SYNCOPE

Relevant Guidelines

2017 ACC/AHA/HRS Guideline on syncope

2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope. JACC 2017

ESC 2018 guidelines on syncope

2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J 2018.

ESC 2021 guidelines on pacing and cardiac resynchronization

2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021.

AHA/ACC 2025 guideline on hypertension.

AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2025.

AHA 2019 Update to the guideline for First Aid

2019 American Heart Association and American Red Cross Focused Update for First Aid: Presyncope: An Update to the American Heart Association and American Red Cross Guidelines for First Aid. *Circulation*. 2019;140:e931-e938.

SYNCOPE

Definition

Syncope is a transient, complete loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.[1, 2]

Epidemiology

The lifetime cumulative incidence of syncope is up to ≥35%, and the prevalence of syncope as a presenting symptom to the emergency department ranges from 0.8% to 2.4%. There is a higher prevalence of first faints in patients between 10 and 30 years, and after the age of 70. [1, 3] In the United States, 1 to 2 million patients are evaluated for syncope annually, 1% to 5% of emergency department visits are for syncope evaluation, and 1% to 6% of urgent hospital admissions are for syncope.[1, 3]

Classification

Neurally-mediated or reflex syncope is the commonest form of syncope and can be vasodepressor, cardioinhibitory, or mixed type (Tables 1 and 2 and Figure 1).

Vasovagal syncope refers to "common faint" that is mediated by emotion or orthostatic stress, is seen in young adults (about 1% of toddlers nay have a form of vasovagal syncope), and may be preceded by prodromal symptoms of autonomic activation. There is absence of heart disease, and syncope occurs after prolonged standing in crowded, hot places, during a meal or post-prandial, with head rotation, pressure on carotid sinus or after exertion. Vasovagal syncope seldom occurs when a person is seated or reclining or, especially, during exercise.

Orthostatic hypotension is defined by a sustained reduction of systolic BP ≥20 mm Hg or diastolic BP ≥10 mm Hg within 3 minutes of active standing or on a head-up tilt test ≥60°.[4] Abnormal BP responses taking longer than 30 seconds to stabilize during standing increase significantly with age, affecting 40% of those ≥80 years of age.[5] The prevalence of orthostatic hypotension in the general population is strongly correlated with age, ranging from <5% below age 50% to 20% above age 70.[4] Common causes are include volume depletion (from vomiting, diarrhea, blood loss, and inadequate oral intake, among others) and medications such as vasodilators and diuretic agents that decrease effective circulating blood volume (**cardiogenic orthostatic hypotension**).

Neurogenic orthostatic hypotension is a highly prevalent and disabling feature of autonomic failure due to both peripheral and central neurodegenerative diseases, associated by high morbidity and mortality.[6] It is due to impairment of baroreflex-mediated vasoconstriction of the skeletal muscle and splanchnic circulation and is caused by damage or dysfunction at central and/or peripheral sites in the baroreflex efferent pathway. Causes are neurodegenerative disorders such as Parkinsonism, dementia with Lewy bodies, multiple system atrophy, and pure autonomic failure.[6]

Other forms

Mixed forms of orthostatic hypotension encompassing conditions characterized by low systemic vascular resistance and low cardiac output may also be seen. ***Initial*** (ie immediate decrease (>40 mmHg) and restoration of blood pressure, and ***delayed*** (progressive decrease without bradycardiac reflex) orthostatic hypotension seen in the elderly, are atypical forms.[7]

Postprandial hypotension is a BP drop, with or without standing, after eating usually occurring in the elderly. Symptoms appear within 2 hours after food ingestion, particularly, with large and high carbohydrate meals or alcohol intake. The pathogenesis appears related to gastric and esophageal distension, release of vasodilatory peptides, and splanchnic blood pooling.[4]

Postural orthostatic tachycardia syndrome (POTS) is a clinical syndrome characterized by (1) frequent symptoms that occur with standing, such as light- headedness, palpitations, tremor, generalized weakness, blurred vision, exercise intolerance, and fatigue; (2) an increase in heart rate of >=30 beats per minute (bpm) when moving from a recumbent to a standing position (or >=40 bpm in individuals 12 to 19 years of age); and (3) the absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure).[8] Dependent acrocyanosis of the legs that occurs with standing may be present and is characteristic of POTS.[9] The aetiology of this condition is still eluting and has been attributed to various forms of autonomic dysfunction, although in young ages a small-size heart in the context of reduced blood volume may also be responsible.[10]

Cardiac syncope is the second most common cause and is mostly due to arrhythmias, and less due to sick sinus or AV nodal disease (Stokes-Adams syndrome). Structural heart disease may cause syncope due to restricted cardiac output and inappropriate reflex vasodilation and arrhythmia.

In patients with **unexplained syncope**, first-ever syncope incidence has a bimodal lifetime pattern with peaks at 15 and 70 years. The majority of older patients experience their first syncope when older and orthostatic hypotension and carotid sinus syndrome are more common in this group.[11]

Pathophysiology

Syncope is due to a fall in systemic blood pressure (systolic BP to 60 mmHg or lower) with resultant decrease in global cerebral blood flow that can be as short as of 6-8 s. Systemic BP is determined by cardiac output and total peripheral vascular resistance. A low peripheral resistance can be due to inappropriate reflex activity causing vasodilatation and bradycardia, or to drug-induced, primary and secondary autonomic nervous system failure. Low cardiac output can be due to reflex bradycardia, arrhythmia, structural heart disease (ie aortic stenosis or pulmonary embolus), and inadequate venous return due to volume depletion or venous pooling. Reflex syncope patients demonstrate distinctly higher prevalence of daytime SBP drops compared with non-syncopal subjects.[12] In vasovagal reflex syncope there is initially sympathetic activation and increased ventricular contractility, followed by vagal afferent and subsequently afferent activation with sympathetic inhibition. In teenagers and young adults, progressive hypotension is driven by vasodilatation or falling cardiac output. The fall in cardiac output is secondary to a progressive decrease in stroke volume because blood is pooled in the splanchnic veins. In adults a fall in cardiac output is the dominant hypotensive mechanism because systemic vascular resistance always remains above baseline levels.[13]

A genetic substrate associating syncope with other cardiovascular disease has been suggested.[14]

Presentation and Initial Evaluation

Typically syncope is brief and occurs without warning, and recovery is characterized by immediate restoration of appropriate behavior and orientation. In some forms, however, prodromal symptoms (lightheadedness, nausea, visual disturbances) may be present and the episode may last longer, rarely even minutes. Minor injury, such as laceration and bruises, and trauma are reported in 29% of patients with syncope, and in 5% of them trauma is severe.[15] Recurrent syncope has serious effects on quality of life. A detailed history and physical examination, and resting 12-lead ECG should be performed for the initial evaluation of patients with syncope. A 12-lead ECG may display conduction disturbances (atrioventricular or intraventricular block), preexcited complexes, or signs of cardiomyopathy or genetic channelopathies. Specific recommendations are provided in Figures 2 and 3.

Aetiologic Diagnosis

The causes of syncope are highly age dependent. Pediatric and young patients are most likely to have neurocardiogenic syncope, conversion reactions (psychiatric causes), and primary arrhythmic causes such as genetic channelopathies, and Wolff-Parkinson-White syndrome. In middle age, neurocardiogenic syncope remains the most frequent cause of syncope. Elderly

patients have a higher frequency of syncope caused by obstructions to cardiac output, eg, aortic stenosis and pulmonary embolus, arrhythmias resulting from underlying heart disease, orthostatic hypotension, and carotid sinus syndrome.[15, 16] In older patients with syncope complicated by a severe trauma, carotid sinus syndrome is the most common cause.[15] Pulmonary embolism may be seen in up to 17% of elderly patients (especially >70years of age).[17] In patients with LVEF<35% and an ICD, syncope is caused by arrhythmias in 40% of cases, whereas 60% of all syncopal events are caused by nonarrhythmic events, such as orthostatic hypotension syncope or vasodepressor reflex syncope (MADIT RIT study).[18] Initial evaluation, especially in multidisciplinary syncope units,[16] defines the cause of syncope in 23-50% of patient, whereas diagnosis is not established in up to 40% of cases. Conditions incorrectly diagnosed as syncope are presented in Table 3, and diagnostic criteria are presented in Tables 4-6. A careful history about the onset and end of the attack, the circumstances under which syncope occurred and the medical background of the patient are crucial for diagnosis.[19] Pseudosyncope usually occurs without a recognizable trigger, many times in a day, and lasts longer than syncope (up to15 minutes). Trauma is more common in pseudoseizures. The eyes are usually open in epileptic seizures and syncope but are usually closed in functional transient loss of consciousness. During tilt testing, the combination of apparent unconsciousness with loss of motor control, normal BP, HR, and EEG rules out syncope and most forms of epilepsy. Differentiation from epilepsy is presented in Table 7. Early impotence, disturbed micturition, and later parkinsonism and ataxia suggest autonomic failure.

Risk stratification

The prognosis is good provided that structural heart disease and genetic channelopathies are excluded (Tables 8-13 and Figures 4 and 5). Other risk stratification tolls such as the Canadian Syncope Risk Score (CSRS) have also been developed. The CSRS is a useful clinical decision tool to identify adult patients with syncope who are at risk of a serious adverse event within 30 days after disposition from the emergency department (Table 9).[20] Orthostatic hypotension, however, is associated with increased total and cardiac mortality.[21] In patients with heart failure and ICD, syncope is associated with increased mortality irrespective of the cause.[18] In the EGSYS 2 trial, death of any cause occurred in 9.2% of patients with syncope during a mean follow-up of 614 days; 82% had an abnormal ECG and/or heart disease, and only 6 deaths (3%) occurred in patients without any apparent cardiac abnormality.[22]

Investigations

Additional evaluation is summarized in Figure 6. Patients with congenital heart disease should be referred to ACHD specialists (ACC/AHA/HRS 2017 GL on syncope, IIa-C-EO).

Blood testing recommendations are presented in Table 14. Thyroid function tests may be useful in patients investigated for POTS.[8] In the BASEL IX study, the prognostic accuracy of BNP, NT-proBNP, hs-cTnI, and hs-cTnT for major adverse cardiac events was moderate-to-good (area under the curve, 0.75–0.79), superior to ROSE, OESIL, and SFSR, and inferior to CSRS scores.[20]

Echocardiography is necessary to diagnose structural disease and evaluate the LVEF (Table 15).

TOE, computed tomography or magnetic resonance may be needed in selected cases (suspicion of aortic dissection, pulmonary embolus, etc) (Table 16).

Exercise testing is indicated in syncope during or after exertion (Table 17).

Carotid sinus massage. Diagnosis of CSS requires the reproduction of spontaneous symptoms during 5 s sequential right and left carotid sinus pressure performed supine and erect, under continuous monitoring of HR and periodic measurement of BP, permitting better evaluation of the vasodepressor component (Table 18). In up to 30% of patients, an abnormal reflex is present only in the upright position.

Orthostatic challenge produces a displacement of blood from the thorax to the lower limbs with resultant decrease in venous return and cardiac output (Tables 19 and 20). ***Active stand test*** (5–10 min quiet standing evaluated with sphygmomanometers) is indicated in patients with suspected orthostatic hypotension or postural orthostatic tachycardia syndrome. It can distinguish patients with early orthostatic hypotension versus delayed orthostatic hypotension (ie, blood pressure reduction >3 min after assuming the standing position).

Tilt testing reproduces a neurally mediated reflex but syncope during the test is not specific, thus limiting its diagnostic usefulness.[23] It is useful by means of showing asystole occurring after transient loss of consciousness and thus permitting avoidance of unnecessary pacing. Asystole before or coincides with hypotension points to symptomatic improvement with pacing.[24] A fast version reducing the duration of the test from 40 to 25 min is equally effective.[25]

Referral for **autonomic evaluation** may be needed in patients with known or suspected neurodegenerative disease and autonomic failure. However, basic autonomic function tests can be undertaken by the cardiologist (Table 21 and Figure 7).[26] A two-step assessment including 24-h ambulatory blood pressure monitoring and short cardiovascular autonomic function assessment allows identification of the haemodynamic mechanism of loss of consciousness in most patients with autonomic syncope.[27]

Electrocardiographic monitoring indications are presented in Table 22. Usually, underlying arrhythmia is identified within the first 2-6 h after arrival at the hospital, but in high-risk patients cardiac rhythm monitoring of up to 15 days may be necessary.[28] However, in the ASPIRED RCT among patients with syncope that remained unexplained after evaluation in the emergency department, the use of 14-day ambulatory ECG monitoring did not result in significantly fewer patient-reported syncope episodes at 1 year.[29]

Implantable loop recorders (ILR) may be necessary in patients with unexplained falls, suspected AV block or VT, or unsuccessful treatment for suspected epilepsy.[30, 31] A high incidence of bradyarrhythmias and asystole, ie convulsive cardio inhibitory reflex syncope has been found with the use of ILR in patients previously diagnosed with epilepsy.[32] Wireless monitoring devices may also be useful in this respect.[33] Cardiac rhythm monitors are summarized in Table 23.

Video recording of the event may also be helpful (Table 24).

Tests for ischemia are indicated in clinical suspicion of IHD, and **coronary angiography** may be needed (Table 25).

Electrophysiology study. Sensitivity and specificity of EPS is not good, and positive results occur predominantly in patients with structural heart disease.[34, 35] Indications are presented in Table 26. Values of sinus node recovery time (SNRT) ≥1.6 s or of corrected SNRT ≥ 525 ms are defined as abnormal responses, but the prognostic value of sinus node recovery time is not well defined. Although a history of syncope and prolonged HV interval increase the risk of subsequent AV block in patients with BBB, neither of these factors are associated with a higher risk of death as opposed to increasing age, congestive heart failure, and coronary-artery disease.[35, 36] Furthermore, the absence of these findings does not exclude the development of AV block and the prognostic value of a pharmacologically prolonged HV interval to a value ≥ 120 ms without induction of AV block is uncertain. In patients with previous myocardial infarction and preserved LVEF (>40%), induction of sustained monomorphic VT is strongly predictive of the cause of syncope,[37] whereas the induction of ventricular fibrillation may be a non-specific finding, particularly when three extrastimuli are used.[38] However, the absence of induction of ventricular arrhythmias identifies a group of patients at lower risk of arrhythmic syncope.[39] The adenosine triphosphate test is no longer recommended for selection of patients for cardiac pacing. However, there has been recent evidence that in elderly patients with syncope of unknown origin and a positive ATP (20 mg IV bolus causing pause due to sinoatrial or atrioventricular block >10 sec) may benefit from DDD pacing.[40]

Carotid Doppler ultrasonography is rarely indicated, since TIA related to carotid artery disease do not cause loss of consciousness.

Subclavian ultrasonography may detect “steal” due to sublavian artery stenosis (usually

left), but most cases are asymptomatic.

Vertebral artery ultrasonography may reveal stenosis that usually cause focal signs and occulomotor palsies and possibly also loss of consciousness.

Neurological evaluation may also be needed (Table 27). Encephalography is indicated only when epilepsy is suspected. **Psychiatric** consultation may also be considered in selected cases.

Brain imaging (CT or MRI) are not indicated unless based on a neurological evaluation.

Therapy

Syncopal recurrences often decrease spontaneously after medical assessment, even in the absence of a specific therapy; in general, syncope recurs in <50% of patients within 1–2 years, and the decrease seems to be more evident when there is a lack of a clear anatomical substrate for syncope, such as in the case of reflex syncope and unexplained syncope.[2] A general framework of therapy is presented in Figure 8.

Reflex syncope

Avoiding precipitating factors, maintaining hydration, and non-pharmacologic physical isometric **counter-pressure manouvres** are the treatment of choice (Tables 28 and 29 and Figures 9 and 10).[41, 42] The value of **drugs** is not established.[43] ***Midodrine*** (5-20 mg tds) is the only agent that has been proven to prevent hypotension and syncope during tilt tests in patients with vasovagal syncope, and may be used, especially as first line treatment in the young.[44-47] ***Beta blockers*** are not generally effective,[47-50] although they might be useful in middle-aged men >42 years old.[51] ***Fludrocortisone*** **(**0.1-0.3 mg od) may also be effective in the young,[52] but there is a risk of hypokalemia or adrenal suppression with doses >0.3 mg daily.[1] Selective serotonin reuptake inhibitors such as ***paroxetine*** in the elderly,[53] might also be of value. The value of **pacing** has been controversial (Figure 9-12). [49 54, 55] In vasovagal syncope most patients lose consciousness due to hypotension before bradycardia develops, and pacing is helpful only in (usually older) older patients with clearly documented cardioinhibition.[56, 57] ***Rate drop pacing*** that increases the heart rate early after abrupt heart rate decline, has been effective in reducing recurrence of syncope in patients >=40 years with severe asystolic neurally mediated syncope (syncope with >=3 s asystole or >= 6 s asystole without syncope recorded by monitoring-ISSUE-3 trial).[58] In an ACC/AHA/HRS review, evidence for pacing was documented only for patients with recurrent vasovagal syncope and asystole documented by implantable loop recorder.[59] However, in the SPAIN randomised trial, ***DDDR pacing with closed loop stimulation*** significantly reduced syncope in patients aged ≥40 years, with high burden syncope (≥5 episodes, ≥2 episodes in the past year), and a cardioinhibitory head-up tilt test (bradycardia <40 beats/min for 10 s or asystole >3 s).[60] The

closed loop stimulation algorithm detects relative changes in right ventricular contractility and increases the heart rate in the early stage of vasovagal reflex, before full-fledged syncope occurs. In the BIOSync CLS randomised trial, dual-chamber pacemaker with closed loop stimulation was also effective in reducing the recurrences of syncope in patients aged 40 years or older affected by severe recurrent vasovagal syncope and tilt-induced asystole.[61]

Carotid sinus massage causing a pause >3 sec is also an indication for pacing (DDD or VVI)[62] in symptomatic patients (Table 24). In patients >40 year old with recurrent attacks without a prodrome, a policy of carotid sinus massage, followed by tilt testing, followed by an implantable loop recorder, may identify up those patients (up to 47%) who may benefit from cardiac pacing.[63]

Cardioneuroablation (ie ablation of the cardiac ganglionated plexi) is also a promising approach for young patients with cardioinhibitory or mixed vasovagal syncope and positive atropine test.[64-66]

Orthostatic intolerance syndromes

Counter-pressure manouvres are a simple and effective way to improve symptoms and prevent syncope in adults with presyncope of vasovagal or orthostatic origin.[42] The principal treatment strategy in drug-induced autonomic dysfunction is elimination of the offending agent. Expansion of extracellular volume is important (Table 30 and Figures 13 and 14). In the absence of hypertension, patients should be instructed to take sufficient salt and water intake, targeting **2–3 L of fluids per day and 10 g of NaCl**. Rapid cool water ingestion is reported to be effective in orthostatic intolerance and post-prandial hypotension.[67] The norepinephrine precursor **droxidopa** (100-600 mg tds) has been approved by the FDA for the therapy of orthostatic hypotension.[68] **Midodrine** (5-20 mg tds) may also be effective ,[69, 70 71] but this is has not been verified in a subsequent meta-analysis.[72] The norepinephrine transporter blockade **atomoxetin**e has been found superior to midodrine for the treatment of orthostatic hypotension in autonomic failure.[73] **Fluorocortisone** (0.1-0.3 mg od-see above) and compression stockings may also be effective. Other drugs may also be tried.[4]

Regular exercise, compressive garments and sleep with the head elevated may also be helpful as first steps in neurogenic orthostatic hypotension, but sympathomimetics and volume expanders as previously described are usually needed.[6] Thigh-high lower limb compression using elastic compression stockings is not useful.[74]

Cardiac arrhythmias

Recommendations for treatment are provided in Table 31 and Figure 15. Pacing has not been shown to prevent recurrences in patients, especially of young age, with unexplained falls, and ILR monitoring is probably the optimal diagnostic strategy. Further detailed recommendations are also presented in chapters on bradyarrhythmias, heart failure,

cardiomyopathies, and channelopathies. ICD may be indicated and reduces arrhythmic death but may not prevent syncope. However, appropriate shocks in patients with heart failure are more likely in patients with syncope.[75] Device malfunction and pacemaker syndrome should also be considered.

Dehydration and drugs

Syncope related to medication is more prevalent in older adults with multiple comorbidities. Dehydration may manifest along a spectrum of symptoms, ranging from tachycardia to shock, depending on whether a person has compensated or uncompensated hypovolemia (Table 32). Orthostatic tolerance worsens with dehydration and is exacerbated by heat stress, which promotes vasodilation.[1]

Syncope in the elderly and in patients with frailty

The most common causes of syncope in the elderly are orthostatic hypotension, reflex syncope, especially CSS, and cardiac arrhythmias. In syncope complicated by a severe trauma, carotid sinus syndrome is the most common cause.[15] Syncope occurring in the morning favors orthostatic hypotension. Symptoms such as nausea, blurred vision, and sweating are predictive of noncardiac syncope, whereas only dyspnea is predictive of cardiac syncope in elderly people.[76] One-third of individuals over 65 years are taking three or more prescribed medications, which may cause or contribute to syncope. Their withdrawal reduces recurrences of syncope and falls.[77] Medication history should include the time relationship with onset of syncope. History should include co-morbidity, association with physical frailty, and locomotor disability. Gait, balance instability, and slow protective reflexes are present in 20–50% of community-dwelling elderly. In these circumstances moderate haemodynamic changes, insufficient to cause syncope, may result in falls.[77] Cognitive impairment is present in 5% of 65 year old and 20% of 80 year old. This may attenuate the patient's memory of syncope and falls. Elderly should be managed according to the identified cause (Table 33).

Suspected (undocumented) syncope

Recommendations for pacing are presented in Table 34.

Syncope in athletes

Recommendations are presented in Table 35. Athlete's heart is discussed in detail in the relevant Chapter.

Other conditions

Management of syncope in structural heart disease and other conditions is discussed in relevant chapters. Syncope is an ominous sign in hypertrophic cardiomyopathy, ARVC, and, most probably, genetic channelopathies, although not as much as documented cardiac arrest. (see relevant chapters for specific recommendations). Uncommon conditions associated with syncope are presented in Table 36.

Pseudosyncope

Psychogenic pseudosyncope is a syndrome of apparent (not true) loss of consciousness occurring in the absence of impaired cerebral perfusion or function. [1] It is believed to be a conversion disorder, ie an external somatic manifestation or response to internal psychological stresses. Patients are often young females with a higher prevalence of preexisting VVS or a history of physical and/or sexual abuse. The apparent duration of loss of consciousness is often long (5 to 20 minutes), and episodes are frequent. Some common characteristics include closed eyes, lack of pallor and diaphoresis, and usually little physical harm. Although many patients with pseudosyncope can be diagnosed with a careful history, occasionally tilt-table testing with or without transcranial Doppler and monitoring of an EEG is helpful (Table 37).

Driving

Healthcare providers managing patients with syncope should be aware of the driving laws and restrictions in their regions and discuss implications with the patient (ACC/AHA/HRS 2017 GL on syncope, IIa-C-EO). Recommendations are provided in Table 38.

Pregnancy

Pregnant patients with new onset of unexplained syncope, especially if it occurs in the first trimester or recurs during pregnancy, are at higher risk of adverse pregnancy outcomes and should receive enhanced evaluation, including echocardiogram, followed by close periodic monitoring.[78] Specific recommendations are presented in Figure 16.

Syncope Unit

Proposed structure and facilities in dedicated syncope units are presented in Table 39.

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