillator.^{26,27} Patient who are non-inducible have a better survival (10% mortality at 3 years, usually due to non-arrhythmic deaths) and are at low risk for future cardiac arrest. Diagnostic EP studies are performed by placing catheters in the heart via the femoral veins; as the arterial circulation is not entered the risks associated with diagnostic EP studies are substantially less than those associated with diagnostic cardiac catheterisation.

Indication

An EP study is indicated in patients with recurrent syncope and structural heart disease.

Tilt table testing

Head up passive tilt testing (HUTT) has assisted the diagnosis of vasovagal syncope since 1986.²⁸ The test protocol typically involves testing the patient in the morning having fasted. After lying supine for 30 min, the patient is tilted to 60–80° for <45 min (strapped in and with arm rest support), and asked to report any symptoms; BP and heart rate are recorded throughout.²⁹

A test is positive (vasovagal syncope diagnosed) only if the patient's original pre-syncope or syncopal symptoms are reproduced entirely, and accompanied by arterial hypotension (BP fall >20 mmHg: vasodepressor response), bradycardia (HR fall >10% baseline: cardio-inhibitory response) or both (mixed response). Haemodynamic changes without symptoms comprise a negative test. If the initial HUTT is non-diagnostic, pharmacological provocations, e.g. nitrates, isoproterenol, can shorten the test duration, though they reduce its specificity. A drug-free HUTT is positive in approximately 50% of patients with suspected vasovagal syncope;³⁰ medications (e.g. isoproterenol) increase the yield to 64%.³¹ Relative contraindications to HUTT include proximal coronary artery disease, critical mitral stenosis, clinically severe left ventricular outflow obstruction and severe cerebrovascular disease. HUTT commonly provokes attacks in patients with psychogenic episodes.

Indication

HUTT is indicated in patients with recurrent unexplained syncope (likely to be vasovagal) where structural heart disease is either not suspected or has been excluded as the cause. It is indicated after a single episode only if syncope occurred in a high-risk setting, e.g. while driving, or causing significant injury. It may also be helpful even when vasovagal syncope is clinically definite, if demonstration of specific haemodynamic changes might alter management, e.g. permanent pacemaker therapy in cardio-inhibitory vasovagal syncope.³² Anecdotally, a positive HUTT helps the patient to understand the symptoms and can lead to improvement in syncope frequency.

Carotid sinus massage

Carotid sinus hypersensitivity is diagnosed by recording the heart rate and BP responses to carotid sinus massage, ideally using continuous ECG and phasic BP monitoring. The carotid artery should be auscultated first. Carotid sinus massage should not be attempted in patients with suspected or known carotid vascular disease. With the patient initially supine and the neck slightly extended, the artery is massaged (not compressed) for up to 5 s. If the response is negative or non-diagnostic, the contralateral artery is massaged after 15 s rest. Bilateral simultaneous carotid massage should never be attempted. The incidence of neurological complications of this procedure is very low at around 0.14%.³²

Carotid sinus syndrome is diagnosed when massage reproduces the patient's spontaneous

symptoms together with asystole for >3 s (cardioinhibitory), a systolic BP fall of >50 mmHg (vasodepressive) or both (mixed).³³ Haemodynamic changes without symptoms (carotid sinus hypersensitivity) comprise a negative test and is inducible in about 10% of the general elderly population.

Indication

Carotid sinus massage is indicated in elderly patients with recurrent unexplained syncope or falls ("drop attacks"), especially if the symptoms suggest carotid sinus syndrome.

Electroencephalogram (EEG)

Neurological investigations have a generally low yield in patients with syncope, if there are no symptoms or signs suggestive of seizure.³⁴ Up to 0.5–2% of healthy young adults have epileptiform changes on inter-ictal EEG.

Indication

EEG is unnecessary in patients with syncope. However, it may be useful where the diagnosis of syncope is uncertain and a spontaneous epileptic seizure is suspected,³⁵ especially in a patient below the age of 25 years.

Simultaneous ECG and EEG monitoring

Simultaneous ECG and EEG may help to diagnose frequent attacks, which cannot be distinguished as syncope or seizure. Video EEG recording (telemetry) might usefully include an ECG channel in the recording montage to identify accompanying arrhythmias during seizures. Ambulatory EEG and ECG without simultaneous video is less useful, and has other problems including the limited number of available recording channels, and movement artefact that sometimes simulates epileptic activity.

Indication

Simultaneously ECG and EEG monitoring may be indicated in patients with frequent attacks, which cannot be distinguished on clinical grounds as either syncope or seizure.

Brain imaging

Computed tomography or magnetic resonance brain scans are usually unnecessary for patients presenting with syncope. Intermittent obstructive hydrocephalus caused by structural intracranial lesions is a rare cause of syncope. Seizures with underlying cerebral lesions may occasionally be mistaken for syncope. Day et al. found a diagnostic yield of

only 4% among patients presenting to an emergency unit with transient loss of consciousness;³⁶ all those with positive findings had either focal neurological findings or a witnessed seizure.

Indication

Brain imaging is indicated in patients with syncope only if there is a significant likelihood of seizure, new onset focal neurological symptoms or signs, or if headache consistently precedes the episodes.

Carotid imaging

Carotid transient ischaemic attacks are not accompanied by loss of consciousness. Carotid Doppler ultrasonography is not indicated in patients with syncope.

Autonomic function tests

Bedside autonomic function tests are helpful to diagnose autonomic dysfunction. The major tests are the supine and erect BP and heart rate at 0, 1 and 2 min. Other simple bedside autonomic function tests include observing heart rate changes (or absence of changes in autonomic neuropathy) on ECG monitoring during the Valsalva manoeuvre, deep breathing or sustained handgrip.³⁷ Diurnal and environmental factors influence the orthostatic response and so a single BP measurement unchanged by posture does not exclude intermittent orthostatic hypotension.

Indication

Bedside autonomic function tests are indicated where syncope occurs immediately on standing (especially in the elderly) or if there are other autonomic symptoms, e.g. dry mouth, urinary urgency/incontinence/retention, impotence, and constipation.

Hyperventilation test

Panic disorder and hyperventilation are identified in around a quarter of patients with unexplained syncope.³⁸ It can be helpful (to patient and clinician) to provoke the physical symptoms of hyperventilation in the clinic.

Hyperventilation testing involves either increasing the ventilation rate to 60 min⁻¹ or simply deep breathing for 3 min.³⁹ Dizziness, unsteadiness, and blurred vision commonly develop within 20–30 s, especially when standing; paraesthesiae in the fingers and face start later. About half report chest pain after three minutes of hyperventilation. Care is needed in interpreting the result since these symp-

toms occur in anyone who hyperventilates well. The hyperventilation syndrome is diagnosed only if the patient's typical symptoms are reproduced by the manoeuvre. For some patients with hyperventilation syndrome, symptoms cannot be reliably reproduced during the hyperventilation test, even on consecutive visits.

Indication

A hyperventilation test (usually with a short screening questionnaire for depression, anxiety and panic attacks) is recommended in patients with recurrent unexplained syncope.⁴⁰ The hyperventilation test should not be performed in patients with ischaemic heart disease, cerebrovascular disease, pulmonary insufficiency, hyperviscosity states, significant anaemia or uncontrolled hypertension.

Blood tests

Routine blood tests, e.g. full blood count, electrolytes, glucose, rarely give diagnostically useful information in patients with syncope¹⁷ unless there is clinical suspicion of anaemia or a metabolic disorder. In suspected insulinoma, a 72-h fast typically induces hypoglycaemic attacks with inappropriately high endogenous insulin concentrations.

Indication

Metabolic blood tests are only indicated for syncope in special circumstances, e.g. suspected insulinoma.

Conclusion

The diagnosis of syncope is critically dependent upon careful history taking—in most patients a diagnosis can be established without complicated and expensive investigations. Nevertheless, an ECG should be routine for all patients presenting with syncope, and clinicians investigating such patients must be familiar with the common and potentially serious ECG abnormalities that may be associated with syncope. Neurologists are likely to be helped by working closely with a cardiologist when investigating syncope. The selection of investigations beyond ECG depends upon the certainty of diagnosis, the frequency and severity of attacks, and the likelihood of an underlying cardiac cause. When cardiac disease is likely, echocardiography, prolonged ECG monitoring, invasive EP studies or exercise testing may be appropriate. Where cardiac disease is not considered the likely cause of syncope, and the episodes are frequent, a head up tilt table test (for vasovagal syncope) may be helpful. If syncope con-

tinues despite normal investigations, psychogenic causes should be considered. Despite the wealth of available investigations, however, retaking the history is still likely to be the most valuable investigation in a patient with undiagnosed blackouts.

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