ANNALS OF INTERNAL MECINE

CLINICAL GUIDELINE: Diagnosing Syncope: Part 1: Value of History, Physical Examination, and Electrocardiography

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15 June 1997 | Volume 126 Issue 12 | Pages 989-996

Purpose: To review the literature on diagnostic testing in syncope and provide recommendations for a comprehensive, cost-effective approach to establishing its cause.

Data Sources: Studies were identified through a MEDLINE search (1980 to present) and a manual review of bibliographies of identified articles.

Study Selection: Papers were eligible if they addressed diagnostic testing in syncope or near syncope and reported results for at least 10 patients.

Data Extraction: The usefulness of tests was assessed by calculating diagnostic yield: the number of patients with diagnostically positive test results divided by the number of patients tested or, in the case of monitoring studies, the sum of true-positive and true-negative test results divided by the number of patients tested.

Data Synthesis: Despite the absence of a diagnostic gold standard and the paucity of data from randomized trials, several points emerge. First, history, physical examination, and electrocardiography are the core of the syncope workup (combined diagnostic yield, 50%). Second, neurologic testing is rarely helpful unless additional neurologic signs or symptoms are present (diagnostic yield of electroencephalography, computed tomography, and Doppler ultrasonography, 2% to 6%). Third, patients in whom heart disease is known or suspected or those with exertional syncope are at higher risk for adverse outcomes and should have cardiac testing, including echocardiography, stress testing, Holter monitoring, or intracardiac electrophysiologic studies, alone or in combination (diagnostic yields, 5% to 35%). Fourth, syncope in the elderly often results from polypharmacy and abnormal physiologic responses to daily events. Fifth, long-term loop electrocardiography (diagnostic yield, 25% to 35%) and tilt testing (diagnostic yield ≤60%) are most useful in patients with recurrent syncope in whom heart disease is not suspected. Sixth, psychiatric evaluation can detect mental disorders associated with syncope in up to 25% of cases. Seventh, hospitalization may be indicated for patients at high risk for cardiac syncope (those with an abnormal electrocardiogram, organic heart disease, chest pain, history of arrhythmia, age >70 years) or with acute neurologic signs.

Conclusions: Many tests for syncope have a low diagnostic yield. A careful history, physical examination, and electrocardiography will provide a diagnosis or determine whether diagnostic testing is necessary in most patients.

Syncope is a transient loss of consciousness that is accompanied by loss of postural tone. It is common [1] and can be dangerous [2], disabling [3], and difficult to diagnose [4]. Thousands of dollars can be spent evaluating a patient with syncope, only to result in a series of negative test results and a patient who continues to faint. Because the range of prognoses in syncope is wide, the physician's principal initial task is to distinguish between benign and life-threatening causes of syncope. We intend primarily to help clinicians maximize the diagnostic yield in the workup of syncope. Our secondary purpose is to summarize the literature that will aid clinicians in assessing risk to enable them to target hospitalization and invasive testing for the patient with syncope who is at high risk for an adverse outcome. The questions addressed by this two-part study are 1) Which diagnostic techniques are the most valuable for patients with syncope? 2) How can the clinical history help focus the workup for patients with syncope? and 3) When should patients with syncope be hospitalized?

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Methods

We used the MEDLINE database to identify articles related to syncope and diagnostic testing. References that evaluated the diagnostic test in near syncope and dizziness were included if they also used the test in patients with syncope. When a medical subject heading did not identify a sufficient number of references about a particular diagnostic test (such as neurovascular testing or carotid Doppler ultrasonography), keyword searches (using such terms as transcranial Doppler) were done. To be included in the review, articles had to be published in the English language between 1980 and 1995. The studies had to be randomized trials, observational studies, cohort studies, or case series of more than 10 patients (review articles and case reports were excluded); had to focus on or include patients with syncope; and had to examine only patients 18 years of age or older (except for tilt-Table studies, which often included adult and pediatric cases in the same articles).

Articles that were candidates for review were evaluated in detail by one of the authors. Articles that met the selection criteria were used to prepare summary tables or paragraphs. Comparisons between groups (for example, the proportion of patients with and without heart disease who had tachyarrhythmias diagnosed by electrophysiologic testing) were made using the Fisher exact test.

Selected national experts in cardiology and neurology were asked to review the findings in their area of expertise. The opinions of these experts were incorporated into the recommendations.

Limitations of the Literature on Syncope

In syncope, there is no diagnostic gold standard against which other diagnostic tests may be measured; thus, sensitivity and specificity may not be easily calculated. Moreover, the presence of a disease, such as coronary disease, in a patient who has fainted does not prove that the disease caused the syncope. Syncope is, at its core, a symptom and not a disease. Therefore, this review is not organized around a technology or a disease entity but focuses on the physiologic states that lead to a sudden, transient loss of consciousness.

The literature that discusses syncope predominantly comprises case series or cohort studies based on referrals to tertiary care centers. We classified studies into three types: population-based studies (including unselected patients from the general population who were hospitalized or seen in emergency departments and other outpatient settings), referral-based studies (including patients referred to specialized centers for syncope workups), and small case series. To our knowledge, no randomized trials of the diagnostic workup or management strategies for patients with syncope have been done. A summary of the types of studies conducted in patients with syncope (Table 1) shows that most have been referral studies or case series.

View this table: [in this window] [in a new window]	Table 1. **Sample Characteristics of Studies of Diagnostic Tests and Syncope**

Definitions

Organic Heart Disease

Whenever possible, our definition of organic heart disease included coronary artery disease, congestive heart failure, valvular heart disease, cardiomyopathy, and congenital heart disease. Because conduction system disease is a separate predictor of the need for special diagnostic testing, it was kept apart except where indicated. Patients who had a history and physical examination that were negative for cardiovascular symptoms or signs and a normal electrocardiogram were considered to have normal hearts; however, we recognize that some investigators think that echocardiography should be done before patients are declared free of organic heart disease.

Diagnostic Yield

For most tests, the diagnostic yield reflects the number of patients with positive diagnostic test results divided by the number of tested patients. For Holter and loop monitoring, the numerator includes the sum of the true-positive test results (arrhythmias during fainting) plus the true-negative test results (normal rhythm during symptoms). This expanded definition reflects the prognostic importance of a negative result on electrocardiography during syncope. For certain tests, the absolute value of the diagnostic yield may not be as important as the ability of the test to exclude a serious diagnosis (for example, intracardiac electrophysiologic studies may be of considerable benefit when they exclude ventricular tachycardia in a patient in whom that diagnosis was strongly considered).

Data Synthesis

Differential Diagnosis

The first category of syncope is neurally mediated syncope, which results from reflex mechanisms that are associated with inappropriate vasodilatation, bradycardia, or both (Table 2). This category includes vasovagal, vasodepressor, situational, and carotid sinus syncope. Neurocardiogenic mechanisms are also implicated in syncope associated with ventricular outflow obstruction (such as with aortic stenosis and pulmonary embolism) as well as supraventricular tachyarrhythmias [5-9]. The second category is orthostatic hypotension, which may result from age-related physiologic changes, volume depletion, medication, and autonomic insufficiency [10, 11]. Psychiatric disorders related to syncope (such as anxiety, depression, and conversion disorders) form a third category. The fourth category includes neurologic disorders, although these rarely cause syncope unless patients with seizures are included. Neurologic causes of syncope include transient ischemia (almost exclusively involving the vertebrobasilar territory), migraines (basilar artery), and seizures (atonic seizures, temporal lobe epilepsy, and unwitnessed grand mal seizures) [12].

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Table 2. **Causes of Syncope**

Cardiac causes of syncope include coronary disease, congenital and valvular heart disease, cardiomyopathy, arrhythmias, and conduction system disorders. Coronary disease, congestive heart failure, ventricular hypertrophy, and myocarditis may set the stage for arrhythmia and syncope. Exertional syncope results from heart disease characterized by a fixed cardiac output that does not increase with exercise. Exertional syncope may also reflect arrhythmic or neurocardiogenic disorders or an anomalous coronary

artery. Syncope may be the presenting symptom in elderly patients with acute myocardial infarction [13]; it rarely occurs with coronary artery spasm and aortic dissection.

We used five population-based studies of unselected patients to estimate the prevalence of various causes of syncope [14-18]; the summary of these studies is necessarily limited by the variability in diagnostic criteria. The most common causes of syncope were vasovagal episode, heart disease and arrhythmias, orthostatic hypotension, and seizures. The cause of syncope could not be determined in approximately 34% of patients. All of these studies were done several years ago, and the proportion of patients with unexplained syncope is probably lower now, given wider use of event monitoring, tilt testing, electrophysiologic studies, attention to psychiatric illnesses, and recognition that the cause of syncope in elderly patients may be multifactorial.

Approach to Syncope

The algorithm depicted in Figure 1 provides a diagnostic approach to syncope. It is intended to provide a framework for clinical judgment, not to replace it. Key points in the algorithm that will be discussed in the text include the following.

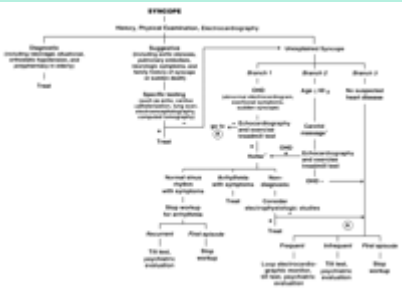

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Figure 1. **Algorithm for diagnosing syncope.** *Carotid massage can be performed in an office setting only in the absence of bruits, ventricular tachycardia, recent stroke, or recent myocardial infarction. Carotid hypersensitivity should be diagnosed only if clinical history is suggestive and massage is diagnostically positive (asystole ≥3 seconds, hypertension, or both). † May be replaced by inpatient telemetry if there is concern about serious arrhythmia. Echo = echocardiography; OHD = organic heart disease.

1. History, physical examination, and electrocardiography are the core of the workup for patients with syncope.

2. Carotid sinus massage may be useful in elderly patients but should not be done by the generalist if bruits are present, if the patient has a history of ventricular tachycardia, or in the setting of a recent stroke or myocardial infarction. A false-positive test result should be suspected if carotid massage is positive but the history does not suggest carotid hypersensitivity.

3. Special issues for elderly patients include the multifactorial nature of syncope, polypharmacy, use of carotid sinus massage, and cardiac testing (exercise stress test and echocardiography) to exclude cardiac disease.

4. Nondiagnostic arrhythmias found on Holter monitor readings should not usually be treated.

5. Intracardiac electrophysiologic studies are most useful in patients who have organic heart disease and otherwise unexplained syncope.

6. In a patient with exertional syncope, echocardiography should precede exercise stress testing.

7. The assessment of patients with a normal heart who have frequent episodes of syncope should include a loop recorder and psychiatric evaluation.

8. The workup of patients with a normal heart who have infrequent episodes of syncope should include a tilt test and psychiatric evaluation.

9. Neurologic testing, including electroencephalography, computed tomography, and carotid and transcranial Doppler ultrasonography, should be reserved for patients who have neurologic signs or symptoms or carotid bruits.

History and Physical Examination

Table 3, which includes data from six population-based studies, shows that the history and physical examination identify a potential cause of syncope in 45% of patients whose primary disorder can be diagnosed. Furthermore, organic cardiac diseases that cause syncope (such as aortic stenosis, idiopathic hypertrophic subaortic stenosis, or pulmonary embolism) and neurologic diseases (such as the subclavian steal syndrome) are frequently suspected on the basis of the history and physical examination. One study reported that suggestive findings on the history and physical examination were helpful in assigning a cause by directed testing in 8% of additional patients. History taking should focus on postural symptoms (orthostatic or vasovagal syncope), exertional symptoms or a positive family history (cardiac syncope, such as prolonged QT syndromes), palpitations (arrhythmia), postictal symptoms (neurologic syncope), situational symptoms (such as defecation and urination), use of medication, and history of organic heart disease (predisposing to arrhythmias or ischemia). A seizure without typical postictal symptoms may suggest an alternative cause, such as hypotension caused by arrhythmia or vasovagal syncope. A history taken from a family member or witness can be helpful.

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Table 3. **Causes of Syncope Found by History and Physical Examination or Electrocardiography**

Physical findings that are useful in diagnosing syncope include orthostatic hypotension, cardiovascular signs, and neurologic signs. Orthostatic hypotension is implicated in 8% of patients with syncope (range, 4% to 12%) [4, 14-19]. One study [20] found that 31% of patients with syncope had orthostasis (defined as a decline of 20 mm Hg in systolic blood pressure after standing). In 90% of patients, this was apparent within 2 minutes of standing up-right. Other important cardiovascular findings include differences in blood pressure in each arm or signs of aortic stenosis, idiopathic hypertrophic subaortic stenosis, pulmonary hypertension, myxomas, and aortic dissection.

Some patients with syncope have a history of concomitant dizziness (lightheadedness). In one study, a psychiatric cause for symptoms was implicated in many of these patients, especially those who had a history of vertigo (24% of patients with syncope and dizziness compared with 5% of patients with syncope alone [$P < 0.01$]) [21]. However, syncope and dizziness can also be a sign of cardiac arrhythmias. A thorough history and physical examination are thus mandatory [22] and should focus on cardiac, neurologic, and medication-related issues. In younger patients who have normal hearts, Holter monitors, loop monitors, or head-up tilt-Table testing can help determine whether symptoms are caused by a cardiac or vasovagal abnormality. Older patients may have more serious cardiac arrhythmias, orthostatic hypotension, or neurologic causes.

Medications frequently cause syncope, especially in elderly patients who are receiving several medications [23]. In a referral study of adverse drug reactions and syncope [23], antihypertensive and antidepressant agents were most commonly implicated. Other medications that are often associated with syncope include antianginal agents, analgesics, and central nervous system depressants. Blood levels of medication may be useful for diagnosis, but the most important ways to confirm medication-induced syncope are to document side effects of medication (such as bradycardia or orthostatic hypotension) that can lead to syncope or to discontinue the medication and follow the patient for remission of syncope. Concerns about medications that

might predispose patients to malignant arrhythmias (for example, concern about quinidine producing torsades de pointes) would mandate hospitalization. Ambulatory monitoring of blood pressure may document episodes of medication-induced orthostasis.

Although syncope may be relatively common in pregnancy, remarkably few researchers have attempted to assess its cause, natural history, and workup in this setting. Although we found more than 52 000 papers on pregnancy in a MEDLINE search of the literature published since 1980, only 7 articles focused on syncope. All of these were small case series involving seven or fewer patients. Aortocaval compression by an enlarged uterus, especially in the supine position, may lead to syncope in the third trimester [24]. Pregnant patients with known heart disease or arrhythmias, a pathologic murmur, exertional syncope, or palpitations with syncope clearly require further evaluation [25]. Further research is needed to help clinicians assess risk and the need for diagnostic evaluation in other pregnant women.

Electrocardiography at Baseline

An abnormal electrocardiogram is found in many patients with syncope. Common findings include bundle-branch block, previous myocardial infarction, and left ventricular hypertrophy [16]. It should be noted that most patients with these findings do not have an identifiable cardiac cause for syncope. Indeed, as shown in Table 3, causes of syncope were determined in only 5% of patients by electrocardiography, by rhythm strip done by paramedics, or in the emergency department [4, 14-18], primarily because of the transient nature of arrhythmias. The most common diagnoses included ventricular tachycardia; bradyarrhythmias; and, less commonly, acute myocardial infarction. Findings of first-degree heart block, bundle-branch block, and sinus bradycardia may predict a cause for syncope attributable to bradycardia, whereas previous myocardial infarction or pronounced left ventricular hypertrophy in hypertrophic cardiomyopathy may be associated with ventricular tachycardia.

Although the yield of electrocardiography is low (5%), the test is risk free and relatively inexpensive. Moreover, finding such abnormalities as bundle-branch block, previous myocardial infarction, and nonsustained ventricular tachycardia will guide further evaluation that may detect life-threatening disorders. Electrocardiography is therefore recommended in almost all patients with syncope.

Basic Laboratory Testing

Routine blood tests (blood count and tests for electrolytes, blood urea nitrogen concentration, creatinine concentration, and glucose level) rarely yield diagnostically useful information. In studies that included patients with seizures, 2% to 3% of patients had hypoglycemia, hyponatremia, hypocalcemia, or renal failure [4, 14-18]. Routine blood tests usually confirmed a clinical suspicion; in one study [14], only one unexpected finding was discovered (hyponatremia with seizures). Bleeding as a cause of syncope was usually diagnosed clinically.

Routine use of basic laboratory tests is not recommended; these tests should be done only if they are specifically suggested by the results of the history or physical examination. Pregnancy testing should be considered in women of child-bearing age, especially those for whom tilt-Table or electrophysiologic testing is being considered.

Patients with a Suggestive History

Patients with exertional syncope (in whom detection of serious cardiac disease requires echocardiography and stress testing), valvular heart disease, a history that suggests pulmonary emboli or pulmonary hypertension, neurologic signs or symptoms of syncope, or a positive family history of syncope or sudden death (prolonged QT syndromes) are included in the broad category of patients with a suggestive history. This category contains patients in whom the clinician strongly suspects a diagnosis after history, physical examination, and electrocardiography. Because many of the cardiac testing indications are discussed in part II of this paper, this section focuses on indications for neurologic testing.

Neurologic Testing

Neurologic tests used for patients with syncope include electroencephalography, brain imaging (computed tomography or magnetic resonance imaging), and neurovascular studies (carotid and transcranial oppler ultrasonographic studies). To determine which patients may benefit from neurologic testing, physicians should take a particularly careful neurologic history (for example, patients should be asked about a history of seizure activity, prolonged loss of consciousness, diplopia, headache, and postictal symptoms) and perform a thorough, focused physical examination (including a search for bruits or focal neurologic signs).

Electroencephalography

In the early 1980s, electroencephalography was one of the cornerstones of the workup for patients with syncope [26]. However, several studies [4, 15, 26-29] conclusively showed that electroencephalographic monitoring was of little use in unselected patients with syncope. In the absence of a history of seizure activity, electroencephalography has provided few diagnoses in more than 500 patients reported in the literature (Table 4). Eight of 534 patients were diagnosed using electroencephalography; 2 of these 8 patients had clinical data provided, and both had a history of seizures. Thus, electroencephalography is not recommended for patients with routine syncope and may only be beneficial in patients with a history of seizures.

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Table 4. **Diagnostic Results of Electroencephalography and Computed Tomography in Syncope***

Computed Tomography and Magnetic Resonance Imaging

No identifiable studies have specifically evaluated the use of brain imaging for patients with syncope. Early case series of such patients [4, 12, 14, 15, 27] (Table 4) found that computed tomography produced new information only in patients with focal neurologic signs. Of 195 patients who were studied, the average yield of computed tomography was 4%; all patients who had positive scans had a focal neurologic examination or a witnessed seizure. The diagnostic utility of magnetic resonance imaging in syncope has not been studied. Thus, computed tomography and magnetic resonance imaging should be avoided unless physical or historical features of central nervous system focality are present.

Neurovascular Studies

No single study has focused on the usefulness of transcranial Doppler ultrasonography for patients with syncope. The available studies [30-32] are insufficient to evaluate the usefulness of this test, perhaps because transient ischemic attacks involving the vertebral and basilar arteries rarely result in isolated syncope. Drop attacks (that is, sudden losses of postural tone without a clear-cut loss of consciousness) [33] can be vertebrobasilar in origin, but it is unclear whether transcranial Doppler ultrasonography can identify the cause of these events.

Anterior cerebral circulatory events rarely cause syncope. To create optimal conditions for an anterior circulatory event that could result in syncope, complete occlusion of one carotid artery and nearly complete occlusion of the other would have to occur. Few studies have evaluated carotid Doppler ultrasonography in certain neurologic conditions, including syncope, and no study has examined the usefulness of this test in syncope. One referral study found occlusive plaques in the carotid artery of 3 of 46 patients who had syncope after pacemaker implantation [32], but it is uncertain whether these plaques would have caused syncope. We know of no other studies that suggest that carotid Doppler ultrasonography is beneficial for patients with syncope, unless signs of cerebrovascular disease (such as previous strokes or bruits) are present.

Neurologic testing in syncope should be guided by the history and physical findings. Specifically, if evidence of seizure activity is present, electroencephalography may be useful. Focal neurologic signs mandate brain imaging, usually with computed tomography. Carotid or transcranial Doppler ultrasonography may be performed in the presence of bruits or when the history suggests vertebrobasilar insufficiency (for example, prolonged loss of consciousness, diplopia, nausea, or hemiparesis). Patients who have seizure activity, normal results on electroencephalography, and no postictal symptoms and patients with seizures who do not respond to anticonvulsant medications should be evaluated for possible cardiac syncope [34].

Appendix

The following are members of the Clinical Efficacy Assessment Subcommittee of the Health and Public Policy Committee of the American College of Physicians: George E. Thibault, MD, Chair, John R. Feussner, MD, Co-Chair, Anne-Marie J. Audet, MD; Gottlieb C. Friesinger Jr., MD; Daniel L. Kent, MD; Keith I. Marton, MD; Valerie Anne Palda, MD; John J. Whyte, MD; and Preston L. Winters, MD.

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Note: The Clinical Efficacy Assessment Project (CEAP) of the American College of Physicians is designed to evaluate and inform College members and others about the safety and efficacy of diagnostic and therapeutic methods.
Acknowledgments: The authors thank Dr. Edward L.C. Pritchett for comments on the cardiologic sections of the manuscript; Dr. Benjamin Eidelman for comments on the neurologic sections; Dr. David Katz for comments on an earlier version of the manuscript; Thomas Havighurst, MS, for statistical analysis; and Cindy Gilles for secretarial assistance.
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CLINICAL GUIDELINE: Diagnosing Syncope: Part 1: Value of History, Physical Examination, and ElectrocardiographyCLINICAL GUIDELINE: Diagnosing Syncope: Part 2: Unexplained Syncope

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1 July 1997 | Volume 127 Issue 1 | Pages 76-86**Purpose:** To review the literature on diagnostic testing in syncope that remains unexplained after initial clinical assessment.

Data Sources: MEDLINE search.

Study Selection: Published papers were selected if they addressed diagnostic testing in syncope, near syncope, or dizziness.

Data Extraction: Studies were identified as population studies, referral studies, or case series.

Data Synthesis: After a thorough history, physical examination, and electrocardiography, the cause of syncope remains undiagnosed in 50% of patients. In such patients, information may be derived from the results of carefully selected diagnostic tests, especially 1) electrophysiologic studies in patients with organic heart disease, 2) Holter monitoring or telemetry in patients known to have or suspected of having heart disease, 3) loop monitoring in patients with frequent events and normal hearts, 4) psychiatric evaluation in patients with frequent events and no injury, and 5) tilt-table testing in patients who have infrequent events or in whom vasovagal syncope is suspected. Hospitalization is indicated for high-risk patients, especially those with known heart disease and elderly patients.

Conclusions: A flexible, focused approach is required to diagnose syncope. Features of the initial history and physical examination help guide diagnostic testing.

In the first part of this two-part study [1], the differential diagnosis of syncope was examined with respect to the information provided by results of the history, physical examination, and electrocardiography; an algorithmic approach to the diagnosis of syncope was also introduced. A careful history and physical examination are mandatory in all patients with syncope because they are the keys to determining whether additional diagnostic testing is required. Electrocardiography is recommended for almost all patients with syncope, whereas specialized neurologic testing is suggested only in certain circumstances: for example, computed tomography for patients with focal neurologic signs, electroencephalography for patients with

seizure activity, or carotid or transcranial Doppler ultrasonography for patients with carotid bruits or a history of neurovascular symptoms. This paper addresses the workup of patients with syncope that is unexplained by the results of history, physical examination, or surface 12-lead electrocardiography.

Unexplained Syncope

Syncope that remains unexplained after initial clinical assessment is of considerable concern to the practicing clinician. The algorithm that we developed provides three branches for unexplained syncope: one for patients known to have or suspected of having heart disease, one for elderly patients, and one for patients not known to have or suspected of having heart disease (Figure 1).

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Figure 1. **Algorithm for diagnosing syncope.** * Carotid massage can be performed in an office setting only in the absence of bruits, a history of ventricular tachycardia, recent stroke, or recent myocardial infarction. Carotid hypersensitivity should be diagnosed only if clinical history is suggestive and massage is diagnostically positive (asystole ≥3 seconds, hypertension, or both). †May be replaced by inpatient telemetry if there is concern about serious arrhythmia. OHD = organic heart disease.

Branch 1: Unexplained Syncope with Clinical Organic Heart Disease or Abnormal Electrocardiogram

Organic heart disease is often known, discovered, or suspected in patients who have sudden or exertional syncope. Evaluation of patients known to have or suspected of having heart disease often begins with echocardiography or an exercise stress test to determine and quantify the degree of heart disease. If the results of these tests are negative, further cardiac testing can often be avoided. If the results are positive, however, subsequent testing may include Holter monitoring or telemetry, signal-averaged electrocardiography, and intracardiac electrophysiologic studies.

Echocardiography

No studies have been specifically designed to assess the usefulness of echocardiography in syncope. In patients known to have or suspected of having heart disease, patients suspected of having arrhythmias, or patients with abnormal electrocardiograms, echocardiography is an important initial step in diagnostic testing. Unsuspected findings on echocardiography are reported in only 5% to 10% of unselected patients [2]. This yield is similar to that of 12-lead electrocardiography, but echocardiography is 7 times more expensive. The cost-effectiveness of echocardiography in diagnosing the cause of syncope has yet to be determined.

Exercise Testing

Exercise stress testing can be used for the evaluation of exertional syncope to diagnose ischemia or exercise-induced tachyarrhythmias or to reproduce exercise-associated or postexertional syncope. In one population study of patients with syncope, the yield of the exercise stress test was less than 1% [3]. No data

are available to determine the yield for ischemia or exercise-induced tachyarrhythmias or to define the test's usefulness in diagnosing exercise-associated syncope. Tilt-table testing has been used to diagnose neurally mediated syncope, which may manifest as postexertional syncope [4, 5].

Exercise stress testing is recommended if patients have exercise-associated syncope and if the results of clinical evaluation suggest ischemic heart disease. In patients with exertional syncope, echocardiography should be done first to exclude hypertrophic cardiomyopathy.

24-Hour Holter Monitoring

We summarize the results of ambulatory monitoring in syncope by determining the presence or absence of arrhythmias in patients who develop symptoms during monitoring [6]. In studies that evaluated syncope or presyncope with 12 or more hours of monitoring and reported on symptoms, 4% of patients had correlation of symptoms with arrhythmias (Table 1) [7-14]. In about 15% of patients, symptoms were not associated with arrhythmias; this finding excluded rhythm disturbance as a cause for syncope in these patients (overall diagnostic yield in 8 studies, 4% + 15% = 19%). No symptoms occurred in approximately 79% of patients, but arrhythmias were found in 14% [7-14]. The causal relation between most of these arrhythmias and syncope is uncertain, although certain uncommon asymptomatic arrhythmias (prolonged sinus pauses, Mobitz type II block, and sustained ventricular tachycardia during sleep) usually prompt appropriate treatment. If no arrhythmias are found and no symptoms occur during monitoring, arrhythmic syncope is not necessarily excluded; this is because of the episodic nature of arrhythmias. In patients with a high pretest likelihood of arrhythmias (for example, patients who have brief loss of consciousness with short or absent prodrome, an abnormal electrocardiogram, or organic heart disease), further evaluation for arrhythmias should be pursued by event monitoring or electrophysiologic studies.

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Table 1. **Yield of Prolonged Electrocardiographic (Holter) Monitoring in Syncope**

Only one study evaluated the effect of duration of monitoring on diagnostic yield [7]. Extending monitoring to 72 hours increased the number of arrhythmias detected (14.7% on the first day, an additional 11.1% the second day, and an additional 4.2% the third day) but not the yield for arrhythmias associated with symptoms.

A 24-hour Holter monitor or inpatient telemetry is recommended when symptoms suggest arrhythmic syncope (brief loss of consciousness, no prodrome, palpitations with syncope) and in patients who have syncope of unexplained cause, heart disease, or an abnormal electrocardiogram. Loop monitoring may be a reasonable alternative in patients with recurrent syncope and a normal heart.

Intracardiac Electrophysiologic Studies

Although they are relatively safe in patients with syncope [15], electrophysiologic studies are expensive and invasive. Such studies are associated with low risks for pulmonary embolism, cardiac perforation, arteriovenous fistulae, and myocardial infarction (cumulative risk < 3%) [16]. Electrophysiologic studies use electric stimulation and monitoring to discover conduction abnormalities that predispose patients to bradyarrhythmias and to determine a patient's propensity for developing tachyarrhythmias (both ventricular and supraventricular). Most protocols for programmed stimulation include three extrastimuli at one or two ventricular sites. More aggressive protocols, including the use of isoproterenol, may increase the sensitivity but decrease the specificity of tests for detecting tachyarrhythmias.

The most important outcome of electrophysiologic testing is the diagnosis of ventricular tachycardia. Other potentially important diagnostic outcomes include supraventricular tachycardias and bradyarrhythmias.

Because only a few studies have used 24-hour Holter monitoring to confirm results of electrophysiologic studies [17, 18], the true diagnostic yield of this testing is generally unknown. Nevertheless, it is agreed that the results of an electrophysiologic test are considered positive if the test uncovers any of the following: 1) sustained monomorphic ventricular tachycardia [not including polymorphic ventricular tachycardia or ventricular fibrillation, which may be nonspecific responses], 2) a prolonged corrected sinus node recovery time longer than 1000 milliseconds, 3) markedly prolonged HV intervals longer than 90 milliseconds, 4) spontaneous or induced infra-Hisian block, and 5) supraventricular tachycardia with hypotension.

For the accompanying analysis, we used the above definitions wherever possible, excluding supraventricular tachycardias (which are relatively uncommon outcomes of electrophysiologic testing in syncope and can be diagnosed by other means). Our primary purpose was to classify study results to determine predictors of positive results on electrophysiologic studies. Key predictors that we assessed were presence of organic heart disease and brady-arrhythmic abnormalities (such as conduction-system disease) found on 12-lead electrocardiography.

Fourteen studies evaluating 1423 patients provided information on electrophysiologic outcomes but had insufficient detail to assess the importance of organic heart disease and baseline electrocardiography [19-32]. Heart disease was present in slightly more than half of the patients. Ventricular tachycardia was diagnosed in 14%, whereas a bradycardic outcome was observed in 21%. Because some patients (about 10%) had both tachycardic and bradycardic outcomes, the overall diagnostic yield in these studies (in which a high prevalence of patients had organic heart disease) was approximately 32% [14% ventricular tachycardia + 21% bradycardias –10% x (14 + 21)].

Table 2 summarizes eight additional studies in which the contribution of organic heart disease to a positive test result could be assessed [15, 17, 18, 33-37]. In these studies, 625 patients underwent electrophysiologic testing for syncope. Of the 406 patients with organic heart disease or an abnormal electrocardiogram, 21% had ventricular tachycardia and 34% had a bradycardia during the electrophysiologic study. Of the 219 patients with normal hearts, only 1% had ventricular tachycardia and 10% had a documented bradycardia ($P < 0.001$ for both comparisons). In these studies, approximately 14% of patients who could be given a diagnosis had both ventricular tachycardia and bradycardia. Thus, the diagnostic yield of electrophysiologic studies was almost 50% in patients with organic heart disease and about 10% in patients with a normal heart.

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Table 2. **Diagnostic Yield of Intracardiac Electrophysiologic Studies in Syncope: Importance of Organic Heart Disease***

These data are further elucidated by Table 3, which describes six referral studies of electrophysiologic testing in syncope [38-43]. In this table, the independent contributions of organic heart disease and electrocardiographic abnormalities are evaluated in predicting outcome. Most of the electrocardiographic abnormalities were evidence of serious conduction system disease (bundle-branch block, first-degree heart block, or sinus bradycardia). A few patients had nonspecific ST-segment and T-wave findings, left ventricular hypertrophy, or atrial and ventricular ectopy. Of 213 patients, 126 had organic heart disease; of the patients with organic heart disease, 19% had ventricular tachycardia and 17% had a bradycardia discovered during the electrophysiologic study. In the subgroup with conduction system abnormalities ($n = 36$), only 3% of patients had ventricular tachycardia but 19% received a diagnosis of bradycardia. Finally, of the 51 patients with normal hearts and normal electrocardiograms, 4% ($n = 2$) had ventricular tachycardia and 10% ($n = 5$) had bradycardia. None of the patients in these studies had multiple diagnoses. Although these differences are significant for ventricular tachycardia ($P < 0.005$), the differences in the prevalence of bradycardias among the three groups did not reach statistical significance ($P > 0.2$), perhaps because of small sample sizes.

View this table: [in this window] [in a new window]	Table 3. **Electrophysiologic Studies in Syncope: Importance of Electrocardiographic Abnormalities**

These data show that positive results on electrophysiologic examinations occur predominantly in patients who have organic heart disease. Evidence of bradycardia is more likely to be found on electrophysiologic testing in patients who have conduction disease on their electrocardiograms; however, the yield of electrophysiologic studies in detecting bradyarrhythmias is limited [23]. Most important is that meaningful abnormal outcomes are rarely discovered during electrophysiologic testing in patients with clinically normal hearts and normal electrocardiograms.

Patients who have clinically normal hearts and normal electrocardiograms should rarely undergo electrophysiologic testing. Patients with syncope and serious organic heart disease, especially those who have had myocardial infarctions or congestive heart failure [26, 29, 31], and patients with preexcitation should be hospitalized and should probably undergo electrophysiologic studies. Patients with clinically normal hearts in whom conduction system disease (for example, first-degree heart block, sinus pauses, or bundle-branch block) is found on electrocardiography or Holter monitoring can be studied electrophysiologically or by loop monitoring. Elderly patients with conduction disease who are at high risk for morbid events (such as hip fracture) during syncope may be better evaluated initially with electrophysiologic studies than with noninvasive testing. These recommendations are concordant with the recent guidelines by the American College of Cardiology/American Heart Association Task Force [44]. Patients suspected of having arrhythmic syncope should not drive during their evaluation.

Signal-Averaged Electrocardiography

Low-amplitude signals (late potentials) are detected by signal-averaged electrocardiography. Three referral studies [45-47] show that this test has a sensitivity of 73% to 89% and a specificity of 89% to 100% for the prediction of inducible ventricular tachycardia in patients with syncope. However, no studies of the usefulness of signal-averaged electrocardiography have been done in unselected patients with unexplained syncope. It is also unclear whether it is safe to avoid electrophysiologic studies in patients with negative signal-averaged electrocardiography results and significant organic heart disease (such as depressed left ventricular function or previous myocardial infarction) [48].

Signal-averaged electrocardiography may be useful in selecting patients for electrophysiologic studies when coronary disease is present and ventricular tachycardia is suspected. This role should be ascertained in prospective studies of unselected patients with syncope before the use of this test is routinely recommended.

Branch 2: Unexplained Syncope in Elderly Patients

Causes

Syncope in elderly persons is associated with many daily situations (situational syncope). Syncope in association with micturition, defecation, postural changes, and meals was found in 20% of institutionalized elderly patients (mean age, 87 years) [49-52]. Other provocative situations include coughing, laughing, and swallowing. Postprandial hypotension can result in syncope during or after a meal [53]. Orthostatic hypotension is also common in elderly persons, particularly when it is caused by medications that may result in symptoms even if standard therapeutic doses are administered. In a study that compared community-dwelling elderly persons (mean age, 71 years) with young persons (mean age, 39 years), arrhythmias were diagnosed in 28% of the elderly persons and only 13% of the young persons [54]. Several entities, including aortic stenosis, myocardial infarction, transient ischemic attack, and carotid sinus syncope, were primarily found in the elderly persons [54].

Diagnostic Testing

In one population study of syncope in elderly persons (mean age, 71 years), a history and physical examination led to 40% of the diagnoses that could be assigned [54]. Furthermore, a diagnosis was suggested in an additional 15% of patients according to the results of a history and physical examination and was confirmed by specific tests, such as echocardiography or cardiac catheterization. Electrocardiography led to a diagnosis in 9% of elderly patients and 4% of younger patients.

Five recent referral studies of carotid sinus massage in syncope [55-59] show that carotid massage has its greatest clinical utility in elderly patients (mean age, 60 to 81 years). The test appears to be safe if it is done in the office in patients who do not have carotid bruits, recent myocardial infarction, recent stroke, or a history of ventricular tachycardia (incidence of neurologic complications < 0.2%) [60]. Intravenous access during the maneuver is not necessary. Patients who have cardioinhibitory hypersensitivity of the carotid sinus (that is, asystolic arrest lasting ≥3 seconds) were effectively treated by the implantation of an artificial pacemaker. The yield in these studies of referral-based populations was remarkably high (average yield for positive carotid massage, 46%). However, because the positive predictive value of carotid massage remains undefined (and may decline with age), a clinician who finds a sensitive carotid sinus should still consider other prognostically important causes of syncope, depending on the nature of the episodes of syncope and the presence of comorbid conditions.

Arrhythmias were diagnosed by monitoring more frequently in elderly patients than in younger patients. In elderly patients, diagnosing heart disease may require such noninvasive diagnostic tests as stress tests or echocardiography. Referral studies of upright tilt-table testing in elderly patients with syncope (mean age ≥60 years) show positive responses to tilt in 54% of these patients (range, 26% to 90%) [61]. The rate of positive responses to tilt (number of positive test results divided by total number of patients tested) in elderly controls without syncope was 11% (range, 0% to 100%) [61].

In elderly patients, an inability to compensate for common situational stresses in the setting of several medical problems, medications, and physiologic impairments may combine to cause syncope [62]. If a single cause is not identified but many potential processes are found, management should be directed toward correcting these factors.

Branch 3: Unexplained Syncope in Patients Not Known To Have or Suspected of Having Heart Disease

In patients not known to have or suspected of having heart disease and syncope, primary diagnostic tests include long-term ambulatory loop electrocardiography, tilt-table testing, and psychiatric evaluation. Considerations in making the decision to perform Holter monitoring, loop monitoring, or tilt-table testing are presented in Table 4.

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Table 4. **Indications for 24-Hour Holter Monitoring, Long-Term Ambulatory Loop Electrocardiography, and Tilt-Table Testing**

Long-term Ambulatory Loop Electrocardiography

Loop electrocardiographic monitoring can be done for 30 days or more. A loop recorder is a type of event monitor. Whereas some event monitors may be carried in a pocket and applied to the chest at the moment symptoms occur, loop monitors use two chest electrocardiographic leads that are continuously worn and connected to a small (beeper-sized) monitor. The monitor constantly records and erases the cardiac rhythm.

Loop monitors can be activated after syncope by pressing a button that freezes in memory the previous 2 to 5 minutes and the subsequent 60 seconds of heart rhythm; the tracing can then be transmitted by telephone. Loop recorders are thus preferable to other types of event monitors because they can capture "retrospective" rhythm.

Three referral studies have evaluated loop monitoring in syncope, near syncope, dizziness, and palpitations [63-65]. The duration of monitoring ranged from 1 day to 4.5 months. True-positive test results (arrhythmia detected during syncope) were relatively frequent, occurring in 8% to 20% of patients. True negative results (normal cardiac rhythm during syncope) occurred in 12% to 27% of patients. The diagnostic yield (true-positive plus true-negative results) varied from 24% to 47%; the highest yield was seen in patients with palpitations.

Loop monitoring was most effective in patients with recurrent events (median number of events in two studies, 15 and 30 events/patient) [63, 64]. Because patients must comply with using the device (putting it on each morning, pushing a button after the episode of syncope, and transmitting the rhythm over the telephone), difficulties caused by human error limited diagnostic efficacy in as many as 32% of patients.

Loop recording is a noninvasive method of cardiac monitoring that requires a compliant patient. It is most beneficial in patients with frequent episodes of syncope. Loop monitoring is often deferred in favor of electrophysiologic studies in patients with serious organic heart disease who are at a high risk for fatal ventricular arrhythmias.

Head-up Tilt-Table Testing

In 25 studies of tilt-table testing in syncope, we assessed the most widely used procedures: passive tilt without pharmacologic stimulation [59, 66-73] and isoproterenol infusion after passive tilt [33, 58, 61, 74-85]. Studies that used other provocative or protective agents [86-88] were not reviewed because of limited data.

Methods. Most protocols for tilt-table testing use footboard support. During passive protocols and after baseline measurements of blood pressure and continuous monitoring of heart rate while patients are supine, patients are suddenly brought semiupright. Most studies used a tilt angle of 60 degrees. Fitzpatrick and colleagues [67] currently recommend that patients be kept in this position for 45 minutes; this period is two SDs from the mean time that is required to produce a positive response (approximately 24 minutes) [67].

All testing protocols that incorporate isoproterenol also include a passive phase of testing that usually lasts 10 to 15 minutes; in this phase, the patient is tilted upright without receiving intravenous medication. If an end point (syncope or hypotension) is not reached during tilting, the patient is brought to the supine position and isoproterenol infusion is started at 1 micro g/min. The patient is then retilted and isoproterenol infusion is continued. If an end point is still not reached, the patient is again brought to the supine position, the infusion rate is increased, and the patient is retilted. This procedure is continued with increasing doses of isoproterenol until a positive response or another end point (such as maximum dose, adverse effects, or development of severe tachycardia) is reached. The maximum dose of isoproterenol is 3 to 5 micro g/min.

Sensitivity and specificity. The sensitivity of tilt-table testing in two small referral-based studies of patients who had clinical vasovagal syncope was 67% to 83% [89, 90]. Specificity has been evaluated by performing upright tilt-table testing in patients without previous syncope. With passive tilt-table testing, specificity has ranged between 0% and 100%, although an overall rate is approximately 90% [61]. As protocols with longer duration are used and the dose of isoproterenol is increased, specificity declines. The overall specificity of upright tilt-table testing with isoproterenol is approximately 75% (range, 35% to 100%). The specificity was lowest when isoproterenol was used in young patients.

Positive responses in patients with unexplained syncope. In studies that used passive tilting, 49% of 425 patients (range, 26% to 90%) had a positive response to tilt-table testing. In 806 patients studied with isoproterenol, however, positive responses were seen in 62% (range, 39% to 87%). Approximately two thirds of the positive responses occurred during the isoproterenol phase. When either type of testing was used, approximately two thirds of the responses seemed to be cardioinhibitory; the rest were pure vasodepressor hypotensive reactions. Greater tilt angles and longer durations of testing were associated with a greater rate of positive responses.

On the basis of a recently published analysis of pooled data [61] and the data discussed above, passive upright tilt-table testing at 60 degrees for 45 minutes is recommended in patients with unexplained recurrent syncope in whom cardiac causes of syncope, including arrhythmias, have been excluded. In patients with negative results on a passive tilt-table test who have a high pretest probability of neurally mediated syncope (for example, young patients with a prodrome of nausea or warmth), tilt-table testing with isoproterenol is recommended. The test results should be considered positive only if a patient's typical symptoms are reproduced. Many laboratories suggest that women of childbearing age should have a pregnancy test and that men older than 45 years of age and women older than 55 years of age have stress testing before tilt-table testing. Positive test results would preclude tilt-table testing.

Psychiatric Evaluation

Aside from psychological issues that would predispose a patient to vasovagal syncope [91], psychiatric disorders as causes of syncope were previously considered to be uncommon [92-95]. In 1989, a high prevalence of psychiatric disorders (24%), especially anxiety and depressive disorders, was shown in a referral study of patients with syncope [96]. Syncope had been unexplained in many of the patients, and a large proportion of the patients who received treatment for their psychiatric disorder showed a marked diminution in syncope. More recently, a population-based study [97] showed a high prevalence of psychiatric disorders (35%) in unselected patients with syncope. The most common disorders were generalized anxiety disorder (8.6%), panic disorder (4.3%), and major depression (12.2%). Alcohol dependence was found in 9.2% of patients. Patients with psychiatric disorders were younger, generally did not have underlying heart disease, and had more frequent syncope. At a 1-year follow-up examination, patients with psychiatric illnesses were found to have a higher rate of recurrence of syncope than were those with other causes of syncope [97].

As Hackel and associates [69] and Grubb and colleagues [98] have shown, such psychiatric disorders as conversion disorders can be reproduced with a psychosomatic response to tilt-table testing (apparent syncope with normal vital signs). Thus, the manifestations of at least three types of psychiatric disorders, beyond the vasovagal response, can include syncope: anxiety, depression, and conversion disorders.

Two referral studies examined the usefulness of a hyperventilation maneuver in syncope [99, 100]. These studies showed a significant correlation between a positive maneuver (open-mouthed hyperventilation for 2 to 3 minutes, resulting in near syncope or true syncope) and psychiatric causes of syncope. This was particularly useful in young patients (positive predictive value, 59%) [100].

Psychiatric disorders as potential causes of syncope should be sought in young patients who faint frequently, patients in whom syncope does not cause injury, and patients who present with many symptoms (for example, nausea, lightheadedness, numbness, and fear or dread) [96, 97]. The hyperventilation maneuver and screening instruments for common mental disorders are recommended [101].

Miscellaneous Tests

Lung ventilation-perfusion scanning should be reserved for patients in whom pulmonary embolism is likely (for example, patients who have recently had surgery or patients who have syncope with dyspnea or chest pain, abnormal arterial blood gases, or signs of pulmonary hypertension on physical examination). However, the overall prevalence of pulmonary embolism as a cause of syncope is low. Glucose tolerance testing is rarely indicated [102] because hypoglycemia is an uncommon cause of syncope (prevalence < 1%).

Special Issues in Evaluating Patients with Syncope

Risk Stratification

Patients with syncope are admitted to the hospital primarily for observation and prevention of the consequences of a more serious subsequent episode or to rule out myocardial infarction or a new stroke. In

the United States, the degree of variation in rates of hospitalization for syncope is high [103]. Eagle and colleagues' early research on prognostic classification of patients who present to the emergency department with syncope [95] began to address the issue, but the conclusion was that patients with cardiac syncope (which could not always be diagnosed on presentation) were at the highest risk for dying within 1 to 6 months.

The situation is clearest for patients who are at risk for myocardial infarction or malignant arrhythmias. On the basis of data from six population-based series of patients with syncope who presented to emergency departments (Table 5), we suggest that patients with syncope be hospitalized if they have evidence of organic heart disease, chest pain, or a history of arrhythmias or if they take medications that are associated with malignant arrhythmias [54, 94, 95, 104-106]. In patients who have myocardial infarction presenting as syncope, the electrocardiogram is usually abnormal [105]. This was seen in a study of 251 patients with syncope who presented to emergency departments, 18 of whom had acute cardiac ischemia and an abnormal electrocardiogram (sensitivity of electrocardiography, 100%; lower limit of 95% CI, 78%). Trauma caused by syncope has not been uniformly shown to correlate with prognostic seriousness [95]. Patients with syncope and neurologic symptoms that suggest a transient ischemic attack or stroke should be hospitalized [104].

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Table 5. **Indications for Hospital Admission in Patients with Syncope***

Elderly patients are often hospitalized for syncope, especially when it is serious or of recent onset. Elderly patients with situational syncope (such as syncope with micturition) may not require hospitalization. Research in this area would be valuable. Patients should also be hospitalized if rare causes of syncope (such as pericardial tamponade or pulmonary embolism) that would be imminently dangerous are suspected.

Driving

The occurrence of syncope during driving could have serious consequences for the patient and other persons who might be harmed by the patient's vehicle. The physician and patient should carefully consider the risks when deciding whether the patient should continue to drive while syncope is being evaluated. State laws vary with respect to the physician's and the patient's responsibilities for reporting medical conditions that affect the ability to drive. Physicians should be aware of the pertinent laws in their own state.

Charges for Diagnostic Studies

Table 6 shows current charges for tests that are used to diagnose syncope. The most efficient test is the combination of history and physical examination. In elderly patients, carotid sinus massage is inexpensive but may be nonspecific. Twelve-lead electrocardiography is recommended for most patients with syncope. Loop electrocardiography and psychiatric evaluations are appropriate for patients who have normal hearts. Echocardiography may be useful in detecting occult cardiac abnormalities, but it is moderately expensive. Most of the other tests are comparatively expensive (>$400) and should be used only when specifically indicated.

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Table 6. **Summary of Charges for Diagnostic Tests in Syncope***

Future Research

To improve our knowledge of the efficacy of diagnostic tests in syncope, future studies should have strong study designs and should focus on such topics as implantable loop recorders [107], testing protocols that provide a rapid diagnosis, risk stratification, and the cost-effectiveness of echocardiography [108].

Conclusions

The prognosis in syncope ranges from benign to life endangering. Risk stratification should be based on the results of history, physical examination, electrocardiography, and selected noninvasive tests. Electrophysiologic studies should be reserved for high-risk patients who have organic heart disease. Patients at low risk who nonetheless have frequent episodes of syncope may have serious impairments in quality of life [109, 110]; an aggressive (although noninvasive) approach may be warranted in such patients. An individualized approach is required to diagnose syncope, but the core of the syncope workup remains a detailed history and physical examination.

Appendix

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Acknowledgments: The authors thank Dr. Edward L.C. Pritchett for his comments on the cardiologic sections of the manuscript; Dr. Benjamin Eidelman for his comments on the neurologic sections; Dr. David Katz for his comments on an earlier version of the manuscript; Thomas Havighurst, MS, for statistical analysis; and Cindy Gilles for secretarial assistance.
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