Syncope: Evaluation and Differential Diagnosis

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Syncope is an abrupt and transient loss of consciousness caused by cerebral hypoperfusion. It accounts for 1% to 1.5% of emergency department visits, resulting in high hospital admission rates and significant medical costs. Syncope is classified as neurally mediated, cardiac, and orthostatic hypotension. Neurally mediated syncope is the most common type and has a benign course, whereas cardiac syncope is associated with increased morbidity and mortality. Patients with presyncope have similar prognoses to those with syncope and should undergo a similar evaluation. A standardized approach to syncope evaluation reduces hospital admissions and medical costs, and increases diagnostic accuracy. The initial assessment for all patients presenting with syncope includes a detailed history, physical examination, and electrocardiography. The initial evaluation may diagnose up to 50% of patients and allows immediate short-term risk stratification. Laboratory testing and neuroimaging have a low diagnostic yield and should be ordered only if clinically indicated. Several comparable clinical decision rules can be used to assess the short-term risk of death and the need for hospital admission. Low-risk patients with a single episode of syncope can often be reassured with no further investigation. High-risk patients with cardiovascular or structural heart disease, history concerning for arrhythmia, abnormal electrocardiographic findings, or severe comorbidities should be admitted to the hospital for further evaluation. In cases of unexplained syncope, provocative testing and prolonged electrocardiographic monitoring strategies can be diagnostic. The treatment of neurally mediated and orthostatic hypotension syncope is largely supportive, although severe cases may require pharmacotherapy. Cardiac syncope may require cardiac device placement or ablation. (*Am Fam Physician*. 2017;95(5):303-312. Copyright © 2017 American Academy of Family Physicians.)

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▶ **Patient information:** A handout on this topic is available at http://www.aafp.org/afp/2017/0301/p303-s1.html.

Syncope is a sudden, brief, and transient loss of consciousness caused by cerebral hypoperfusion.[1] Other nontraumatic loss of consciousness syndromes include seizures, cataplexy, metabolic disorders, acute intoxications, vertebrobasilar insufficiency, transient ischemic attack, cerebrovascular accident, and psychogenic pseudosyncope.[2,3]

Syncope accounts for 1% to 1.5% of all emergency department visits, 250,000 annual hospital admissions, and a median hospital cost of $8,500.[4,5] Approximately 40% of the U.S. population will experience a syncopal episode in their lifetimes, and 30% to 50% will be admitted to the hospital for further evaluation.[6,7] The etiology is unexplained in up to one-third of cases.[8]

Although syncope is associated with serious risks, short-term mortality is low (i.e., 0.7% at 10 days and 1.6% at 30 days). At one year, the mortality rate is 8.4%; one-third of these are attributed to cardiovascular causes. Approximately 25% of patients with syncope will experience another event within two years.[8,9] Historically, neurally mediated and orthostatic hypotension syncope have not conferred an increased risk of death[10]; however, in a recent study, healthy adults with a diagnosis of syncope had higher rates of all-cause mortality, recurrent syncope, cardiovascular events, and pacemaker or implantable cardioverter-defibrillator placement compared with matched controls. Patients 44 to 75 years of age had the highest risk.[11,12]

Management of syncope remains a challenge, particularly in identifying patients with potentially life-threatening etiologies. Lack of physician knowledge, a desire to reassure the patient or clinician, and the fear of medicolegal ramifications result in overuse of diagnostic tests.[13] A standardized approach for evaluating patients with syncope reduces admissions, hospital costs, and number of tests performed, and increases accuracy of diagnosis.[14] Only 10% to 15% of patients will remain undiagnosed after a comprehensive evaluation using current guidelines.[15,16]

Classification and Etiology

Syncope is classified as cardiac, neurally mediated (reflex), and orthostatic hypotension *(Table 1)*.[1,17] The differential diagnosis should include nontraumatic causes of transient loss of consciousness. Rare causes include subclavian steal syndrome, pulmonary embolism, acute myocardial infarction, acute aortic dissection, leaking aortic aneurysm, subarachnoid hemorrhage, and cardiac tamponade.[2,3]

Neurally mediated syncope is the most common type, comprising approximately 45% of cases.[6,10,18] It can be vasovagal, situational, or secondary to carotid sinus hypersensitivity. The pathophysiology is complex, consisting of an interaction between autonomic systems paradoxically favoring parasympathetic or vagal tone, which causes bradycardia and hypotension.

Cardiac syncope occurs in approximately 20% of syncope presentations. It is most often caused by an arrhythmia, and less often by a structural cardiac abnormality. In a prospective cohort study, patients with cardiac syncope had a twofold increase in mortality over 17 years.[10] The presence of cardiovascular disease predicts a cardiac etiology of syncope with 85% to 94% sensitivity and 64% to 83% specificity.[16]

Orthostatic hypotension syncope has an incidence of approximately 10% and is typically characterized by posturally induced hypotension, most often related to impaired increase in systemic vascular resistance. Associated factors include medication effects, volume depletion, acute hemorrhage, and autonomic dysfunction. Postural tachycardia syndrome is the most prevalent form of orthostatic intolerance, affecting approximately 500,000 persons in the United States. Younger adults, predominantly women who report symptoms of postural presyncope, are more likely to have this condition.[19]

PRESYNCOPE

Presyncope is poorly studied, and the true incidence is unknown. A study of 881 patients presenting to the emergency department with presyncope showed a 30-day risk of serious outcomes of 5% and a mortality rate of 0.3%.[20] Emergency physicians had difficulty stratifying patients at increased risk of adverse outcomes, regardless of presumed etiology. A prospective observational study (n = 244) compared adverse outcomes and

BEST PRACTICES IN NEUROLOGY: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN	
Recommendation	*Sponsoring organization*
Avoid computed tomography of the head in asymptomatic adult patients in the emergency department with syncope, insignificant trauma, and a normal neurologic evaluation.	American College of Emergency Physicians
In the evaluation of simple syncope and a normal neurologic evaluation, do not obtain brain imaging studies (computed tomography or magnetic resonance imaging).	American College of Physicians
Do not perform imaging of the carotid arteries for simple syncope without other neurologic symptoms.	American Academy of Neurology

Source: For more information on the Choosing Wisely Campaign, see http://www.choosingwisely.org. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see http://www.aafp.org/afp/recommendations/search.htm.

Table 1. Classification of Syncope

Syncope type	Scenario	Clinical features
Cardiac syncope		
Arrhythmia (e.g., bradyarrhythmias, ventricular tachyarrhythmias, supraventricular tachyarrhythmias), pacemaker dysfunction, channelopathies	Generally abrupt and unprovoked; palpitations may precede symptoms	Abnormal electrocardiographic findings, family history of sudden death, personal history of heart disease, sudden onset of palpitations, symptoms during or after exertion while in supine or prone position
Obstructive cardiomyopathy	Hypertrophic cardiomyopathy or exertional syncope in persons with a family history of sudden cardiac death	Often asymptomatic; may cause arrhythmias, chest pain, shortness of breath, or syncope; dynamic systolic murmur that intensifies from squatting to standing or during Valsalva maneuver
Structural cardiac disease	Acute myocardial infarction or ischemia	Diaphoresis, exertional chest pain, nausea, shortness of breath; rare cause of syncope
	Arrhythmogenic right ventricular cardiomyopathy	Asymptomatic, atypical chest pain, dizziness, exertional syncope, family history of sudden cardiac death, palpitations, right ventricular structural abnormalities
	Infiltrative (e.g., amyloidosis, hemochromatosis, sarcoidosis)	Arrhythmias, heart block, heart failure
	Valvular disease (e.g., aortic stenosis, mitral stenosis, pulmonary stenosis)	Symptoms dependent on severity; severe aortic stenosis can manifest with congestive heart failure, exertional angina, or syncope
Other structural disease	Acute aortic dissection	Hypotension or shock, severe sharp chest pain with or without radiation to the back, history of hypertension
	Cardiac masses (e.g., atrial myxoma, cardiac tumors)	Arrhythmia via direct invasion, embolization, heart failure, systemic symptoms, valvular regurgitation
	Cardiac tamponade	Elevated jugular venous pressure, hypotension, pulsus paradoxus, sinus tachycardia
	Pulmonary hypertension	Often asymptomatic; may cause fatigue and shortness of breath
	Saddle pulmonary embolus	Acute shortness of breath, chest pain, hypoxia, right heart strain, sinus tachycardia
Neurally mediated (reflex) syncope		
Carotid sinus syndrome/hypersensitivity	Head rotation or pressure on the carotid sinus (e.g., from shaving or tight collar) can reproduce symptoms; consider in patients with unexplained falls	Ventricular pause or decreased systolic blood pressure after carotid sinus massage; may coincide with syncope
Situational	Brought on by coughing, defecation, gastrointestinal stimulation, or urination; may occur after exercise or meals	Absence of heart disease; history of similar syncope; prolonged standing, eating, or voiding
Vasovagal	Mediated by fear, heat exposure, noxious stimuli, pain, or stress	Prodromal symptoms (e.g., diaphoresis, dizziness, nausea), precipitating factors
Orthostatic hypotension syncope		
Drug induced	Alcohol, antianginal agents, antidepressants, antidiabetic agents, antihypertensives, antiparkinsonian agents, diuretics, flibanserin (Addyi), insulin	Initiation or change in dosage
Postural tachycardia syndrome	Young adults (predominantly female); associated with chronic fatigue syndrome and mitral valve prolapse	Severe orthostatic intolerance with marked tachycardia
Primary autonomic failure	Multiple sclerosis, multiple system atrophy (e.g., Shy-Drager syndrome), Parkinson disease/parkinsonism, Wernicke encephalopathy	Orthostatic hypotension with postural change
Secondary autonomic failure	Amyloidosis, chronic inflammatory demyelinating polyneuropathy, connective tissue diseases, diabetes mellitus, Lewy body dementia, older age, spinal cord injury, uremia	Orthostatic hypotension with postural change
Volume depletion	Acute blood loss (e.g., gastrointestinal bleeding, ectopic pregnancy), diarrhea, inadequate fluid intake, vomiting	Hypotension, tachycardia, history of volume/blood loss, dehydration on examination

Information from references 1 and 17.

hospitalizations in patients who presented with presyncope and syncope.[21] Adverse outcomes occurred in 49 of 244 patients (20%) with presyncope compared with 68 of 293 patients (23%) with syncope. Admission rates were 49% and 69%, respectively. Because rates of adverse outcomes are similar in patients with presyncope and syncope, both groups should receive a similar evaluation.

Risk Stratification

The decision to perform an expedited and monitored evaluation of patients presenting with syncope is based on the likelihood of short-term adverse outcomes. Unnecessary admissions for patients meeting low-risk criteria result in high medical costs without improvements in morbidity and mortality, patient safety, or quality of life.[22]

Several clinical decision rules have been developed to risk stratify patients presenting to the emergency department with syncope. Each has differing variables, and no single rule has proved significantly superior[23,24] (eTable A). The San Francisco Syncope Rule, Evaluation of Guidelines in Syncope Study, and Osservatorio Epidemiologico sulla Sincope nel Lazio are the only rules that have been externally validated. High-risk patients should be admitted for further evaluation (Table 2).[1,25]

Diagnostic Approach

Guidelines from the Canadian Cardiovascular Society, European Society of Cardiology, and the American College of Emergency Physicians recommend obtaining a detailed history and performing a physical examination, standard 12-lead electrocardiography (ECG), and orthostatic blood pressure measurement in patients presenting with syncope.[1,25-28] Additional testing should be individualized. Figure 1 provides a general framework, emphasizing classification and risk stratification to standardize the evaluation of syncope.[2] High-risk patients should be admitted for monitoring and further workup. Low-risk patients with a first episode of syncope may be reassured without further workup.[1,25,27,29]

HISTORY

A detailed history will suggest a diagnosis in up to 50% of patients and is the most important diagnostic tool in the evaluation of syncope.[1] The history should focus on three key elements: (1) Is the loss of consciousness attributable to syncope? (2) Is there a history of cardiovascular disease? (3) Are there clinical features to suggest a specific cause of syncope?[30] Pertinent historical elements are listed in Table 3.[18,30-33] Medication reconciliation is relevant because medications are contributory in 5% to 15% of syncope cases, typically causing orthostatic hypotension, sedation, symptomatic bradycardia, or QT interval prolongation.[34] The history should also assist in classifying patients as low or high risk.

PHYSICAL EXAMINATION

Most patients with syncope will have normal physical examination findings, with the exception of any trauma incurred from the syncopal event. The examination should focus on initial vital signs; orthostatic blood pressure measurements[35]; and vascular (pulses and carotid bruits), cardiac, pulmonary (evidence of congestive heart failure), abdominal, rectal, and skin/nail (anemia) signs. Any new focal neurologic findings suggest a primary central nervous system lesion.

Table 2. Risk Stratification in Patients with Syncope

High risk (hospital admission recommended)*

Clinical history suggestive of arrhythmic syncope (e.g., syncope during exercise, palpitations, or syncope without warning or prodrome)

Comorbidities (e.g., severe anemia, electrolyte abnormalities)

Electrocardiographic history suggestive of arrhythmic syncope (e.g., bifascicular block, sinus bradycardia < 40 beats per minute in absence of sinoatrial block or medication use, QRS preexcitation, abnormal QT interval, ST segment elevation leads V_1 through V_3 [Brugada pattern], negative T wave in right precordial leads and epsilon wave [arrhythmogenic right ventricular dysplasia/cardiomyopathy])

Family history of sudden death

Hypotension (systolic blood pressure < 90 mm Hg)

Older age†

Severe structural heart disease, congestive heart failure, or coronary artery disease

Low risk (outpatient evaluation recommended)‡

Age less than 50 years†

No history of cardiovascular disease

Normal electrocardiographic findings

Symptoms consistent with neurally mediated or orthostatic hypotension syncope
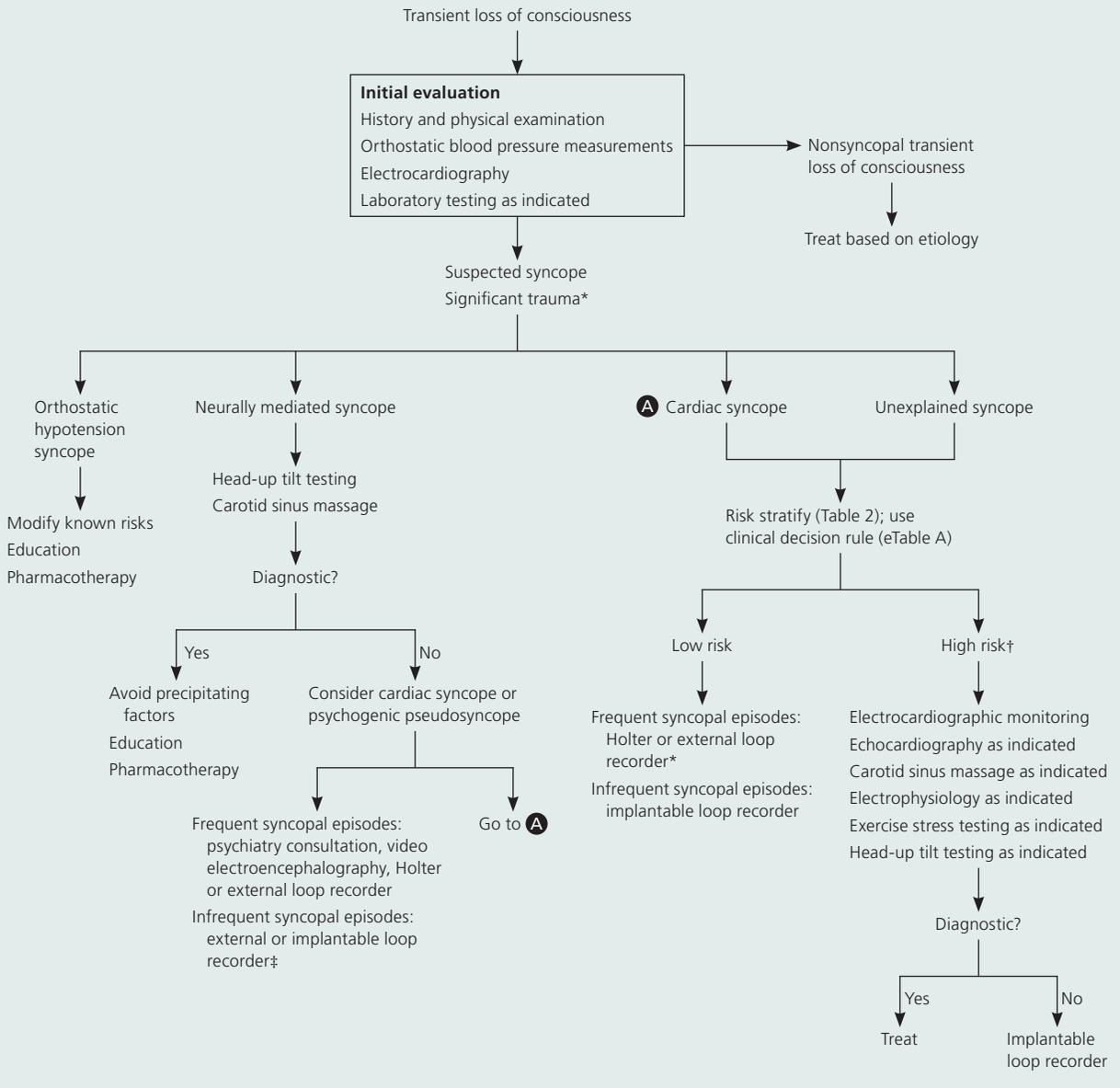
Unremarkable cardiovascular findings

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*—Patient is at high risk if any of the criteria are met.

†—Different age thresholds have been used in studies for decision making. Older age largely reflects the patient's cardiovascular health.

‡—Patient is at low risk only if all criteria are met.

Information from references 1 and 25.

Evaluation of Syncope

Transient loss of consciousness

↓

Initial evaluation
History and physical examination
Orthostatic blood pressure measurements
Electrocardiography
Laboratory testing as indicated

→ Nonsyncopal transient loss of consciousness

↓

Treat based on etiology

↓

Suspected syncope
Significant trauma*

Orthostatic hypotension syncope

↓

Modify known risks
Education
Pharmacotherapy

Neurally mediated syncope

↓

Head-up tilt testing
Carotid sinus massage

↓

Diagnostic?

Yes → Avoid precipitating factors
Education
Pharmacotherapy

No → Consider cardiac syncope or psychogenic pseudosyncope

Frequent syncopal episodes: psychiatry consultation, video electroencephalography, Holter or external loop recorder
Infrequent syncopal episodes: external or implantable loop recorder‡

Go to (A)

(A) Cardiac syncope   **Unexplained syncope**

↓

Risk stratify (Table 2); use clinical decision rule (eTable A)

Low risk

Frequent syncopal episodes: Holter or external loop recorder*
Infrequent syncopal episodes: implantable loop recorder

High risk†

Electrocardiographic monitoring
Echocardiography as indicated
Carotid sinus massage as indicated
Electrophysiology as indicated
Exercise stress testing as indicated
Head-up tilt testing as indicated

↓

Diagnostic?

Yes → Treat
No → Implantable loop recorder

*—Consider admission for patients with significant trauma and those with frequent syncopal episodes.
†—Admission is recommended for high-risk patients.
‡—In the absence of injuries, consider no further evaluation.

Figure 1. Algorithm for the evaluation of syncope.

Information from reference 2.

DIAGNOSTIC TESTING

Carotid sinus massage can be considered in patients older than 40 years to confirm the diagnosis of carotid sinus hypersensitivity. The maneuver is positive when it produces an asystolic or ventricular pause longer than three seconds or a decrease in systolic blood pressure of at least 50 mm Hg. The test is performed while the patient is supine, with five to 10 seconds of massage consecutively to each carotid sinus. It should be per- formed initially on the right because the maneuver is more often positive on this side. If results are negative, it should be repeated with the patient upright at approxi- mately 60 to 70 degrees.[36] This maneuver should be avoided in patients who have had a stroke or transient ischemic attack in the past three months and in patients with carotid bruits. If a positive carotid hypersensitiv- ity test is associated with patient symptoms, then the patient has carotid sinus syndrome.

Syncope

Routine laboratory studies have low diagnostic yield and should be ordered only if clinically indicated. Laboratory tests can distinguish syncope from other suspected nontraumatic etiologies of loss of consciousness. Elevated troponin and brain natriuretic peptide levels have been shown to predict a higher likelihood of adverse outcomes but should be used only if cardiovascular disease is clinically suspected.[26,37,38]

ECG generally has a low diagnostic yield (approximately 3% to 5%) but is recommended for all patients with syncope.[39,40] Although arrhythmias are unlikely to be detected on a single ECG, ischemic, structural, or conduction abnormalities may be identified. Any ECG abnormality or change from baseline increases the risk of arrhythmia or death within one year of the syncopal event.[41]

Echocardiography is essential to evaluate suspected structural abnormalities, but it generally has low diagnostic yield. Two studies (n = more than 310) found echocardiography to be clinically useful in patients with syncope if there is a history of cardiac disease, abnormal ECG findings, or suspected significant valvular disease.[42,43]

Continuous cardiac monitoring is the diagnostic standard to establish a correlation between symptoms and ECG findings. Devices include Holter monitors (generally up to 72 hours), external loop recorders (typically four to six weeks), and implantable loop recorders (up to three years). The diagnostic yield improves with prolonged monitoring. Up to 50% of patients who present with syncope in the absence of heart disease will have an arrhythmia when an implantable loop recorder is placed.[44] These devices may increase diagnostic yield, decrease time to diagnosis, and improve cost-effectiveness. Some guidelines recommend them early in the diagnostic workup of unexplained syncope.[45-48] Patients most likely to benefit from these devices are those with cardiovascular disease, abnormal baseline ECG findings, cardiac symptoms surrounding the syncopal event, and a family history of sudden cardiac death.[39]

Table 3. Pertinent Historical Information in the Evaluation of Syncope

Features	Possible diagnosis
Position before syncope	
Prolonged standing	Neurally mediated syncope (vasovagal), orthostatic hypotension syncope
Sudden change in posture*	Orthostatic hypotension syncope
Supine*	Cardiac syncope (arrhythmia, structural heart disease)
Postsyncope	
Amnesia regarding loss of consciousness	Seizure or neurally mediated syncope (vasovagal) in older patients
Eyes closed during event*	Pseudoseizure, psychogenic pseudosyncope
Eyes open during event	Seizure or syncope (any cause)
Fatigue, nausea, vomiting*	Neurally mediated syncope (vasovagal)
Focal neurologic deficit	Neurogenic syncope (cerebrovascular accident or transient ischemic attack)
Immediate complete recovery	Cardiac syncope (arrhythmia), psychogenic pseudosyncope
Incontinence	Seizure (uncommon in syncope; vasovagal syncope most likely)
Myoclonic, tonic-clonic movement	Neurally mediated syncope (vasovagal), seizure
Prolonged confusion*	Seizure
Prolonged syncope	Seizure, neurogenic, metabolic, infectious
Slow pulse	Cardiac syncope (bradyarrhythmia)
Tongue biting*	Seizure
Transient disorientation	Neurally mediated syncope (vasovagal)
Precipitating factors	
Activities such as coughing, defecation, eating, laughing, urination*	Neurally mediated syncope (situational)
Emotional distress, fear, pain, prolonged standing, warm or crowded area*	Neurally mediated syncope (vasovagal)
Exertion*	Cardiac syncope (arrhythmia, structural heart disease)
Hand or upper extremity exercise	Subclavian steal syndrome
Head movement, shaving, tight collar*	Neurally mediated syncope (carotid sinus)
Medication use	
Antiarrhythmics	Cardiac syncope (arrhythmia, prolonged QT interval)
Antihypertensives	Orthostatic hypotension syncope, cardiac syncope (prolonged QT interval)
Macrolides, antiemetics, antipsychotics, tricyclic antidepressants	Cardiac syncope (prolonged QT interval)
Postexertion	Neurally mediated syncope (vasovagal), cardiac syncope (arrhythmia)
Standing after prolonged sitting	Orthostatic hypotension syncope
Unexplained fall	Neurally mediated syncope (carotid sinus), cardiac syncope (arrhythmia, structural heart disease)

continues

—Salient features from history for differentiation.

Table 3. Pertinent Historical Information in the Evaluation of Syncope *(continued)*

Features	Possible diagnosis
Preexisting disease	
Alcoholism, diabetes mellitus, Parkinson disease, renal replacement therapy	Orthostatic hypotension syncope
Family history of sudden cardiac death	Cardiac syncope (long QT syndrome, Brugada syndrome, arrhythmogenic right ventricular dysplasia/cardiomyopathy, structural heart disease)
Heart disease	Cardiac syncope
History of frequent and prolonged syncopal events	Psychogenic pseudosyncope, neurally mediated syncope (vasovagal)
Older age with dementia	Orthostatic hypotension syncope, cardiac syncope
Psychiatric illness	Psychogenic pseudosyncope
Prodrome	
Abdominal pain, diaphoresis, nausea*	Neurally mediated syncope (vasovagal)
Aura	Seizure
Blurred vision, dizziness, lightheadedness, vertigo	Neurally mediated syncope (vasovagal), orthostatic hypotension syncope
Chest pain, dyspnea	Cardiac syncope (structural heart disease, pulmonary embolus, acute myocardial infarction)
Fluttering or palpitations*	Cardiac syncope (arrhythmia)
Focal neurologic deficit	Cerebrovascular accident, transient ischemic attack
Headache	Subarachnoid hemorrhage
Slow pulse	Neurally mediated syncope (vasovagal), cardiac syncope (bradyarrhythmia)
Tonic-clonic movement or posture	Seizure
None	Vasovagal or cardiac syncope in older patients, cardiac syncope in younger patients

*—Salient features from history for differentiation.

Adapted with permission from Parry SW, Tan MP. An approach to the evaluation and management of syncope in adults. BMJ. 2010;340:c880, with additional information from references 18, 30, 32 and 33.

Provocative testing strategies include head-up tilt testing, exercise testing, and electrophysiologic studies. The head-up tilt test is a safe procedure designed to precipitate hypotension and bradycardia and is used to confirm the diagnosis of neurally mediated syncope in patients with an intermediate pretest probability.[11] Persons in high-risk settings with unexplained syncope should also be considered for testing. Protocols using isoproterenol or nitroglycerin have an overall sensitivity of 92% to 94%; however, specificity is low.[1,49] Exercise testing is useful in exertional syncope, ischemia, and arrhythmia evaluation. Less than 2% of patients referred to cardiologists for evaluation of unexplained syncope undergo electrophysiologic studies.[1] These studies have poor sensitivity and specificity except in the setting of structural heart disease; they have been replaced by noninvasive tools such as prolonged ECG monitoring.[1,7] Patients who have an indication for implantable cardioverter-defibrillator placement do not require electrophysiologic studies.

Cranial or cardiac imaging, carotid ultrasonography, electroencephalography, and cardiac enzyme testing are rarely helpful in determining the cause of syncope and should not be ordered routinely. These tests affect diagnosis and management in less than 2% of older patients presenting to the emergency department.[40] For most patients with tests results that were significant and affected management, the patient's history indicated the diagnosis.[50,51] *Table 4* provides an overview of the available testing modalities.[1,11]

Treatment

The treatment of syncope is directed at the underlying cause. Morbidity and mortality are generally low except in cardiac syncope; therefore, patient reassurance is an important part of treatment.

NEURALLY MEDIATED SYNCOPE

Treatment of neurally mediated syncope includes reassurance, education, and physical therapy.[1] In situational syncope, it is important to avoid potential triggers. Physical counterpressure maneuvers such as leg crossing, squatting, and tensing the lower extremities are effective at the onset of prodromal symptoms.[7] One randomized trial showed that these maneuvers reduce syncope by 39%.[52] Tilt training involves standing for prolonged periods, and compliance is generally poor.[7]

Pharmacologic therapy with beta blockers, alpha agonists, and fludrocortisone has shown no effectiveness or conflicting results in reducing vasovagal syncope.[1] In one small randomized trial of patients with a history of recurrent vasovagal syncope, paroxetine (Paxil) prevented additional episodes in 82.4% compared with 47.1% in the placebo group over two years ($P < .001$), although guidelines recommend its use only in patients with concurrent psychiatric disease.[53] In patients with severe asystole from neurally mediated syncope, a double-blind, randomized, placebo-controlled trial showed that the use of permanent dual chamber pacing reduced the risk of recurrent syncope.[54]

Table 4. Diagnostic Evaluation of Syncope

Test	Indication	Comments
Basic laboratory testing	As clinically indicated	Rarely helpful; complete blood count, brain natriuretic peptide testing, fecal occult blood testing, human chorionic gonadotropin testing in women of childbearing age; troponin testing may be beneficial to identify cardiac etiology
Carotid sinus massage	Syncope of unknown etiology in patients older than 40 years[1]	Diagnostic if ventricular pause is more than three seconds or if systolic blood pressure decreases by more than 50 mm Hg; contraindicated in patients with bruits or a history of transient ischemic attack/cerebrovascular accident within the past three months
ECG	All patients with syncope	Diagnostic yield is 3% to 5%, but can aid in diagnosing arrhythmia, ischemia, pulmonary embolus (increased pulmonary pressures or right ventricular enlargement), hypertrophic cardiomyopathy, and Brugada syndrome; findings suggestive of arrhythmia include bundle branch block, intraventricular conduction delay, sinus bradycardia (less than 50 beats per minute), prolonged QT interval, QRS preexcitation, Q waves
	Recurrent syncope with unremarkable initial evaluation; clinical or ECG features suggestive of arrhythmic syncope; unexplained falls	Holter monitoring for 24 to 48 hours, external loop recorders for four to six weeks, implantable loop recorders for up to three years; consider testing in patients with suspected epilepsy not responsive to therapy; implantable loop recorders have high diagnostic yield in recurrent unexplained syncope[1]
Echocardiography	Suspected structural cardiac disease or when history, examination, and ECG are not diagnostic	Diagnostic in aortic stenosis, pericardial tamponade, obstructive cardiac tumors or thrombi, aortic dissection, hypertrophic cardiomyopathy, congenital anomalies of the coronary arteries, acute right ventricular strain (in pulmonary embolism)
Electrophysiology	Arrhythmogenic right ventricular cardiomyopathy, Brugada syndrome, high-risk occupations, suspected intermittent bradycardia, syncope in patients with bundle branch block,[1] syncope preceded by palpitations suspicious for sinus tachycardia	Not recommended in patients without underlying heart disease; consider in high-risk patients with recurrent unexplained syncope
Exercise testing	Hemodynamic and ECG abnormalities with syncope during exercise, syncope reproduced with exercise, polymorphic ventricular tachycardia, prolonged QT interval, to precipitate a Mobitz type 2 second- or third-degree block during exercise[1]	Inadequate blood pressure increase in younger patients suggests hypertrophic cardiomyopathy or ischemia; similar findings in older persons may suggest autonomic dysfunction; may unmask ECG changes of channelopathies
Head-up tilt test	Neurally mediated syncope, recurrent unexplained falls, frequent syncopal episodes, psychiatric disease, to distinguish between neurally mediated and orthostatic hypotension syncope, to differentiate syncope with jerking movements from seizure[1]	Used in patients with negative initial findings, normal cardiac structure, and no evidence of ischemia; contraindicated in patients with ischemic heart disease, uncontrolled hypertension, left ventricular outflow tract obstruction, or aortic stenosis
Neurologic testing*	Suspected seizures, cerebrovascular event, neurodegenerative disorder, increased intracranial pressure	Seizure can be confirmed with electroencephalography; cranial imaging studies as clinically indicated; 20% to 30% of seizures with transient loss of consciousness could be the result of syncope; tonic-clonic limb movements and muscle twitching may occur in cardiac and neurally mediated syncope
Orthostatic blood pressure measurement	Neurally mediated syncope, postural tachycardia syndrome, orthostatic hypotension syncope[1]	Diagnostic if systolic blood pressure is less than 90 mm Hg or decreases by 20 mm Hg or more (10 mm Hg or more in symptomatic patients); increase of 30 beats per minute suggests postural tachycardia syndrome; up to 40% of asymptomatic adults older than 70 years and 23% of patients younger than 60 years will have positive orthostatic blood pressure measurements
Psychiatric evaluation	Suspected psychogenic pseudosyncope[1]	Consider with concurrent electroencephalography and video monitoring

ECG = electrocardiography.

*—Includes electroencephalography, computed tomography, magnetic resonance imaging, or carotid ultrasonography.

Information from references 1 and 11.

ORTHOSTATIC HYPOTENSION

Treatment of orthostatic hypotension includes education and lifestyle modifications, such as slowly transitioning from a supine or sitting position to standing and increasing fluid and sodium intake.[1] Contributing medications should be discontinued or decreased, if possible. Other treatment modalities include elevating the head of the bed by 10 degrees, compression stockings/abdominal binders, and counterpressure maneuvers.[1] If these do not mitigate symptoms, midodrine and fludrocortisone are effective treatments.[55]

CARDIAC SYNCOPE

Management of cardiac syncope is directed at the underlying etiology. Options include antiarrhythmic drugs, cardiac pacing, catheter-directed ablation, and, rarely, implantable cardioverter-defibrillator placement.[1]

This article updates previous articles on this topic by Gauer,[56] and by Miller and Kruse.[57]

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eTable A. Major Clinical Decision Rules for Syncope

Study	Population	Predictor variables	Outcome measured
Boston Syncope Rule, 2007 (short-term risk)	Derivation: a priori Validation: 362 ED patients with syncope	Signs of volume depletion Persistent abnormal vital signs in the ED Signs and symptoms of acute coronary syndrome Signs of conduction disease Worrisome cardiac history Family history of sudden death Primary central nervous system event Valvular heart disease (from history or physical examination)	Critical intervention or adverse outcome at 30 days
Canadian Syncope Risk Rule, 2016 (short-term risk)	Derivation: 4,030 ED patients with syncope Validation: pending	Predisposition to vasovagal syncope (prodrome/trigger) History of heart disease Systolic blood pressure < 90 mm Hg or > 180 mm Hg Elevated troponin level Abnormal QRS axis (< 30 or > 110 degrees) QRS duration > 130 milliseconds Corrected QT interval > 480 milliseconds ED diagnosis of vasovagal syncope ED diagnosis of cardiac syncope	Serious event at 30 days: death, arrhythmia, MI, PE, aortic dissection, CVA, or procedural intervention for syncope
EGSYS score, 2008 (short- and long-term risk)	Derivation: 260 ED patients with syncope Validation: 258 ED patients with syncope	Palpitations preceding syncope (4 points) Abnormal ECG findings* or history of heart disease (3 points) Syncope during effort (3 points) or when supine (2 points) Autonomic prodromes (–1 point) Precipitating and/or predisposing factors (–1 point)	Probability of cardiogenic syncope at two years
OESIL risk score, 2003 (long-term risk)	Derivation: 270 ED patients with syncope Validation: 328 ED patients with syncope	Abnormal ECG findings* Absence of prodromal syndrome Age > 65 years History of cardiac disease	Mortality at one year
ROSE study, 2010 (short-term risk)	Derivation: 550 ED patients with syncope Validation: 550 ED patients with syncope	Anemia (hemoglobin ≤ 9 g per dL [90 g per L]) Bradycardia (< 50 beats per minute) Brain natriuretic peptide ≥ 300 pg per mL (300 ng per L) Chest pain with syncope ECG showing Q waves (except in lead III) Oxygen saturation < 94% on room air Rectal examination showing occult blood (if gastrointestinal bleeding suspected)	Serious events at one month: death, acute MI, PE, CVA, arrhythmias, hemorrhage requiring transfusion of two or more units, subarachnoid hemorrhage, acute procedure, need for pacemaker in first month
San Francisco Syncope Rule, 2004 (short-term risk)	Derivation: 684 ED patients with syncope or near syncope Validation: 791 ED patients with syncope or near syncope	Abnormal ECG findings* Congestive heart failure Hematocrit < 30% Shortness of breath Systolic blood pressure < 90 mm Hg	Serious events at seven days: acute MI, PE, CVA, arrhythmias, subarachnoid hemorrhage, return ED visit, readmission

Information from: Colivicchi F, Ammirati F, Melina D, Guido V, Imperoli G, Santini M; OESIL (Osservatorio Epidemiologico sulla Sincope nel Lazio) Study Investigators. Development and prospective validation of a risk stratification system for patients with syncope in the emergency department: the OESIL risk score. *Eur Heart J.* 2003;24(9):811-819.

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Score results	Validation	Comments
Consider admission for one or more variables	Internal: 97% sensitivity, 62% specificity External: none	25 variables in eight categories make it less practical
Estimated risk of serious adverse event at 30 days	Pending	Largest prospective study, outcomes consistent with guidelines, clarifies abnormal ECG findings, pending validation to support use of rule
Consider admission for score of 3 or higher	Internal: 92% sensitivity, 69% specificity External: 56% sensitivity, 84% specificity	Mortality at two years was 2% in patients with scores < 3 and 21% for scores ≥ 3
Consider admission for one or more variables	Internal: 100% sensitivity, 22% specificity External: 95% sensitivity, 31% specificity	Positive variables: 0: 0% mortality 1: 0.6% mortality 2: 14% mortality 3: 29% mortality 4: 53% mortality
Consider admission for one or more variables	Internal: 87% sensitivity, 66% specificity One-year outcomes: 72% sensitivity, 71% specificity External: none	Not useful for predicting outcomes at one year; first study to use a biomarker in risk stratification
Consider admission for one or more variables	Internal: 98% sensitivity, 56% specificity External: 87% sensitivity, 52% specificity	First tool for short-term events (seven days); inconsistencies in validation scores, but the most studied decision tool

CVA = cerebrovascular accident; ECG = electrocardiography; ED = emergency department; EGSYS = Evaluation of Guidelines in Syncope Study; MI = myocardial infarction; OESIL = Osservatorio Epidemiologico sulla Sincope nel Lazio; PE = pulmonary embolism; ROSE = Risk Stratification of Syncope in the Emergency Department.

*—Abnormal ECG definitions varied with each study.