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Syncope: Etiology and diagnostic approach

ABSTRACT

There are three major types of syncope: neurally mediated (the most common), orthostatic hypotensive, and cardiac (the most worrisome). Several studies have shown a normal long-term survival rate in patients with syncope who have no structural heart disease, which is the most important predictor of death and ventricular arrhythmia. The workup of unexplained syncope depends on the presence or absence of heart disease: electrophysiologic study if the patient has heart disease, tilt-table testing in those without heart disease, and prolonged rhythm monitoring in both cases if syncope remains unexplained.

KEY POINTS

Neurally mediated forms of syncope, such as vasovagal, result from autonomic reflexes that respond inappropriately, leading to vasodilation and relative bradycardia.

Orthostatic hypotension is the most common cause of syncope in the elderly and may be due to autonomic dysfunction, volume depletion, or drugs that block autonomic effects or cause hypovolemia, such as vasodilators, beta-blockers, diuretics, neuropsychiatric medications, and alcohol.

The likelihood of cardiac syncope is low in patients with normal electrocardiographic and echocardiographic findings.

Hospitalization is indicated in patients with syncope who have or are suspected of having structural heart disease.

SYNCOPE is a transient loss of consciousness and postural tone with spontaneous, complete recovery. There are three major types: neurally mediated, orthostatic, and cardiac (TABLE 1).

■ NEURALLY MEDIATED SYNCOPE

Neurally mediated (reflex) syncope is the most common type, accounting for two-thirds of cases.¹⁻³ It results from autonomic reflexes that respond inappropriately, leading to vasodilation and bradycardia.

See related patient-education handout, page 767

Neurally mediated syncope is usually preceded by premonitory symptoms such as lightheadedness, diaphoresis, nausea, malaise, abdominal discomfort, and tunnel vision. However, this may not be the case in one-third of patients, especially in elderly patients, who may not recognize or remember the warning symptoms. Palpitations are frequently reported with neurally mediated syncope and do not necessarily imply that the syncope is due to an arrhythmia.^{4,5} Neurally mediated syncope does not usually occur in the supine position^{4,5} but can occur in the seated position.⁶

Subtypes of neurally mediated syncope are as follows:

Vasovagal syncope

Vasovagal syncope is usually triggered by sudden emotional stress, prolonged sitting or standing, dehydration, or a warm environment, but it can also occur without a trigger. It is the most common type of syncope in young patients (more so in females than in males), but contrary to a common misconception, it can also occur in the elderly.⁷ Usually, it is not

TABLE 1

Types of syncope

Neurally mediated (60%–70%)

- Vasovagal
- Situational
- Carotid sinus hypersensitivity
- Postexertional

Orthostatic (10%)

Cardiac (10%–20%)

- Structural heart disease with cardiac obstruction
- Ventricular tachycardia (structural heart disease or primary electrical disease)
- Bradyarrhythmias (degenerative conduction disease, drug effect, structural heart disease)

Other

- Acute illness
- Arterial occlusion with neurologic deficit (carotid, vertebrobasilar, proximal subclavian)
- Psychogenic

Palpitations do not necessarily imply that syncope is due to an arrhythmia

only preceded by but also followed by nausea, malaise, fatigue, and diaphoresis^{4,5,8}; full recovery may be slow. If the syncope lasts longer than 30 to 60 seconds, clonic movements and loss of bladder control are common.⁹

Mechanism. Vasovagal syncope is initiated by anything that leads to strong myocardial contractions in an “empty” heart. Emotional stress, reduced venous return (from dehydration or prolonged standing), or vasodilation (caused by a hot environment) stimulates the sympathetic nervous system and reduces the left ventricular cavity size, which leads to strong hyperdynamic contractions in a relatively empty heart. This hyperdynamic cavity obliteration activates myocardial mechanoreceptors, initiating a paradoxical vagal reflex with vasodilation and relative bradycardia.¹⁰ Vasodilation is usually the predominant mechanism (vasodepressor response), particularly in older patients, but severe bradycardia is also possible (cardioinhibitory response), particularly in younger patients.⁷ Diuretic and vasodilator therapies increase the predisposition to vasovagal syncope, particularly in the elderly.

On tilt-table testing, vasovagal syncope is characterized by hypotension and relative bradycardia, sometimes severe (see **NOTE ON TILT-TABLE TESTING**).^{10–12}

Situational syncope

Situational syncope is caused by a reflex triggered in specific circumstances such as micturition, defecation, coughing, weight-lifting, laughing, or deglutition. The reflex may be initiated by a receptor on the visceral wall (eg, the bladder wall) or by straining that reduces venous return.

Carotid sinus hypersensitivity

Carotid sinus hypersensitivity is an abnormal response to carotid massage, predominantly occurring in patients over the age of 50. In *spontaneous carotid sinus syndrome*, syncope clearly occurs in a situation that stimulates the carotid sinus, such as head rotation, head extension, shaving, or wearing a tight collar. It is a rare cause of syncope, responsible for about 1% of cases. Conversely, *induced carotid sinus syndrome* is much more common and represents carotid sinus hypersensitivity in a patient with unexplained syncope and without obvious triggers; the abnormal response is mainly *induced* during carotid massage rather than spontaneously. In the latter case, carotid sinus hypersensitivity is a marker of a diseased sinus node or atrioventricular node that cannot withstand any inhibition. This diseased node is the true cause of syncope rather than carotid sinus hypersensitivity per se, and carotid massage is a “stress test” that unveils conduction disease.

Thus, carotid massage is indicated in cases of unexplained syncope regardless of circumstantial triggers. This test consists of applying a firm pressure over each carotid bifurcation (just below the angle of the jaw) consecutively for 10 seconds. It is performed at the bedside, and may be performed with the patient in both supine and erect positions during tilt-table testing; erect positioning of the patient increases the sensitivity of this test.

An abnormal response to carotid sinus massage is defined as any of the following^{13–15}:

- Vasodepressor response: the systolic blood pressure decreases by at least 50 mm Hg
- Cardioinhibitory response: sinus or atrioventricular block causes the heartbeat to pause for 3 or more seconds
- Mixed vasodepressor and cardioinhibitory response.

Overall, a cardioinhibitory component is

Note on tilt-table testing

Tilt-table testing consists of strapping the patient to a table that is then inclined to nearly vertical for up to 45 minutes. It is a form of orthostatic stress that simulates prolonged standing and is actually more stressful than standing, as the patient is deprived of the skeletal muscle pumping that normally occurs with standing. The stress level may be increased by infusing isoproterenol or administering sublingual nitroglycerin, which increases the likelihood of syncope during testing. Continuous, beat-to-beat noninvasive blood pressure monitoring is usually performed. Possible findings and what they imply are outlined below.^{10,11}

The specificity of tilt-table testing for vasovagal syncope is up to 90% and the false-positive rate is about 10% (the specificity is reduced with pharmacologic facilitation). The sensitivity is about 80%, and the test is positive in up to 66% of patients with unexplained syncope.^{10,12} The false-positive rate is higher in patients with structural heart disease, left bundle branch block, or right bundle branch block; in fact, tilt-table testing in patients with arrhythmic syncope and abnormal electrophysiologic studies elicits syncope in up to 25% of these patients.

The yield of tilt-testing is highest in patients with an intermediate pretest probability of vasovagal syncope, such as those without structural heart disease who have an unexplained malignant or recurrent syncope, elderly patients with unexplained syncope or falling, and patients with structural heart disease (eg, treated coronary artery disease, left ventricular hypertrophy) but a normal or only mildly reduced ejection fraction, no significant valvular disease, and normal electrophysiologic study results. Patients with a high or low pretest probability of vasovagal syncope have the lowest yield from tilt-table testing.

The test is contraindicated in patients with recent stroke, recent myocardial infarction, and severe coronary or carotid disease.

TYPES OF RESPONSE TO TILT-TABLE TESTING^a

Vasodepressor syncope: abrupt, rapid hypotension without a significant drop in heart rate (< 10%).

Cardioinhibitory syncope: hypotension with a drop in heart rate to less than 40 beats per minute or a pause of more than 3 seconds. A mixed response is characterized by a significant drop in heart rate that remains, however, faster than 40 beats per minute without a prolonged pause. In all forms of vasovagal syncope, except some cardioinhibitory forms, blood pressure falls before the rate falls. Blood pressure falls suddenly.

Orthostatic hypotension: hypotension within 10 minutes of tilt, without bradycardia (usually a slight increase in heart rate is seen). The drop in blood pressure is more gradual in orthostatic hypotension than in vasovagal syncope.

Postural orthostatic tachycardia syndrome: significant increase in heart rate during the first 10 minutes of tilt (an increase of more than 30 beats per minute or an absolute rate of more than 120 beats per minute). Significant hypotension does not occur (blood pressure is normal or low normal).

Cerebral syncope: no significant hemodynamic change, but intense cerebral vasoconstriction on transcranial Doppler study.

Psychogenic syncope: syncope without hemodynamic or transcranial Doppler change.

^aTo be considered positive for vasovagal syncope, hypotension (with or without bradycardia) needs to occur along with reproduction of syncope or near-syncope. A hemodynamic effect without symptoms is not considered an abnormal tilt-test result.

present in about two-thirds of cases of carotid sinus hypersensitivity.

Carotid sinus hypersensitivity is found in 25% to 50% of patients over age 50 who have had unexplained syncope or a fall, and it is seen almost equally in men and women.¹³

One study correlated carotid sinus hypersensitivity with the later occurrence of asystolic syncope during prolonged internal loop monitoring; subsequent pacemaker therapy reduced the burden of syncope.¹⁴ Another study, in patients over 50 years old with unexplained falls, found that 16% had cardioinhib-

itory carotid sinus hypersensitivity. Pacemaker placement reduced falls and syncope by 70% compared with no pacemaker therapy in these patients.¹⁵

On the other hand, carotid sinus hypersensitivity can be found in 39% of elderly patients who do not have a history of fainting or falling, so it is important to rule out other causes of syncope before attributing it to carotid sinus hypersensitivity.

Postexertional syncope

While syncope on exertion raises the worrisome possibility of a cardiac cause, postexertional

syncope is usually a form of vasovagal syncope. When exercise ceases, venous blood stops getting pumped back to the heart by peripheral muscular contraction. Yet the heart is still exposed to the catecholamine surge induced by exercising, and it hypercontracts on an empty cavity. This triggers a vagal reflex.

Postexertional syncope may also be seen in hypertrophic obstructive cardiomyopathy or aortic stenosis, in which the small left ventricular cavity is less likely to tolerate the reduced preload after exercise and is more likely to obliterate.

■ **ORTHOSTATIC HYPOTENSION**

Orthostatic hypotension accounts for about 10% of cases of syncope.¹⁻³

Normally, after the first few minutes of standing, about 25% to 30% of the blood pools in the veins of the pelvis and the lower extremities, strikingly reducing venous return and stroke volume. Upon more prolonged standing, more blood leaves the vascular space and collects in the extravascular space, further reducing venous return. This normally leads to a reflex increase in sympathetic tone, peripheral and splanchnic vasoconstriction, and an increase in heart rate of 10 to 15 beats per minute. Overall, cardiac output is reduced and vascular resistance is increased while blood pressure is maintained, blood pressure being equal to cardiac output times vascular resistance.

Orthostatic hypotension is characterized by autonomic failure, with a lack of compensatory increase in vascular resistance or heart rate upon orthostasis, or by significant hypovolemia that cannot be overcome by sympathetic mechanisms. It is defined as a drop in systolic blood pressure of 20 mm Hg or more or a drop in diastolic pressure of 10 mm Hg or more after 30 seconds to 5 minutes of upright posture. Blood pressure is checked immediately upon standing and at 3 and 5 minutes. This may be done at the bedside or during tilt-table testing.^{2,4}

Some patients have an immediate drop in blood pressure of more than 40 mm Hg upon standing, with a quick return to normal within 30 seconds. This “initial orthostatic hypotension” may be common in elderly patients

taking antihypertensive drugs and may elude detection during standard blood pressure measurement.² Other patients with milder orthostatic hypotension may develop a more delayed hypotension 10 to 15 minutes later, as more blood pools in the periphery.¹⁶

Along with the drop in blood pressure, a failure of the heart rate to increase identifies autonomic dysfunction. On the other hand, an increase in the heart rate of more than 20 to 30 beats per minute may signify a hypovolemic state even if blood pressure is maintained, the lack of blood pressure drop being related to the excessive heart rate increase.

Orthostatic hypotension is the most common cause of syncope in the elderly and may be due to autonomic dysfunction (related to age, diabetes, uremia, or Parkinson disease), volume depletion, or drugs that block autonomic effects or cause hypovolemia, such as vasodilators, beta-blockers, diuretics, neuro-psychiatric medications, and alcohol.

Since digestion leads to peripheral vasodilation and splanchnic blood pooling, syncope that occurs within 1 hour after eating has a mechanism similar to that of orthostatic syncope.

Supine hypertension with orthostatic hypotension. Some patients with severe autonomic dysfunction and the inability to regulate vascular tone have severe hypertension when supine and significant hypotension when upright.

Postural orthostatic tachycardia syndrome, another form of orthostatic failure, occurs most frequently in young women (under the age of 50). In this syndrome, autonomic dysfunction affects peripheral vascular resistance, which fails to increase in response to orthostatic stress. This autonomic dysfunction does not affect the heart, which manifests a striking compensatory increase in rate of more than 30 beats per minute within the first 10 minutes of orthostasis, or an absolute heart rate greater than 120 beats per minute. Unlike in orthostatic hypotension, blood pressure and cardiac output are maintained through this increase in heart rate, although the patient still develops symptoms of severe fatigue or near-syncope, possibly because of flow maldistribution and reduced cerebral flow.²

While postural orthostatic tachycardia syndrome per se does not induce syncope,² it may be associated with a vasovagal form of syncope

Vasovagal syncope is initiated by anything that leads to strong contractions in an 'empty' heart

that occurs beyond the first 10 minutes of orthostasis in up to 38% of these patients.¹⁷

In a less common, hyperadrenergic form of postural orthostatic tachycardia syndrome, there is no autonomic failure but the sympathetic system is overly activated, with orthostasis leading to excessive tachycardia.^{10,18}

■ CARDIAC SYNCOPE

Accounting for 10% to 20% of cases of syncope, a cardiac cause is the main concern in patients presenting with syncope, as cardiac syncope predicts an increased risk of death and may herald sudden cardiac death.^{1,2,8,19,20} It often occurs suddenly without any warning signs, in which case it is called *malignant syncope*. Unlike what occurs in neurally mediated syncope, the postrecovery period is not usually marked by lingering malaise.

There are three forms of cardiac syncope:

Syncope due to structural heart disease with cardiac obstruction

In cases of aortic stenosis, hypertrophic obstructive cardiomyopathy, or severe pulmonary arterial hypertension, peripheral vasodilation occurs during exercise, but cardiac output cannot increase because of the fixed or dynamic obstruction to the ventricular outflow. Since blood pressure is equal to cardiac output times peripheral vascular resistance, pressure drops with the reduction in peripheral vascular resistance. Exertional ventricular arrhythmias may also occur in these patients. Conversely, postexertional syncope is usually benign.

Syncope due to ventricular tachycardia

Ventricular tachycardia can be secondary to underlying structural heart disease, with or without reduced ejection fraction, such as coronary arterial disease, hypertrophic cardiomyopathy, hypertensive cardiomyopathy, or valvular disease. It can also be secondary to primary electrical disease (eg, long QT syndrome, Wolff-Parkinson-White syndrome, Brugada syndrome, arrhythmogenic right ventricular dysplasia, sarcoidosis).

Occasionally, fast supraventricular tachycardia causes syncope at its onset, before vascular compensation develops. This occurs in patients with underlying heart disease.^{2,8,19}

TABLE 2

Clinical clues to the type of syncope

Position during syncope

Supine: reflex syncope is unlikely

Sitting or standing: any cause is possible

Within a few minutes of sitting or standing: orthostatic hypotension

Prolonged sitting or standing: vasovagal

Situation during syncope

Exertion (strenuous activity, not just walking): cardiac syncope (cardiac obstruction, ventricular arrhythmia)

Postexertion: vasovagal

Postprandial: orthostatic hypotension

Sudden fear, pain, unpleasant sight, hot environment: vasovagal

Strain situation (micturition): reflex syncope

Head-turning, shaving, tight collar: carotid sinus syndrome

Prodromes (abdominal discomfort, malaise, palpitations, nausea, blurred vision)

Yes and > 5 seconds: reflex syncope

No or < 5 seconds: cardiac syncope (but reflex or orthostatic syncope may be associated with prodromes < 5 seconds or no prodrome in 33% to 50% of patients, more so in the elderly)

How consciousness is regained after syncope

Promptly: cardiac syncope

Prolonged fatigue or nausea after syncope: reflex syncope

Confusion: seizure

Color during syncope

Pale, diaphoretic: reflex syncope, orthostatic syncope

Blue: arrhythmia, seizure

Duration

> 5 minutes: seizure, hypoglycemia; not syncope (except occasionally aortic stenosis)

Other factors

Underlying heart disease, chest pain: cardiac syncope

Multiple neuropsychiatric or blood pressure medications: orthostatic syncope (cardiac syncope possible)

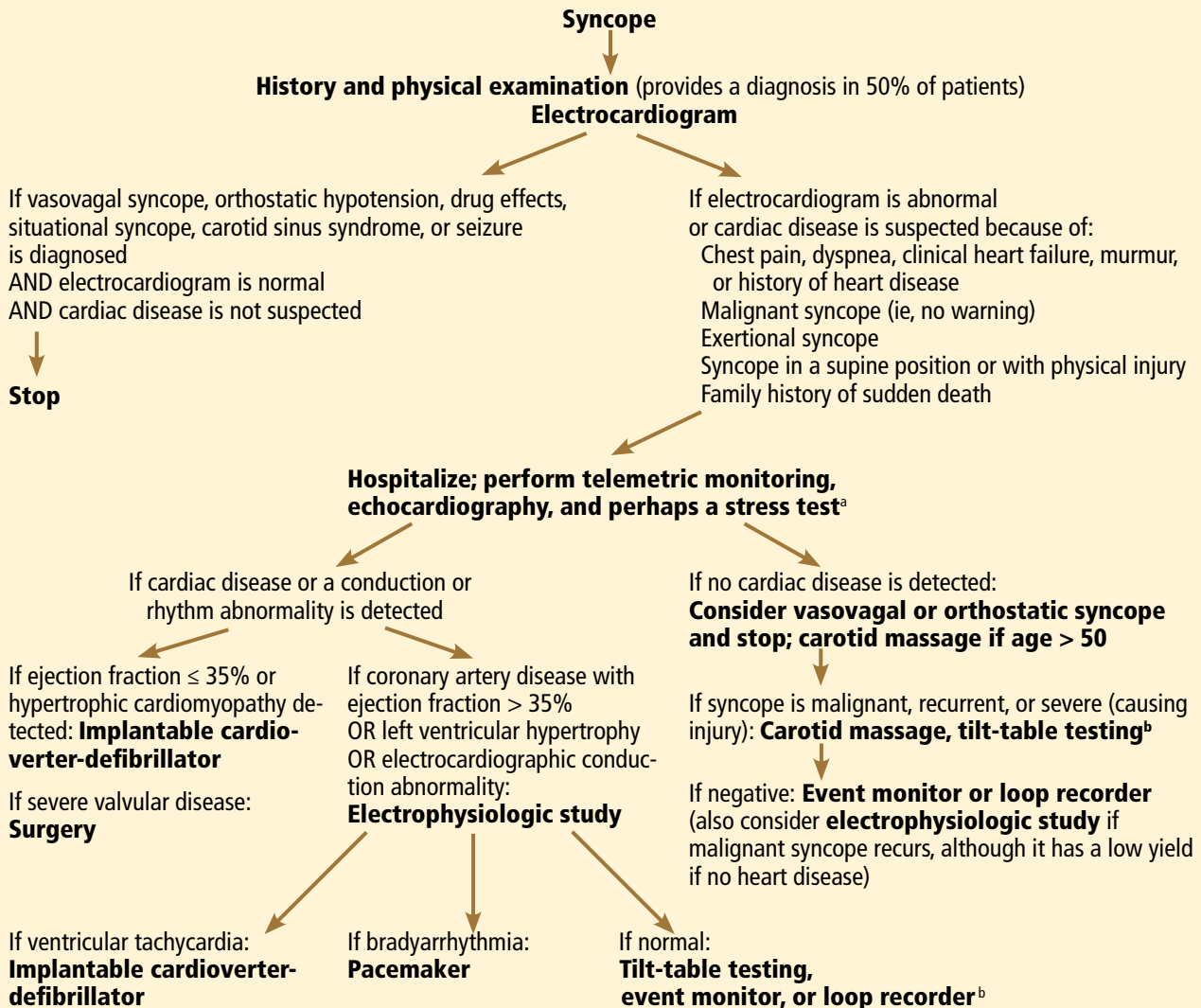
The presence or absence of injury does not help differentiate cardiac from reflex syncope

Multiple syncopal recurrences (\geq three episodes) suggest reflex or orthostatic syncope (one is less likely to survive three episodes of cardiac syncope); this is particularly true if the interval between episodes is > 4 years⁸

INFORMATION FROM REFERENCES 2–5 AND 8.

Syncope from bradyarrhythmias

Bradyarrhythmias can occur with or without underlying structural heart disease. They are most often related to degeneration of the conduction system or to medications rather than to cardiomyopathy.



^a Also consider severe hypovolemia, bleeding, pulmonary embolism, and tamponade and rule them out clinically. Carotid Doppler ultrasonography and computed tomography of the head are not indicated, especially because carotid stenoses per se very rarely lead to syncope.
^b Electrophysiologic study may have missed bradyarrhythmias and some forms of ventricular tachycardia.

FIGURE 1. Management of syncope

Caveats

When a patient with a history of heart failure presents with syncope, the top considerations are ventricular tachycardia and bradyarrhythmia. Nevertheless, about half of cases of syncope in patients with cardiac disease have a noncardiac cause,¹⁹ including the hypotensive or bradycardiac side effect of drugs.

As noted above, most cases of syncope are

neurally mediated. However, long asystolic pauses due to sinus or atrioventricular nodal block are the most frequent mechanism of unexplained syncope and are seen in more than 50% of syncope cases on prolonged rhythm monitoring.^{1,21} These pauses may be related to intrinsic sinus or atrioventricular nodal disease or, more commonly, to extrinsic effects such as the vasovagal mechanism. Some experts favor

classifying and treating syncope on the basis of the final mechanism rather than the initiating process, but this is not universally accepted.^{1,22}

■ OTHER CAUSES OF SYNCOPE

Acute medical or cardiovascular illnesses can cause syncope and are looked for in the appropriate clinical context: severe hypovolemia or gastrointestinal bleeding, large pulmonary embolus with hemodynamic compromise, tamponade, aortic dissection, or hypoglycemia.

Bilateral critical carotid disease or severe vertebrobasilar disease very rarely cause syncope, and, when they do, they are associated with focal neurologic deficits.² Vertebrobasilar disease may cause “drop attacks,” ie, a loss of muscular tone with falling but without loss of consciousness.²³

Severe proximal subclavian disease leads to reversal of the flow in the ipsilateral vertebral artery as blood is shunted toward the upper extremity. It manifests as dizziness and syncope during the ipsilateral upper extremity activity, usually with focal neurologic signs (subclavian steal syndrome).²

Psychogenic pseudosyncope is characterized by frequent attacks that typically last longer than true syncope and occur multiple times per day or week, sometimes with a loss of motor tone.² It occurs in patients with anxiety or somatization disorders.

■ SEIZURE: A SYNCOPE MIMIC

Certain features differentiate seizure from syncope:

- In seizure, unconsciousness often lasts longer than 5 minutes
- After a seizure, the patient may experience postictal confusion or paralysis
- Seizure may include prolonged tonic-clonic movements; although these movements may be seen with any form of syncope lasting more than 30 seconds, the movements during syncope are more limited and brief, lasting less than 15 seconds
- Tongue biting strongly suggests seizure.

Urinary incontinence does not help distinguish the two, as it frequently occurs with syncope as well as seizure.

TABLE 3

Electrocardiographic or Holter findings that suggest cardiac syncope

Bradyarrhythmia-related syncope is *established* with any of the following:

Sinus bradycardia (< 40 beats per minute) or sinus pauses > 3 seconds while awake

Mobitz II, high-grade, or complete atrioventricular block

Alternating left or right bundle branch block on the same electrocardiogram or on electrocardiograms obtained on separate occasions

Bradyarrhythmia-related syncope is *suggested* with:

Isolated right or left bundle branch block (ventricular tachycardia also possible depending on the underlying cardiac disease)

Mobitz I atrioventricular block

Tachyarrhythmia-related syncope is *established* with:

Sustained ventricular tachycardia or fast supraventricular tachycardia (>160 beats per minute)

Underlying heart disease and ventricular tachycardia are *suggested* with:

Q waves

Left bundle branch block, right bundle branch block, QRS > 0.11 seconds

Left ventricular hypertrophy, right ventricular hypertrophy

Large R wave in V₁

Primary electrical disorders are *suggested* with:

Long QTc

Pre-excitation

Right bundle branch block with Brugada pattern

T-wave inversion in V₁–V₃ or epsilon waves (arrhythmogenic right ventricular dysplasia)

Acute ST/T abnormalities

■ DIAGNOSTIC EVALUATION OF SYNCOPE

TABLE 2 lists clinical clues to the type of syncope.^{2–5,8}

Underlying structural heart disease is the most important predictor of ventricular arrhythmia and death.^{20,24–26} Thus, the primary goal of the evaluation is to rule out structural heart disease by history, examination, electrocardiography, and echocardiography (FIGURE 1).

Initial strategy for finding the cause

The cause of syncope is diagnosed by history and physical examination alone in up to 50% of cases, mainly neurally mediated syncope, orthostatic syncope, or seizure.^{2,3,19}

Always check blood pressure with the patient both standing and sitting and in both

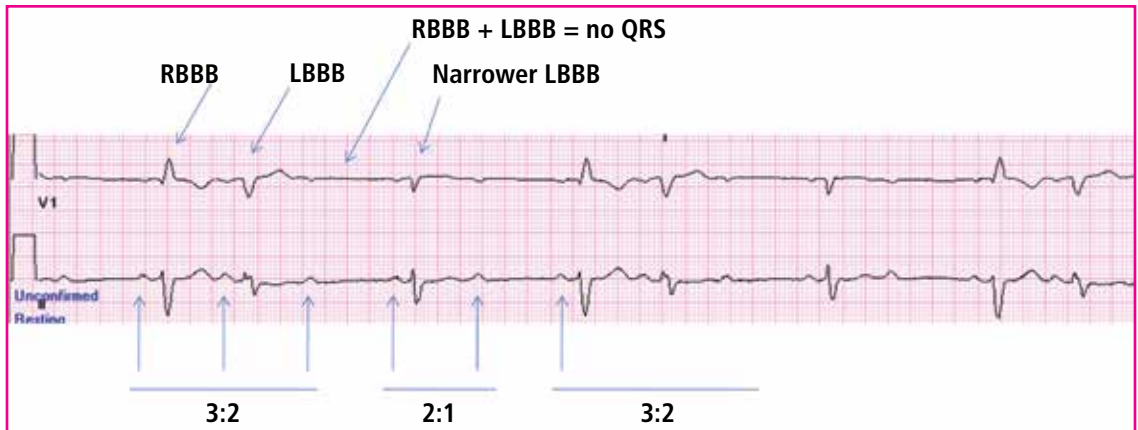


FIGURE 2. Second-degree Mobitz II atrioventricular block, with 3:2 block alternating with 2:1 block (arrows point to P waves). As seen in lead V₁, right bundle branch block alternates with left bundle branch block. Beside Mobitz II block, the alternation of right and left bundle branch block indicates infranodal atrioventricular block. In fact, QRS is dropped when both bundles simultaneously block in a patient with underlying right bundle branch block, left bundle branch block, or alternating right and left bundle branch block. RBBB = right bundle branch block; LBBB = left bundle branch block

Carotid massage is indicated in cases of unexplained syncope regardless of circumstantial triggers

arms, and obtain an electrocardiogram.

Perform carotid massage in all patients over age 50 if syncope is not clearly vasovagal or orthostatic and if cardiac syncope is not likely. Carotid massage is contraindicated if the patient has a carotid bruit or a history of stroke.

Electrocardiography establishes or suggests a diagnosis in 10% of patients (TABLE 3, FIGURE 2).^{1,2,8,19} A normal electrocardiogram or a mild nonspecific ST-T abnormality suggests a low likelihood of cardiac syncope and is associated with an excellent prognosis. Abnormal electrocardiographic findings are seen in 90% of cases of cardiac syncope and in only 6% of cases of neurally mediated syncope.²⁷ In one study of syncope patients with normal electrocardiograms and negative cardiac histories, none had an abnormal echocardiogram.²⁸

If the heart is normal

If the history suggests neurally mediated syncope or orthostatic hypotension and the history, examination, and electrocardiogram do not suggest coronary artery disease or any other cardiac disease, the workup is stopped.

If the patient has signs or symptoms of heart disease

If the patient has signs or symptoms of heart disease (angina, exertional syncope, dyspnea, clinical signs of heart failure, murmur), a his-

tory of heart disease, or exertional, supine, or malignant features, heart disease should be looked for and the following performed:

- **Echocardiography** to assess left ventricular function, severe valvular disease, and left ventricular hypertrophy
- **A stress test** (possibly) in cases of exertional syncope or associated angina; however, the overall yield of stress testing in syncope is low (< 5%).²⁹

If electrocardiography and echocardiography do not suggest heart disease

Often, in this situation, the workup can be stopped and syncope can be considered neurally mediated. The likelihood of cardiac syncope is very low in patients with normal findings on electrocardiography and echocardiography, and several studies have shown that patients with syncope who have no structural heart disease have normal long-term survival rates.^{20,26,30}

The following workup may, however, be ordered if the presentation is atypical and syncope is malignant, recurrent, or associated with physical injury, or occurs in the supine position¹⁹:

Carotid sinus massage in patients over age 50, if not already performed. Up to 50% of these patients with unexplained syncope have carotid sinus hypersensitivity.¹³

24-hour Holter monitoring rarely detects significant arrhythmias, but if syncope or dizziness occurs without any arrhythmia, Holter monitoring rules out arrhythmia as the cause of the symptoms.³¹ The diagnostic yield of Holter monitoring is low (1% to 2%) in patients with infrequent symptoms^{1,2} and is not improved with 72-hour monitoring.³⁰ The yield is higher in patients with very frequent daily symptoms, many of whom have psychogenic pseudosyncope.²

Tilt-table testing to diagnose vasovagal syncope. This test is positive for a vasovagal response in up to 66% of patients with unexplained syncope.^{1,19} Patients with heart disease taking vasodilators or beta-blockers may have abnormal baroreflexes. Therefore, a positive tilt test is less specific in these patients and does not necessarily indicate vasovagal syncope.

Event monitoring. If the etiology remains unclear or there are some concerns about arrhythmia, an event monitor (4 weeks of external rhythm monitoring) or an implantable loop recorder (implanted subcutaneously in the prepectoral area for 1 to 2 years) is placed. These monitors record the rhythm when the rate is lower or higher than predefined cutoffs or when the rhythm is irregular, regardless of symptoms. The patient or an observer can also activate the event monitor during or after an event, which freezes the recording of the 2 to 5 minutes preceding the activation and the 1 minute after it.

In a patient who has had syncope, a pacemaker is indicated for episodes of high-grade atrioventricular block, pauses longer than 3 seconds while awake, or bradycardia (< 40 beats per minute) while awake, and an implantable cardioverter-defibrillator is indicated for sustained ventricular tachycardia, even if syncope does not occur concomitantly with these findings. The finding of nonsustained ventricular tachycardia on monitoring increases the suspicion of ventricular tachycardia as the cause of syncope but does not prove it, nor does it necessarily dictate implantation of a cardioverter-defibrillator device.

An electrophysiologic study has a low yield in patients with normal electrocardiographic and echocardiographic studies. Bradycardia is detected in 10%.³¹

If heart disease or a rhythm abnormality is found

If heart disease is diagnosed by echocardiography or if significant electrocardiographic abnormalities are found, perform the following:

Pacemaker placement for the following electrocardiographic abnormalities^{1,2,19}:

- Second-degree Mobitz II or third-degree atrioventricular block
- Sinus pause (> 3 seconds) or bradycardia (< 40 beats per minute) while awake
- Alternating left bundle branch block and right bundle branch block on the same electrocardiogram or separate ones.

Telemetric monitoring (inpatient).

An electrophysiologic study is valuable mainly for patients with structural heart disease, including an ejection fraction 36% to 49%, coronary artery disease, or left ventricular hypertrophy with a normal ejection fraction.³² Overall, in patients with structural heart disease and unexplained syncope, the yield is 55% (inducible ventricular tachycardia in 21%, abnormal indices of bradycardia in 34%).³¹

However, the yield of electrophysiologic testing is low in bradyarrhythmia and in patients with an ejection fraction of 35% or less.³³ In the latter case, the syncope is often arrhythmia-related and the patient often has an indication for an implantable cardioverter-defibrillator regardless of electrophysiologic study results, especially if the low ejection fraction has persisted despite medical therapy.³²

If the electrophysiologic study is negative

If the electrophysiologic study is negative, the differential diagnosis still includes arrhythmia, as the yield of electrophysiologic study is low for bradyarrhythmias and some ventricular tachycardias, and the differential diagnosis also includes, at this point, neurally mediated syncope.

The next step may be either prolonged rhythm monitoring or tilt-table testing. An event monitor or an implantable loop recorder can be placed for prolonged monitoring. The yield of the 30-day event monitor is highest in patients with frequently recurring syncope, in whom it reaches a yield of up to 40% (10% to 20% will have a positive diagnosis of arrhythmia, while 15% to 20% will have symptoms with a normal rhythm).^{31,34} The implantable

Underlying structural heart disease is the most important predictor of ventricular arrhythmia and death

recorder has a high overall diagnostic yield and is used in patients with infrequent syncopal episodes (yield up to 50%).^{1,35,36}

In brief, there are two diagnostic approaches to unexplained syncope: the monitoring approach (loop recorder) and the testing approach (tilt-table testing). A combination of both strategies is frequently required in patients with unexplained syncope, and, according to some investigators, a loop recorder may be implanted early on.²¹

Heart disease with left ventricular dysfunction and low ejection fraction

In patients with heart disease with left ventricular dysfunction and an ejection fraction of 35% or less, an implantable cardioverter-defibrillator can be placed without the need for an electrophysiologic study. These patients need these devices anyway to prevent sudden death, even if the cause of syncope is not an arrhythmia. Patients with a low ejection fraction and a history of syncope are at a high risk of sudden cardiac death.³² Yet in some patients with newly diagnosed cardiomyopathy, left ventricular function may improve with medical therapy. Because the arrhythmic risk is essentially high during the period of ventricular dysfunction, a wearable external defibrillator may be placed while the decision about an implantable defibrillator is finalized within the ensuing months.

In patients with hypertrophic cardiomyopathy, place an implantable cardioverter-defibrillator after any unexplained syncopal episode.

Valvular heart disease needs surgical correction.

If ischemic heart disease is suspected, coronary angiography is indicated, with revascularization if appropriate. An implantable cardioverter-defibrillator should be placed if the ejection fraction is lower than 35%. Except in a large acute myocardial infarction, the substrate for ventricular tachycardia is not ameliorated with revascularization.^{32,37} Consider an electrophysiologic study when syncope occurs with coronary artery disease and a higher ejection fraction.

A note on left or right bundle branch block

Patients with left or right bundle branch block and unexplained syncope (not clearly vasovagal or orthostatic) likely have syncope related

to intermittent high-grade atrioventricular block.³⁸

One study monitored these patients with an implanted loop recorder and showed that about 40% had a recurrence of syncope within 48 days, often concomitantly with complete atrioventricular block. About 55% of these patients had a major event (syncope or high-grade atrioventricular block).³⁹ Many of the patients had had a positive tilt test; thus, tilt testing is not specific for vasovagal syncope in these patients and should not be used to exclude a bradyarrhythmic syncope. Also, patients selected for this study had undergone carotid sinus massage and an electrophysiology study with a negative result.

In another analysis, an electrophysiologic study detected a proportion of the bradyarrhythmias but, more importantly, it induced ventricular tachycardia in 14% of patients with right or left bundle branch block. Although it is not sensitive enough for bradyarrhythmia, electrophysiologic study was highly specific and fairly sensitive for the occurrence of ventricular tachycardia on follow-up.³⁸ Thus, unexplained syncope in a patient with right or left bundle branch block may warrant carotid sinus massage, then an electrophysiologic study to rule out ventricular tachycardia, followed by placement of a dual-chamber pacemaker if the study is negative for ventricular tachycardia, or at least placement of a loop recorder.

■ INDICATIONS FOR HOSPITALIZATION

Patients should be hospitalized if they have severe hypovolemia or bleeding, or if there is any suspicion of heart disease by history, examination, or electrocardiography, including:

- History of heart failure, low ejection fraction, or coronary artery disease
- An electrocardiogram suggestive of arrhythmia (TABLE 3)
- Family history of sudden death
- Lack of prodromes; occurrence of physical injury, exertional syncope, syncope in a supine position, or syncope associated with dyspnea or chest pain.^{2,40}

In these situations, there is concern about arrhythmia, structural heart disease, or acute myocardial ischemia. The patient

About half of cases of syncope in patients with cardiac disease have a noncardiac cause, such as a side effect of drug therapy

is admitted for immediate telemetric monitoring. Echocardiography and sometimes stress testing are performed. The patient is discharged if this initial workup does not suggest underlying heart disease. Alternatively, an electrophysiologic study is performed or a device is placed in patients found to have structural heart disease. Prolonged rhythm monitoring or tilt-table testing may be performed when syncope with underlying heart disease or worrisome features remains unexplained.

Several Web-based interactive algorithms have been used to determine the indication for hospitalization. They incorporate the above clinical, electrocardiographic, and sometimes echocardiographic features.^{2,24,25,40–42} A cardiology consultation is usually necessary in patients with the above features, as they frequently require specialized cardiac testing.

Among high-risk patients, the risk of sudden death, a major cardiovascular event, or significant arrhythmia is high in the first few days after the index syncopal episode, justifying the hospitalization and inpatient rhythm monitoring and workup in the presence of the above criteria.^{24,40,42}

■ SYNCOPE AND DRIVING

A study has shown that the most common cause of syncope while driving is vasovagal syncope.⁶ In all patients, the risk of another episode of syncope was relatively higher during the first 6 months after the event, with a 12% recurrence rate during this period. However, recurrences were often also seen more than 6 months later (12% recurrence between 6 months and the following few years).⁶ Fortunately, those episodes rarely occurred while the patient was driving. In a study in survivors of ventricular arrhythmia, the risk of recurrence of arrhythmic events was highest during the first 6 to 12 months after the event.⁴³

Thus, in general, patients with syncope should be prohibited from driving for at least the period of time (eg, 6 months) during which the risk of a recurrent episode of syncope is highest and during which serious cardiac disease or arrhythmia, if present, would emerge. Recurrence of syncope is more likely and more dangerous for commercial drivers who spend a significant proportion of their time driving; individualized decisions are made in these cases. ■

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