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Syncope

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Introduction

Despite progress in our knowledge of the patho-physiological causes and treatment of syncope, management of this condition remains variable across healthcare sectors.

Epidemiology

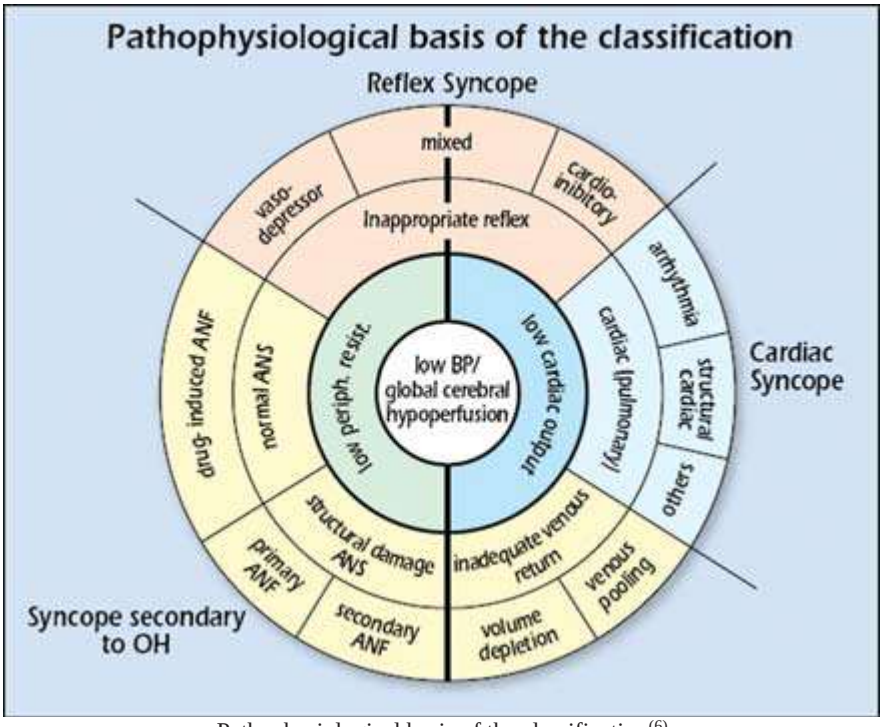
It is estimated that 4.2% of hospital admissions between the ages of 65 and 74 are due to orthostatic hypotension (OH); this increases to 30.5% in patients older than 75 years.[1] Polypharmacy and carotid sinus syndrome are main causes of syncope in particularly among older people.[1] In the Framingham study[2] the incidence of self-reported syncope was 6.2:1000 persons/year. This prevalence increased to 11% for patients in their seventies and to more than 17% in those older than 80 years. A recent study in Utah revealed that 1 in 10 in-patients have syncope.[3] As older people have the higher incidence of syncope ultimately there are more roles for geriatricians in managing these cases.[4]

Definition of Syncope

Syncope is a temporary loss of consciousness (LOC) due to transient global cerebral hypo-perfusion (5). This will lead to a rapid onset, short duration loss of consciousness followed by complete spontaneous recovery. Using this definition a clinician can exclude all other causes of LOC where there is no transient cerebral hypo-perfusion such as an epileptic seizure.

Aura or prodromal symptoms may precede syncope in some cases but in the majority it occurs without warning. There is no way to accurately estimate the period of unconsciousness in syncope but it is generally agreed to last no more than 20 seconds. Short periods of 6 to 8 seconds are sufficient to cause complete LOC.

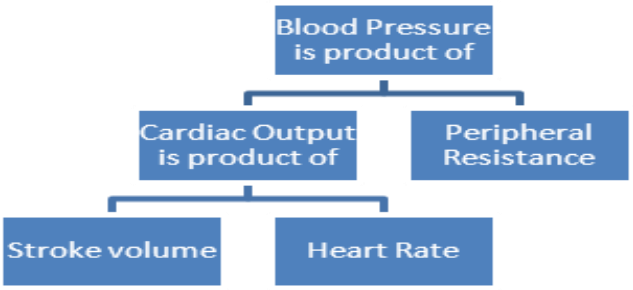
Causes and classification of syncope



Pathophysiological basis of the classification[6]

ANF – autonomic nervous failure; ANS – autonomic nervous system; BP – blood pressure; OH – orthostatic hypotension

A distinctive feature of syncope is cerebral hypo-perfusion, which is always secondary to a sudden decrease in blood pressure (BP).



Therefore a sudden drop in BP is the core cause of syncope. The second circle as in the above diagram is inadequate peripheral resistance and a decrease in cardiac output.

- Inappropriate reflexes in terms of vasodilatation or bradycardia cause syncope either because of vaso-suppression, cardio-inhibition or a mixture of the two.
- Orthostatic hypotension is due to dysfunction of the autonomic system that is either iatrogenic, drug-induced or pathological.[7] Failure to increase total peripheral resistance in the upright position will cause syncope.
- Cardiac dysarrhythmias influence cardiac output e.g. in cases of non-sustained ventricular tachycardia and second- and third-degree heart block.

Inappropriate Reflex, neutrally mediated	Emotional stress or orthostatic stress – vasovagal syncope Situational Cardio-inhibitory syncope and carotid sinus disease.
Orthostatic Hypotension	Primary as in Parkinson disease and Parkinson plus disorders Secondary as in diabetes and spinal cord injury Drug induced as in diuretics, antidepressants, alcohol and vasodilators Volume depleted as in haemorrhage and dehydration
Cardiac Syncope	Conduction disorders Tachycardia as VT and SVT Structure Heart Disease e.g. HOCM

Reflex syncope can be neurally mediated or cardio-inhibitory. This group is associated with transient impairment of the carotid and cardiac reflexes in certain situations. This results in inappropriate vasodilatation and/or bradycardia.[8]

Neurally mediated syncope refers to a temporarily inappropriate reaction by the sympathetic or parasympathetic system that leads to vasodilatation and hypotension. Cardio-inhibitory syncope refers to cases of bradycardia or asystole. This again is due to a temporarily inappropriate response of the sympathetic or parasympathetic system.

Orthostatic hypotension is the result of persistent impairment of sympathetic efferent activities.[5] OH is defined as a drop of 20 mmHg or more in systolic BP.

Syncope mimics

Without global cerebral hypo-perfusion	Epilepsy
	Hypoglycaemia
	Hypoxia
	Vertebrobasilar TIA
	Intoxication
No LOC	Falls
	Cataplexy
	Psychogenic
	TIA carotid origin

Risks associated with syncope

- Life threatening: cardiac syncope can be a warning sign of major structural cardiac disease[9] and conduction heart blocks.[10] OH is an indicator of frailty and other co-morbidities. The mortality rate of patients with OH is twice that of the general population.[11]
- Traumatic injury as a consequence of syncope and falls reduces patient confidence and independence.[12]
- Economic impact of syncope: there is no clear estimate of the cost of hospital admissions and investigations after the onset of syncope. In the USA data extrapolated from the Medicare database suggest costs of US$2.4 billion per year for syncope and pre-syncope. In the UK,[13] it is estimated that a patient with syncope costs £611. Three-quarters of this is for the hospital stay.

Management approach:

- Diagnosis
- Risk stratification
- Investigation
- Treatment

Diagnosis

A thorough history and physical examination are mandatory to establish the correct diagnosis, including lying and standing BP measurements[14] and a 12-lead ECG.[15] The aim is to ascertain syncope, identify the patho-physiological cause and identify red flag cases. An abnormal ECG that involves any degree of heart block, ST changes, T wave abnormality or prolonged QT interval should be treated as a red flag.[14] The aim is not only to diagnose syncope but to identify the mechanism and risks in order to be able to offer appropriate management.[16]

Reproduction of a ventricular pause for 3 seconds or a drop in systolic BP by 50 mmHg or more during carotid sinus massage is diagnostic for carotid hypersensitivity.

Risk stratification

National guidelines[14] recommend referral to specialist clinician within 24 hours for adults with syncope and any of the following:

1. Abnormal ECG
2. New onset or known history of congestive heart failure or unexplained shortness of breath
3. Syncope during exertion
4. Family history of sudden cardiac death
5. Detection of a new heart murmur
6. Age > 65 years with syncope without prodromal symptoms

Investigations

History and Examination at acute setting is to exclude cardiac dysarrythmias supported by relevant investigations. Therefore syncope investigations can simply divide in two major categories.

A. Investigations to exclude cardiac syncope;

1. ECG monitoring is recommended for unexplained syncope to exclude intermittent dysarryhthmias.[17] This can be in the form of a ward cardiac monitor, Holter monitor or implantable loop recorders. Short-term monitoring involving telemetry is particularly useful for those at high risk of cardiac syncope.[16] High risk factors are as follows:
1. Sinus bradycardia <40 beats/min[15]
2. SA node block or sinus pauses for 3 seconds[16]
3. Second-degree Mobitz II or third-degree atrioventricular block
4. Bifasicular or trifasicular blocks
5. SVT >160 or SVT for 32 beats or VT[15]
6. Malfunction PPM or ICD[16]
7. Evidence of new IHD
8. Hypotension with systolic BP <90 mm Hg

The R-test and Holter monitoring are particularly useful in cases of repeated syncope i.e. several times a week.[14] Less frequent syncope is usually missed in short-term monitoring and therefore implantable loop recorders are advisable. However this prolongs the diagnosis and dysarrhythmias may occur while awaiting the results.

2. An echocardiogram is recommended if cardiac syncope is suspected or if the patient is known to have a cardiac disorder. This allows the assessment of structural and functional abnormalities.

B. Investigation to differentiate between inappropriate reflex, inadequate venous return and autonomic failure is Tilt Table Test.

Orthostatic stress triggers neurally mediated syncope. Physiologically low blood pressure concomitant with vasodilatation instead of vasoconstriction followed by parasympathetic over-activity and bradycardia will result in cerebral hypo-perfusion.[18] The tilt table test is not recommended in patients with known postural hypotension or with a diagnosis of OH on clinical examination.[14] This test can also be used for patients who have had multiple syncope episodes with the suspicion of psychiatric problems.[19] Similarly this test can be used in falls assessment especially in older people.[20] The tilt table is one of the safest investigatory tools; however it may be associated with ventricular tachycardia, especially in cases of ischemic heart disease and carotid disease.[21] Other minor side effects may be associated with GTN spray such as headaches.

Recommendations	Class	level
Tilt table is indicated in the case of an unexplained single syncopal episode in high-risk settings (e.g., occurrence of, or potential risk of physical injury or with occupational implications)or recurrent episodes in the absence of organic heart disease, after cardiac causes of syncope have been excluded	I	B
Tilt testing is indicated when it is of clinical value to demonstrate susceptibility to reflex syncope to the patient	I	C
Tilt testing should be considered to discriminate between reflex and orthostatic hypotensive syncope	IIa	C
Tilt testing may be considered for differentiating syncope with jerking movement from epilepsy	IIb	C
Tilt testing may be indicated for evaluating patients with recurrent unexplained falls	IIb	C

Tilt testing may be indicated for evaluating patients with frequent syncope and psychiatric disease	IIb	C

Contraindications

- Unable to obtain consent
- Morbid obesity as technically unsafe
- Pregnancy
- Coma
- Feeble patient unable to stand or painful extremities
- Lower extremity fractures
- Severe anaemia
- Recent stroke (within seven days)
- Recent myocardial infarction (6 months)
- Severe proximal cerebral or coronary arterial disease
- Known severe mitral or aortic stenosis
- Left ventricular outflow tract obstruction
- Hypotensive shock
- Tachyarrhythmias
- Severe metabolic acidosis
- Electrolyte imbalance
- End-stage renal failure
- Severe heart failure

Procedure: Patient should be fast for 2 hours prior to the procedure, empty bladder and remove stocking support. Explains the test to the patient and consented has to be obtained. Patients will lay supine for 15 minutes and the monitoring equipment will be attached. Patients will be tilted at 60-70o upright for 20 minutes.

The following monitoring is carried out during a tilt test:

- Continuous non-invasive beat-to-beat blood pressure
- Intermittent blood pressure (either Dynamap or manual) every 5 minutes
- Continuous 3-lead ECG
- The blood pressure and heart rate during the test should be documented every 2 minutes.
- Crash trolley and resuscitation equipment should be available in the same room as the tilt test. The reason for this is that rarely patients may develop arrhythmias.

The tilt test should be discontinued and the patient laid flat immediately when:

- Systolic blood pressure falls below 80 mmHg - or is falling rapidly
- Heart rate falls below 50 /min - or is falling rapidly
- Heart rate rises above 170 /min
- Acute arrhythmia
- Hyperventilation
- Patient distress or discomfort

Intervention during the test; carotid sinus massage to illicit symptoms related to carotid sinus disease and GTN spray

A. The contraindications to CSM are:

- Patient refusal
- A carotid stenosis of 50%, if a carotid bruit is present then Carotid Doppler ultrasonography should be performed prior to CSM.

Potential complications of CSM

- The main complication is transient neurological signs (TIA) or stroke. Studies report complication rates of between 0.17 and 0.45% (i.e. around 1 in 1000).
- More rarely, CSM can give rise to transient atrial fibrillation. VT or VF never occurred in 16,000 CSMs in one study.

How to do CSM

- Clinician capable to deal with potential complications has to be present when CSM is performed.
- First massage after 5 minutes laying supine and patient already attached to the monitors.
- Anatomically CSM is performed between the thyroid cartilage and the angle of the mandible, for 5 seconds.
- If supine CSM is negative on both sides then the procedure is repeated with the patient tilted upright at 60-70o, at least 60 seconds should be left between each massage.
- After CSM the patient should lay flat for at least 10 minutes, which reduces the likelihood of neurological complications.

Carotid sinus disease is diagnosed

- More than 3 seconds asystole (cardio-inhibitory type)
- More than 50 mmHg fall in systolic BP (vasodepressor type)
- Both of the above (mixed type)
- And the patient has symptoms (dizziness or syncope)

B. Valsalva manoeuvre is mainly to reproduce autonomic failure. Patient is asked to blow in to the outer part of a 20 ml syringe aiming for pressure equivalent to 40 mmHg for 10 seconds.

Normal physiological response

Phase 1 - there is an initial rise in BP as blood is squeezed out of the thorax.

Phase 2 - then the increased intrathoracic pressure causes a reduction in venous return and the BP falls. This stimulates the baroreceptor reflex (vasoconstriction and tachycardia) so the heart rate rises.

Phase 3 - when the person stops exhaling the intrathoracic pressure suddenly drops and blood pools in the pulmonary vessels, so there is a transient further fall in BP.

Phase 4 - BP returns to normal, but there is an overshoot because the compensatory baroreceptor reflex is still operating for a little bit longer.
In case of autonomic failure, the BP falls and remains low until the intrathoracic pressure is released. But there are no changes in heart rate and overshoot is absent.

C. Glyceryl trinitrate

400-800 µg of GTN sublingual spray given to patient in a supine position are administered. The patient remains supine for a further five minutes and is then tilted to 70° for 20 minutes.

Responses to tilt testing

Normal responses if patient asymptomatic accompanied by normal physiological responses.

Cardio-inhibitory

Type A without asystole when heart rate fall below 40/minutes but non asystole

Type B associated with more than 3 seconds asystole.

Neurally mediated hypotension: Reduction in systolic blood pressure 25 mmHg from baseline supine values sustained for at least 1 minute, with no associated increase in heart rate, and accompanied by symptoms of pre-syncope.

Orthostatic (postural) hypotension: Greater than 20-30 mmHg drop in systolic blood pressure plus a greater than 10 mmHg drop in diastolic blood pressure when the head tilt-up >60 degree.

The sympathetic nervous system regulates blood vessel tone by modulating nerve traffic to lower extremity blood vessels. The arterial and venous circulations compensate for pooling by constricting; thus redirecting blood flow from the leg veins back toward the heart. However, poor sympathetic tone to the lower extremity blood vessels can cause the mechanisms of arterial and venous constriction to fail, resulting in a disproportionate pooling of blood in the legs, instead of returning blood to the circulation, resulting in less oxygen supplied to the brain and heart. As a result, a person feels lightheaded and may even faint.

Neurocardiogenic/ Vasodepressor syncope: Acute hypotension >20mmhg without bradycardia but the heart rate does not fall by more than 10% from its peak.

Vasovagal syncope: Acute hypotension with bradycardia i.e. heart rate falls by more than 10% from its peak.

Postural orthostatic tachycardia syndrome (POTS): The occurrence of orthostatic symptoms in association with either a 30 beats/ minute increase in heart rate from baseline within 10 minutes of being tilted upright, sustained for 1 minute or more, or a heart rate of higher than 120 beats/ minute in the same period.

Presyncope: The presence of premonitory symptoms and signs of imminent syncope such as severe weakness, light-headedness, nausea, or diaphoresis.

Syncope: Pan-cerebral hypoperfusion accompanied by a lack of postural tone and unconsciousness without focal neurological deficit.

Psychogenic and Hyperventilation Syncope

Psychogenic syncope or loss of consciousness is in the absence of heart rate, blood pressure or ECG. The clinical features include sudden and dramatic syncope, a prolonged recovery period, and disorientation after the episode, all features rarely seen in vasovagal attacks.[40]

Carotid sinus hypersensitivity: The diagnosis of carotid sinus hypersensitivity rests on the finding of >3 seconds asystole (cardioinhibitory subtype B), >50mmHg fall in systolic blood pressure (vasodepressor) or both during carotid sinus massage.

Writing the report

- The baseline BP and heart rate
- The change in BP and heart rate
- What the BP and heart rate was when the test was stopped
- Which tilt test end points (above) were reached
- Observations

Treatment: Stopping the culprit medication[14] and reducing polypharmacy will reduce the incidence of falls and syncope.[22]

Tilt training: OH will benefit from tilting the head during sleep to reduce the vasovagal reflexes.[23] Outcome is dependent on patient compliance.

Pharmacological therapy: the alpha agonist midodrine (5–20 mg, three times daily)[24,25] reduces reflex syncope. Other medications include fludrocortisone,[26] a mineralocorticoid that expands fluid volume, and is widely used in adult patients with OH, despite weaker clinical evidence than for midodrine. There is no clinical evidence supporting the use of B-blockers[27] or paroxetine.[28]

Cardiac pacing: a meta-analysis found contradictory evidence for the effect of cardiac pacing on neurally mediated syncope.[29] Pacing is very effective for sinus node disease[30] and in AV heart block, LVF and prolonged QRS.[31]

Driving: Patients are advised not to drive while awaiting specialist review. For vasovagal syncope there is no restriction on driving and there is a one-month restriction for those diagnosed with cardiac dysarrhythmias and PPM implanted.[32]

Single point referral

This has been applied in various ways

- The Rapid Access Falls and Syncope Service (FASS) adopted by the Newcastle group is a multidisciplinary approach applying a standardised algorithm.[33] This service was designed for emergency admission outside the emergency department for all age groups attending with falls and syncope. The team consists of clinicians with

an interest in falls and syncope, mainly geriatricians who are equipped with all the necessary tools for investigations with a low threshold for the tilt table test. The team liaises with other specialities in their management plan. This service has reduced admissions and the general costs for syncope.[5] The FASS manages to differentiate the causes of syncope, and out of 180 patients involved in the intervention group 49 patients were likely to be syncope mimics, 16% were diagnosed as cardiac syncope, 70 patients (38%) were regarded as reflex syncope and 18.3% had syncope due to OH.

- A non-blinded RCT in the USA, SEED, proved the benefits of a syncope unit in the emergency department in terms of reducing length of stay and admission rates without compromising patient care and long-term outcome. The patients in this study had an intermediate risk i.e. the researchers excluded patients with an obvious cause of syncope during their initial evaluation and those with other co-factors that required hospitalisation. The patients included in the study were randomly allocated to a syncope unit or to a standard care unit. Those in the syncope unit arm received 6 hours in-patient cardiac monitoring to exclude cardiac syncope. Echocardiogram and tilt table tests were offered in cases of suspected cardiac disease. The team consisted of clinicians and designated nurses. The study revealed the difficulty in establishing solid triage criteria for admission or discharge of syncope cases from the emergency department.[16]
- The largest project assessing the effectiveness of syncope units was in Italy, and evaluated multi-units designated for syncope over 6 months.[34] The majority of patients were received as outpatient referrals and the minority (11%) were referred from the emergency department. Seven hundred patients were recruited in the syncope unit project and diagnosis was achieved in 82% in the initial or early stages. The majority of cases (67%) were due to reflex syncope. The study proved that syncope units may not prevent further syncope attacks but do reduce the rate of admission and total management costs. The costs associated with the management of a patient presenting with syncope as an in-patient was nearly €3000, that is, 10 times the cost of management as an out-patient.

Conclusion and recommendation

- Discharging patients with syncope from emergency department will increase the risk of missing high-risk cases and red flags.[16] Therefore most national guidelines encourage doctors to admit patients with syncope from the emergency department to prevent misdiagnosis, preferably to designated syncope units.
- A syncope clinic or a single point clinic within secondary care has to be able to receive patients from the community and emergency units. Physicians with a special interest in falls and syncope are preferred to lead these clinics. Patients will receive a comprehensive assessment and risk stratification and syncope mimics can be excluded, as recommended by the ECS guideline.[5] This is type of cellular unit patient received new-test-review in one stop.

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