# Review Article

## Syncope: Approach to diagnosis

*Om Murti Anil[1], MD, DM*

From the [1]Division of Interventional Cardiology, Grande International Hospital, Dhapasi, Nepal

**Abstract**

Syncope is a transient loss of consciousness (LOC) due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. Here, the term "transient LOC" encompasses all disorders characterized by self-limited LOC irrespective of the mechanism. Central point in pathophysiology of the development of syncope is fall in systemic blood pressure (BP) with a decrease in global cerebral blood flow. The evaluation and treatment of syncope are very challenging because syncope is not the only cause of transient LOC. Moreover, symptoms of syncope are fleeting, patient is usually asymptomatic at the time of evaluation, and most of the events are often unwitnessed. The guiding principle of assessment is to differentiate syncope from other causes of transient LOC and the more benign causes of syncope from the potentially serious ones. Initial assessment of syncope consists of a detailed history and examination complemented by 12-lead electrocardiography and supine and standing BP. If the cause is suspected, then further investigations may be needed to confirm the particular disorder. A deliberate approach based on initial risk stratification is more likely to give a correct diagnosis. Despite the difficulties, a thorough evaluation of the cause of syncope is warranted in all patients, not just in those deemed to be at high mortality risk. The goal in every case should be to determine the cause with sufficient confidence to provide a reliable assessment of prognosis and treatment options.

**Key Words:** *Loss of consciousness, neurocardiogenic syncope, seizure, vasovagal episode*

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### Introduction

Syncope is a transient loss of consciousness (LOC) due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. Here, the term "transient LOC" encompasses all disorders characterized by self-limited LOC irrespective of the mechanism.[1] Often the cause for a specific event is unclear, and in these patients, the term "transient LOC" should be used.[2] The term "presyncope" or "near-syncope" is often used to describe a state that resembles the prodrome of syncope and is not followed by LOC.[1] This definition emphasizes five important components of syncope:

- LOC is always complete. It is a critical element
- Loss of voluntary muscle tone is inherent with LOC
- Onset is relatively rapid and usually preceded by prodromal symptoms
- Recovery is spontaneous, complete, and usually prompt
- Underlying mechanism for LOC is transient global cerebral hypoperfusion.

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### Pathophysiology of Syncope

Central point in pathophysiology of the development of syncope is fall in systemic blood pressure (BP) with a decrease in global cerebral blood flow. A sudden cessation of cerebral blood flow for as short as 6–8 s has been shown to be sufficient to cause complete LOC. Experience from tilt testing showed that a decrease in systolic BP to 60 mmHg or lower is associated with syncope.[3] Systemic BP is determined by cardiac output (CO) and total peripheral vascular resistance, and a fall in either can cause syncope, but a combination of both mechanisms is often present, even if their relative contributions vary considerably.[1]

### Approach to Diagnostic Evaluation of Syncope

Diagnostic approach in a patient with suspected syncope can be broadly divided into the following four steps:

***Address for correspondence:***
Dr. Om Murti Anil, MD, DM,
Division of Interventional Cardiology,
Grande International Hospital, Dhapasi, Nepal.
E-mail: drommurti@yahoo.com



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- Step 1: Differentiate syncope from other cause of LOC (diagnosis of syncope)
- Step 2: Initial evaluation of syncope (history, clinical examination, and 12-lead electrocardiography [ECG])
- Step 3: Investigations to confirm the underlying diagnosis (i.e., the cause of syncope)
- Step 4: Investigation of unexplained syncope.

## Distinguishing syncope from nonsyncopal conditions

The differentiation between syncope and nonsyncopal[1] conditions with real or apparent LOC can be achieved in most cases with a detailed clinical history. The following questions should be answered.

### Was loss of consciousness complete?

LOC in syncope is always complete. Sometimes, syncope needs to be distinguished from several other symptoms such as dizziness and vertigo, which do not result in an LOC or postural tone. Similarly, in presyncope, consciousness is never lost completely. Falls and cataplexy are not associated with LOC.

### Was loss of consciousness transient with rapid onset and short duration?

LOC in syncope is rapid and usually lasts no longer than 20 s. However, syncope may rarely be longer even as much as several minutes;[4] if LOC is prolonged, then seizure and psychogenic syncope are likely causes.

### Did the patient recover spontaneously, completely, and without sequelae?

Recovery in syncope is prompt. Immediate complete restoration of appropriate behavior and orientation is common. However, sometimes, patient may report prolonged fatigue and headache in postrecovery period, particularly in vasovagal syncope. Retrograde amnesia, particularly in older individuals, is not uncommon.

### Did the patient lose postural tone?

In psychogenic syncope, patients fall frequently and also get injury, but careful history reveals the absence of complete LOC.

If the answers to these questions are positive, the episode has a high likelihood of being syncope. If the answer to one or more of these questions is negative, exclude other forms of LOC before proceeding with syncope evaluation [Table 1].

Distinguishing syncope from seizure is another important step in diagnosis. Detailed history about situation at the time of episode, symptoms immediately before, during and after the episode, especially from a witness, is very helpful [Table 2].[5] The diagnosis of syncope may also be missed in people presenting with falls. Older people being evaluated for falls may have experienced brief syncopal episodes that resulted in loss of postural tone but may not have been aware of LOC.[6] People with sudden falls who cannot remember or explain the fall, and those with facial and head injuries, may benefit from investigation for syncope.[7]

## Causes of syncope

The causes of syncope are highly age dependent.[2] In the general population, the most common cause of syncope is neurocardiogenic, followed by primary arrhythmias.[8] In pediatric and young patients, psychiatric and primary arrhythmic causes should also be considered. While in middle-aged and elderly, situational, orthostatic, and cardiac causes of syncope should be searched. Assessment of the medication list for agents associated with proarrhythmia, for example, Class IA and IC antiarrhythmic drugs [Tables 3 and 4].

### Neurally mediated (reflex) syncope

Neurally mediated syncope describes LOC associated with reflex vasodilation and bradycardia occurring as a response to certain triggers. The main clinical features that distinguish vasovagal syncope from seizures are shown in Table 2. Vasovagal is the most common form of neutrally mediated syncope.[9] It is generally benign and is the usual explanation for fainting in otherwise healthy individuals of all ages, but especially children and young adults. Patients may report certain precipitants and triggers 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.

Warning symptoms (presyncope) that develop over 1–5 min include lightheadedness, nausea, sweating, graying or blacking of vision, muffled hearing, and feeling distant. During the period of unconsciousness, a witness may describe pallor, sweating, and cold skin. Brief convulsive jerks may occur after LOC has set in.[10] Although patients with neurally mediated syncope are orientated soon after recovery, they have typically fatigued for minutes to hours afterward, in contrast to patients with cardiac syncope who recover completely almost immediately on regaining consciousness.

### Carotid sinus syndrome

It is rare below aged 50 years but is an important yet frequently overlooked cause of syncope in the

**Table 1: Causes of nonsyncopal attacks (commonly misdiagnosed as syncope)**

| No impairment of consciousness | Partial or complete LOC without global cerebral hypoperfusion |
|---|---|
| Falls | Metabolic disorders |
| Drop attacks | Hypoglycemia |
| Cataplexy | Hypoxia |
| TIA of carotid origin | Hyperventilation with hypocapnia |
| Psychogenic pseudosyncope | Epilepsy |
| | Intoxications |
| | Vertebrobasilar TIA |

LOC=Loss of consciousness, TIA=Transient ischemic attack

**Table 2: Salient distinguishing features of vasovagal syncope, seizures, and cardiac syncope**

| | Vasovagal syncope | Seizure | Cardiac syncope |
|---|---|---|---|
| Trigger | Common (upright posture, hot environment, pain, fear) | Rare (flashing lights, hyperventilation) | Rare, exertional |
| 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 jerk | Common (brief), occurs after LOC has set in | Common, prolonged, occurs during LOC | Common (brief), occurs after LOC |
| Incontinence | Uncommon | Common | Uncommon |
| Tongue bite | Very rare | Common | Very rare |
| Injury | Less likely | Likely | Less likely |
| Color | Very pale, cold skin | Pale, flushed or blue | Very pale, cold skin |
| Postictal confusion | Rare (wakes on floor), more in elderly | Common (wakes in ambulance) | Rare (wakes on the floor) |
| Recovery | Prompt (if lie flat quickly) | Slow (confused) | Prompt |
| | Fatigue (minutes to hours) | Fatigue (minutes to hours) | No fatigue |

LOC=Loss of consciousness

elderly. 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 (cardiovascular)*

Cardiac syncope is the second most common cause of syncope. Arrhythmias are the most common cardiac causes of syncope. Bradyarrhythmia is a more common cause of syncope than tachyarrhythmia. They induce hemodynamic impairment, which can cause a critical decrease in CO and cerebral blood flow. Syncope or near syncope occurs at the onset of paroxysmal tachycardia before vascular compensation develops.[11,12] Consciousness is, in general, restored before tachycardia terminates.

Usually, prodromal symptoms are lacking. Although exertional syncope points toward cardiac etiology, vasovagal syncope may occur after exertion in healthy heart and cardiac etiology needs to be ruled out by appropriate investigation;[13] however, the majority of patients with conditions such as aortic stenosis or hypertrophic cardiomyopathy experience syncope either at rest or during low-level activity. 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).

### *Orthostatic syncope*

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. Orthostatic syncope occurs most often in the elderly, autonomic dysfunction. Associated dysautonomic symptoms include impotence, urinary incontinence, nocturnal diarrhea, and constipation [Box 1].

### *Psychogenic syncope*

A history should focus on identifying underlying panic (especially with hyperventilation) and dissociative (conversion) disorders. Too frequent syncopal episodes are more likely to be of psychological origin. Usually, psychogenic syncope lacks triggers, situational factors, and prodromal features. Episodes are relatively frequent and may occur in bouts. Typically, syncopal episodes are not brief. Detailed history almost always reveals the absence of complete LOC. Facial and limb tingling are typical and may be lateralized. Accompanying symptoms include anxiety, lightheadedness, breathlessness, palpitation, chest and throat tightness, blurred vision, and carpopedal spasms. Self-injury or postictal confusion is not rare.

## *Initial assessment in a patient with suspected syncope*

Thorough evaluation of the cause of syncope is warranted in all patients. This is important because syncope, although perhaps benign from a mortality perspective in most cases, is rarely a solitary event; recurrences, physical injury, diminished quality-of-life, and possible lifestyle limitations are real concerns.[14,15]

The guiding principle of assessment is to differentiate syncope from other causes of transient LOC and the most benign causes of syncope from the potentially serious. In practice, this means differentiating

**Table 3: Classification of causes of syncope is described in order of frequency**

| |
|---|
| Neurally-mediated reflex syncope |
| Vasovagal ("common") faint |
| Carotid sinus syndrome |
| Situational faints (e.g., cough, defecation, excessive heat, micturition, sneeze, swallow, pain, prolonged upright posture, venipuncture, volume depletion) |
| Postexercise variant |
| Glossopharyngeal and trigeminal neuralgia |
| Other (e.g., brass instrument playing, weightlifting, postprandial) |
| Orthostatic syncope |
| Secondary autonomic failure |
| Diabetes, amyloid, uremia, spinal injury |
| Volume depletion (e.g., hemorrhage, diarrhea, vomiting, Addison's disease) |
| Drug-induced: alcohol, vasodilators, diuretics, antidepressants |
| Primary autonomic failure syndromes (e.g., pure autonomic failure, multiple system atrophy) |
| Postural intolerance syndromes (e.g., POTS) |
| Cardiac arrhythmias as primary cause |
| Sinus node dysfunction |
| Bradycardia/tachycardia syndrome |
| Atrioventricular conduction system disease |
| Paroxysmal supraventricular and ventricular tachycardia |
| Channelopathies (e.g., Long QT syndrome, Brugada syndrome, short QT, arrhythmogenic right ventricular dysplasia) |
| Implanted device (pacemaker, implantable cardioverter-defibrillator) malfunction |
| Drug-induced proarrhythmias |
| Structural cardiac or cardiopulmonary disease |
| Acute myocardial infarction/ischemia |
| Cardiac valvular disease |
| Obstructive cardiomyopathy |
| Acute aortic dissection |
| Pulmonary embolus/pulmonary hypertension |
| Atrial myxoma |
| Pericardial disease/tamponade |
| Cerebrovascular causes |
| Migraine (most often neurally mediated reflex in origin) |
| Vascular steal syndromes |

POTS=Postural orthostatic tachycardia syndrome

**Box 1: Common factors that increase risk of orthostatic syncope**

- Sudden head-up postural change (especially upon waking in the morning)
- Standing still for a prolonged period
- Certain prescription drugs (e.g., diuretics, vasodilators)
- Severe exertion with dehydration
- Diminished "thirst drive" in elderly persons
- Avoidance of fluid intake in older men (to minimize prostate symptoms)
- Excess alcohol or caffeine
- Straining during micturition or defecation
- High environmental temperature (including hot baths, showers, and saunas)
- Large meals (especially with refined carbohydrates)

noncardiac syncope from cardiac syncope, which carries a high mortality in all age groups; consequently, the goal must be to determine the cause of syncope with sufficient confidence to provide a reliable assessment of prognosis, recurrence risk, and treatment options.[16]

Initial assessment of syncope consists of a detailed history and examination complemented by 12-lead ECG and lying and standing BP [Box 2]. It can provide an initial diagnosis in 66% of cases, with a diagnostic accuracy of 88%.[17]

After the initial evaluation, the cause of syncope may be obvious, in which case no tests are needed. If the cause is suspected, then tests may be needed to confirm the particular disorder. If the cause is unexplained, then the next steps depend on how severe and how

**Table 4: Frequency of different causes of syncope**

| Causes of syncope | Mean prevalence (range) percentage |
|---|---|
| Neurally mediated syncope | |
| Vasovagal attack | 18 (8-37) |
| Situational syncope | 5 (1-8) |
| Carotid-sinus syncope | 1 (0-4) |
| Psychiatric disorders | 2 (1-7) |
| Orthostatic hypotension | 8 (4-10) |
| Medications | 3 (1-7) |
| Neurologic disease | 10 (3-32) |
| Cardiac syncope | |
| Organic heart diseases* | 4 (1-8) |
| Arrhythmia | 14 (4-38) |
| Unknown | 34 (13-41) |

*Organic heart disease refers to structural heart disease that causes syncope, such as aortic stenosis, pulmonary hypertension, pulmonary embolism, or myocardial infarction

**Box 2: How to obtain and interpret lying and standing BP measurements**

Record baseline supine BP and heart rate after 10 min of rest

Record BP and heart rate at 1, 2, and 3 min after standing (at 5 min if, POTS suspected)

Inquire about symptoms

Orthostatic hypotension is defined by a drop in systolic BP of 20 mmHg or diastolic BP of 10 mmHg within 3 min of standing

Orthostatic hypotension is considered clinically important if

- The reduction in BP is sustained at or beyond 3 min
- Original symptoms are reproduced during active or passive standing

Heart rate should rise with standing

- Excessive rise in heart rate (≥30 beats/min) or to a rate of ≥120 beats/min is diagnostic of POTS
- Lack of heart rate response suggests autonomic failure, rate limiting drugs, or chronotropic incompetence

POTS=Postural orthostatic tachycardia syndrome, BP=Blood pressure

frequent the attacks are and whether the patient has heart disease.

Initial evaluation can be difficult in elderly. Orthostatic and postprandial hypotension is common in elderly. Prodromal symptoms are uncommon in elderly. Elderly people commonly experience vasovagal or orthostatic syncope while sitting. Prolonged confusion during recovery is particularly common in elderly. This can lead to diagnostic confusion with seizures which are also more common in the elderly population. Elderly may deny history of LOC because they frequently have retrograde amnesia. Carotid sinus hypersensitivity occurs almost exclusively in people over the age of 40 years. Heart disease is common in elderly people, yet noncardiac causes of syncope are still more common. It is normal to find more than one potential cause of syncope after evaluating an elderly person.

A menstrual history should also be taken in women of childbearing age as syncope is a not uncommon presentation of ectopic pregnancy. In addition, neurocardiogenic syncope is relatively common in early pregnancy. A urinary beta-human chorionic gonadotropin test should be considered in all women of childbearing age to rule out an ectopic pregnancy.

Finally, a family history of cardiac disease or sudden unexplained family death or history of syncope raise the possibility of hypertrophic cardiomyopathy, Brugada syndrome, congenital long QT syndrome, and arrhythmogenic right ventricular dysplasia.

A confident diagnosis of vasovagal syncope or orthostatic hypotension (OH) can be made without further investigation if the history is suggestive and cardiac examination and ECG are normal.[1,18] OH, cardiac syncope, and those with noncardiac syncope in whom diagnostic and management difficulties exist should be investigated by clues obtained in the systemic inquiry, physical examination, and routine laboratory tests.

Important pointers in history, categorized as "5Ps," for the evaluation of syncope are summarized in Table 5 and the relevant physical examination findings are summarized in Table 6.

### *Electrocardiography*

The 12-lead ECG and echocardiogram are essential elements of the initial syncope evaluation. Although ECG rarely provides a definitive diagnosis, they might facilitate choice of subsequent tests. ECG is a noninvasive, inexpensive tool for identifying the important causes of syncope. It also predicts prognosis and risk stratify patients, presenting with different types of syncope. Various ECG changes [Box 3] in the appropriate clinical setting provide an answer to the clinician for the syncopal event. A negative ECG itself does not rule out either cardiac pathology or serious etiology. Similarly, incidental ECG findings can be obtained in noncardiac syncope. A corrected QT interval of >470 ms in men, >480 ms in women "rule in" LQTS (100% positive predictive value) , while a QTc of <390 ms in men and <410 ms in women rule out (100% negative predictive value) this syndrome.[19]

Presence of injury, abnormal ECG, absence of symptoms preceding syncope, and male gender were independent risk factors for developing adverse events within 10 days from the index episode in Short-Term Prognosis of Syncope[20] study. Prompt identification of short-term risk factors may help emergency physicians in their decision-making process and in turn reduce the number of inappropriate hospital admission.

**Table 5: Important pointers in history in a patient with syncope: The "5Ps"**

| | Clinical features | Suggested diagnosis |
|---|---|---|
| Precipitants | Warm or crowded environments | Vasovagal attack |
| | Prolonged standing at attention | |
| | Sudden unexpected pain, fear, or unpleasant sight, sound, or smell emotional distress | |
| | After exertion in well-trained athlete without heart disease | |
| | Episodes occur immediately on standing | Orthostatic hypotension |
| | Dehydration (as a result of drugs or illness) | |
| | Episodes occur during or immediately after micturition, cough, swallowing, or defecation | Situational syncope |
| | Episodes occur with head rotation or pressure on carotid sinus (due to tumors, shaving, or tight collars) | Carotid sinus syndrome |
| | Syncope is accompanied by throat or facial pain (glossopharyngeal or trigeminal neuralgia) | Neurally mediated syncope with neuralgia |
| | Patient takes medications that may lead to a long QT interval or orthostasis and bradycardia | Drug-induced syncope |
| | During or immediately after exercise, or no obvious precipitant | Arrhythmia, structural heart disease |
| | Family history of sudden cardiac death | Brugada or Long QT syndrome |
| | Episodes occur with arm exercise | Subclavian steal syndrome |
| | Syncope precipitated by exertion | Aortic stenosis, pulmonary hypertension, mitral stenosis, hypertrophic cardiomyopathy, coronary artery disease |
| Prodromes | Lightheadedness, dizziness, blurred vision | Vasovagal, orthostatic |
| | Syncope with vertigo, dysarthria, or diplopia | Transient ischemic attack, subclavian steal, basilar migraine |
| | Syncope associated with headache | Migraine, seizure |
| | Nausea, sweating, abdominal pain | Vasovagal |
| | Chest pain, shortness of breath, or no prodrome | Cardiac |
| | *Déjà vu, jamais vu* | Seizures |
| Palpitations | Palpitations preceding/during syncope | Arrhythmia |
| Position | Prolonged standing | Vasovagal syncope, orthostatic hypotension, orthostatic hypotension |
| | Sudden changes in posture | |
| | Supine | Arrhythmia, structural heart disease |
| Postevent phenomenon | Nausea, vomiting, fatigue | Vasovagal syncope |
| | Immediate complete recovery | Any cause, common in arrhythmia |
| | Patient is confused after episode, or loss of consciousness lasts >5 min | Seizure |

**Table 6: Physical examination findings helpful in evaluation of syncope**

| Examination finding | Suggested diagnosis |
|---|---|
| Differences are found in BP or pulse between the two arms | Subclavian steal or aortic dissection |
| Murmur occurring with changes of position (from sitting to lying, bending, turning over in bed) | Atrial myxoma or thrombus |
| Patient is confused after episode, or loss of consciousness lasts >5 min | Seizure |
| Abnormalities of cognition and speech, visual fields, motor strength, sensation, tremor, and gait disturbance suggest an underlying neurological disorder | Cerebrovascular cause |
| Cardiac examination for murmurs | Valvular heart disease, or other forms of organic heart disease |
| Loud P2 | Pulmonary hypertension |

BP=Blood pressure

**Box 3: Electrocardiogram findings suggesting cardiac or arrhythmic cause of syncope**

- Third-degree atrioventricular block
- Intermittent atrioventricular block (i.e., high-grade, Mobitz II, Mobitz I in elderly patients)
- Intraventricular conduction abnormality
- Sustained severe sinus bradycardia (<40 beats/min while awake, sinoatrial block, or sinus pause ≥3 s duration)
- Tachyarrhythmia
- Ventricular ectopy or nonsustained ventricular tachycardia
- QT interval (short and long QT syndromes)
- Preexcited QRS complexes (e.g., Wolff–Parkinson–White syndrome)
- Brugada pattern
- Arrhythmogenic right ventricular dysplasia "epsilon waves"
- ST-segment or T-wave changes suggesting acute myocardial infarction/ischemia
- Ventricular hypertrophy
- Pacemaker malfunction

Risk stratification Of Syncope in the Emergency department[21] (ROSE) rule is clinically validated and has got excellent sensitivity and negative predictive value that allows identification of high-risk patients with an emergency presentation of syncope, and it should be to patients in whom a clear diagnosis is not apparent after initial assessment. The ROSE rule correctly identifies 85% of patients whose subsequent serious outcome or death is not apparent in the emergency department (ED). This rule potentially reduces admission rates by 30%. ROSE rule includes B-type natriuretic peptide level ≥300 pg/ml, bradycardia ≤50 in ED or prehospital, rectal examination showing fecal occult blood (if suspicion of gastrointestinal bleed), anemia-hemoglobin ≤90 g/l, chest pain associated with syncope, ECG showing Q-wave (not in lead III), and saturation ≤94% on room air.

### *Role of echocardiography*

An echocardiogram is a helpful screening test if the history, physical examination, and ECG do not provide a diagnosis or if underlying heart disease is suspected. The echocardiogram is an excellent way to identify underlying heart disease. The most common cause of sudden death in athletes is hypertrophic cardiomyopathy, which is readily indicated by echocardiography.[22] Echocardiographic findings of unsuspected left ventricular dysfunction, dynamic left ventricular outflow obstruction, or atrial myxoma/thrombus might provide valuable clues. The second most common cause of sudden death in the young is the presence of an anomalous coronary artery.[22] In young and thin individuals, the coronary ostia may be identified by a transthoracic echocardiogram, and if not visualized, the presence of an anomalous coronary artery may be further evaluated with a transesophageal echocardiogram, cardiac magnetic resonance imaging or computed tomography, or other imaging modality.

### *Predicting cause of syncope*

If the patient has had syncope, a key question is whether he or she has heart disease or not. The presence of structural heart disease is the most important predictor of a cardiac cause of syncope. On the other hand, the absence of structural heart disease rules out a cardiac cause of syncope in 97% of cases.[23] Structural heart disease usually refers to history of previous myocardial infarction or in young people, a family history of sudden cardiac death, clinically significant murmur, and an abnormal ECG. Four variables increase the likelihood of syncope due to primary arrhythmia: Ischemic heart disease, structural heart disease, syncope without prodrome, and left bundle branch block. History of syncope before age of 20 years with a normal baseline ECG, decreases the likelihood of primary arrhythmia.[24]

Thus, the presence or absence of heart disease should be investigated first. In the presence of heart disease, some variables suggest a cardiac cause of syncope, with a high specificity. These are history of blurred vision, syncope occurring in the supine position or during effort, <3 syncopal episodes, time between first and last syncopal episodes <4 years, and convulsive syncope. The presence of these variables increases the pretest probability of a cardiac cause of syncope. In the patients without heart disease, palpitation was the only significant predictor of a cardiac cause. In contrast, a longer gap (>4 years) between two episodes and three or more episodes of syncope, when preceded by abdominal discomfort or followed by nausea and diaphoresis, suggests a neutrally mediated cause of syncope, with a high specificity and an increased posttest probability.[23]

## *Evaluation of specific types of syncope*

### *Exercise testing in syncope*

An evaluation for ischemia is appropriate in patients at risk for or with a history of coronary artery disease. Exercise testing should be performed in the patient with unexplained syncope, especially if the episode was exercise related. Exercise testing provides the opportunity to monitor pulse and BP. In patients <40 years of age, a drop in BP or failure of BP to rise with exercise raises the question of hypertrophic obstructive cardiomyopathy or left main coronary artery disease;[25] in the elderly patient, it may be a manifestation of autonomic failure. Exercise testing also screens for catecholaminergic polymorphic ventricular tachycardia.

### *Noninvasive electrocardiography monitoring*

The gold standard for diagnosing an arrhythmic cause of syncope is ECG documentation of the rhythm disturbance at the time of symptoms. However, it is rare to have documentation of the cardiac rhythm

from the initial episode of syncope. The type and duration of ambulatory ECG monitoring are dictated by the frequency of symptoms. A Holter monitor is appropriate for episodes that occur at least every day. Event monitoring is ideal for episodes that occur at least once a month. An implantable loop monitor allows the correlation of symptoms, with the cardiac rhythm in patients in whom the symptoms are infrequent.

The short duration of the Holter recording limits the diagnostic yield. Such techniques are of limited diagnostic value because they are useful only if symptoms occur during monitoring, which is rare.[26] An asymptomatic arrhythmia does not prove an arrhythmic cause for syncope. Monitoring may be more helpful in excluding arrhythmia as the etiology of syncope if the patient has symptoms while monitored and no arrhythmia is recorded.[26] Presyncope may not be an adequate surrogate for syncope. As a result, therapy should not necessarily be guided by presyncopal findings.

External event recorders appear to be somewhat more helpful than short-term continuous ambulatory monitoring in diagnosing the etiology of syncope or presyncope.[26] External event recorders can provide prospective and/or retrospective (loop) recordings. Prospective recorders often do not provide useful information because the patient must be conscious to activate the unit and record the rhythm at the time of the symptom.[27] Intermittent loop recorders may circumvent this difficulty if the unit has the ability to store several minutes of recording and if the patient activates the device immediately upon regaining consciousness.[28]

Implantable loop recorder (ILR)[29] is typically implanted in the left parasternal or pectoral region and has a battery life of 18–24 months. The ILR stores recorded ECG strips either when the device is activated according to programmed criteria (tachycardia or bradycardia thresholds) or when the patient manually activates it with magnet application. Retrospective recording permits capture of the rhythm during syncope by activation of the ILR after consciousness has returned.

### *Syncope in the patient with a normal evaluation*

Although life-threatening clinical entities are less likely in the presence of a normal evaluation, the possibility of neurocardiogenic syncope, carotid sinus hypersensitivity, paroxysmal bradyarrhythmias, supraventricular tachycardia, ventricular tachycardia, and myriad noncardiac causes of syncope remains.[30]

### *Tilt testing*

The most commonly used protocols are the low-dose intravenous isoproterenol test and the protocol using sublingual nitroglycerine. Both protocols have a similar rate of positive responses (61–69%), with a high specificity (92–94%). When a reflex is induced, according to the predominance of vasodepressor or cardioinhibitory components, the responses have been classified as cardioinhibitory, vasodepressor, or mixed.[31] A negative tilt table response does not exclude the diagnosis of reflex syncope.

Indications:[1] Main indication for tilt testing has been to confirm a diagnosis of reflex syncope in patients in whom this diagnosis was suspected but not confirmed by initial evaluation. Tilt testing is not usually needed in patients whose reflex syncope is already diagnosed by clinical history and in patients with single or rare syncope unless special situations (e.g., injury, anxiety, occupational implications such as aircraft pilots). Tilt testing has no value in assessing the treatment efficacy.

- In patients with organic heart disease high probability of cardiac syncope, when a cardiovascular cause has been reasonably excluded by a comprehensive evaluation
- Discriminating reflex syncope from epilepsy, when history of jerky movement present
- Psychiatric pseudosyncope
- In elderly to distinguish syncope from falls
- Discriminate pure reflex syncope from nonclassical forms of delayed OH
- Demonstrate susceptibility of the patient to reflex syncope before initiating treatment (e.g., physical maneuvers).

Tilt testing is safe. There have been no reported deaths during the test. However, some rare life-threatening ventricular arrhythmias with isoproterenol in the presence of ischemic heart disease[32] have been reported. No complications have been published with the use of nitroglycerine Atrial fibrillation can be induced during or after a positive tilt test and is usually self-limited.[33]

### *Electrophysiological study*

In patients with a normal evaluation for syncope, the yield of electrophysiological testing is approximately 3%.[34] The sensitivity of electrophysiological testing for the detection of bradyarrhythmias is low.[35] Because of the low yield of electrophysiological testing in patients without underlying heart disease, this test is not routinely recommended.[36] However, given the low risk of electrophysiological testing[37] and the high risk of recurrent syncope with potential harm to the patient, the risk-to-benefit ratio may favor electrophysiological testing in patients with a malignant episode of syncope. Important indications of electrophysiological study are abnormal electrocardiogram, suggesting conduction system cause, syncope during exertion or in supine position or with important structural heart disease, syncope with palpitations or angina-like chest pain, family history of sudden death.

### *Carotid sinus massage*

A positive response to carotid sinus massage (CSM) in patients with syncope is highly predictive of the

occurrence of spontaneous asystolic episodes. CSM is indicated in patients with more than 40 years old in syncope of unknown etiology after initial evaluation. CSM is diagnostic if syncope is reproduced in the presence of asystole longer than 3 s and/or systolic BP fall by more than 50 mmHg. The main complications of CSM are neurological (0.29%). CSM should be avoided in patients with previous transient ischemic attack, stroke within the past 3 months, or with carotid bruits, except if carotid Doppler studies excluded significant stenosis.[38]

### *Adenosine triphosphate test*

The test requires the rapid (<2 s) injection of a 20 mg bolus of adenosine triphosphate (ATP) (or adenosine) during ECG monitoring. The induction of atrioventricular (AV) block with ventricular asystole lasting >6 s, or the induction of AV block lasting >10 s, is considered abnormal. ATP testing produced an abnormal response in some patients with syncope of unknown origin (especially older women without structural heart disease), but not in controls, thus suggesting that paroxysmal AV block could be the cause of unexplained syncope. Owing to lack of correlation with spontaneous syncope, ATP test cannot be used as diagnostic test to select patient for cardiac pacing.[1]

## Conclusion

The evaluation and treatment of syncope are very challenging. First, "syncope" is only one of many causes of transient LOC. Second, symptoms are fleeting, and the patient is usually asymptomatic at the time of evaluation. Third, events are often unwitnessed; however, even when witnessed; circumstances might undermine reliability of the account. Finally, there is often an excessive sense of diagnostic "urgency;" these results in a rush to undertake multiple poorly considered "diagnostic" testing procedures. A deliberate approach based on initial risk stratification is more likely to give a correct diagnosis. It is important to spend enough time on history before prescribing investigation.

Despite the difficulties, a thorough evaluation of the cause of syncope is warranted in all patients, not just in those deemed to be at high mortality risk. Conversely, the mere presence of an abnormal finding does not constitute a "diagnosis." The physician must carefully consider whether detected abnormalities are compatible with the clinical circumstances. The goal in every case should be to determine the cause with sufficient confidence to provide a reliable assessment of prognosis and treatment options.

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