Syncope: Diagnosis and Evidence-Based Management

Case Study and Commentary, Shamai A. Grossman, MD, MS, and Rochelle Kohen, BS

Abstract

Syncope accounts for nearly 3% of all emergency department visits and 1% to 6% of all hospital admissions. Cardiac syncope patients have a mortality of 18% to 33%; mortality for those with noncardiac or unexplained syncope is 3% to 4%. In addition, cardiac syncope is an independent predictor of mortality when baseline cardiac conditions such as past congestive heart failure or myocardial infarction are taken into account. Determining the etiology of a syncopal event is frequently difficult. It has been estimated that 30% to 50% of all cases of syncope cannot be given a definable etiology even with extensive medical evaluation. Despite increasing emphasis on evidence-based medicine, efforts to reduce unnecessary and expensive medical testing, and concerns over the rapidly rising costs of medical care, syncope remains a frequent cause for medical admission and costly clinical workup, and more often than not a definitive diagnosis is not made. This article reviews the approach to diagnostic testing and management in the syncope patient.

INSTRUCTIONS

The following article, “Syncope: Diagnosis and Evidence-Based Management,” is a continuing medical education (CME) article. To earn credit, read the article and complete the CME evaluation form on page 46.

OBJECTIVES

After participating in the continuing education activity, primary care physicians should be able to:

1. Be familiar with the clinical presentation of syncope
2. Know the important elements in the history, physical examination, and workup of syncope patients
3. Identify common causes of syncope
4. Know the indications for hospital admission following a syncopal event

Syncope is common and often debilitating in patients of all ages. It accounts for nearly 3% of all emergency department (ED) visits and 1% to 6% of all hospital admissions nationwide [1]. Syncope results from a brief loss in generalized cerebral blood flow [2]. It is defined as a transient loss of consciousness producing a brief period of unresponsiveness and a loss of postural tone, ultimately resulting in spontaneous recovery requiring no resuscitation measures.

The causes of syncope range from the benign to the life-endangering. Thus, it is critical for clinicians to appropriately evaluate and diagnose patients who present with this symptom. Determining the etiology of a syncopal event, however, is frequently difficult. Often the initiating event is unwitnessed and not remembered by the patient, making it difficult to uncover the specific circumstances leading up to and occurring during the syncopal episode [3]. Syncopal events are often transient and may resolve independently, without recurrence. It has been estimated that in 30% to 50% of cases, the cause of syncope remains unexplained despite extensive medical evaluation [4].

CASE STUDY

Initial Presentation

A 28-year-old woman who was found unconscious at the bottom of an isolated stairwell in a local shopping mall is brought to the ED by emergency medical services (EMS). The patient, awake on EMS arrival, does not recall the duration of her loss of consciousness nor the occurrences preceding the event. EMS reports no signs of confusion or lethargy.
Physical Examination

Upon initial examination, the physician notes a blood pressure of 90/68 mm Hg, heart rate of 60 bpm, respiratory rate of 18 breaths/minute, temperature of 96°F, and the presence of anterior and lateral tongue lacerations. With the exception of the lacerations and borderline low blood pressure, the patient has no other signs of trauma. The ED physician notes no gross neurologic deficits.

- What are initial considerations in the patient with possible syncope?
- What factors support a diagnosis of syncope in this patient?

The initial task is to obtain vital signs and determine the need for immediate stabilization. The utility of orthostatic vital signs is controversial, but they are probably helpful in the elderly [5]. Measurement of blood pressure in both arms may be useful to help evaluate for aortic dissection. Most syncope patients are asymptomatic and have normal or near normal vital signs. These patients do not need to be stabilized but require a thorough history and physical examination.

Other diagnoses can mimic syncope (Table 1), and in approaching the syncope patient, one must first determine if the event falls within the definition of syncope. Seizures and stroke can cause loss of consciousness, but both can be distinguished from other etiologies of syncope by history and physical examination. Patients who have had a seizure often suffer from metabolic acidosis [6]. Seizures classically present with prodromal aura or “warning” symptoms and are typically followed by a postictal period in which the patient is often lethargic, agitated, and/or confused, with the patient slowly returning to full consciousness [7]. A loss of consciousness of greater than 5 minutes’ duration and rhythmic movements can be seen in both seizures and syncope but are far more common in patients who have had a seizure [7]. Stroke, if associated with loss of consciousness, will generally not be a self-limited event but would tend to be of extended duration with focal findings on neurologic examination [8].

Critical questions include the precipitating factor, such as pain or anxiety, postural or exertional symptoms, the situations in which episodes occur (e.g., after urination), associated neurologic symptoms, history of cardiac disease, history of psychiatric illness, medications being used, and a family history of sudden death [9].

Physical examination should include meticulous auscultation of the carotid arteries, heart, and lungs as well as careful palpation of the peripheral arteries. Evidence of trauma, such as lacerations from tongue biting or contusions and fractures, should be painstakingly noted.

In this patient, while the lateral tongue lacerations tend to support the existence of tonic-clonic seizures, anterior lacerations are generally the result of a fall from syncope [10]. The patient did not experience a prodrome nor were there focal findings on neurologic exam. In addition, the event was self-limiting and without postictal confusion or agitation. These aspects support a true syncopal episode.

Further History and Examination

The patient is otherwise healthy and not taking any regular medications. She is a long-distance runner but has been more easily tired of late and is no longer competing in races. She notes her last menstrual period was approximately 8 weeks prior, but she has a lengthy history of irregular menses. The patient denies intermittent vaginal bleeding, spotting, lower abdominal pain, and cramping. There was no clear precipitate or prodrome prior to the episode. There is no family history of sudden death or cardiac disease. The patient was told previously that her blood pressure is low. On further examination, the physician notes a systolic ejection murmur at the cardiac apex radiating to the carotid artery.

Electrocardiogram (ECG) demonstrates normal sinus rhythm with normal conduction intervals. A stool specimen is examined for the presence of blood and is negative. A fingerstick test for glucose is negative for hypoglycemia and the patient’s serum bicarbonate levels are normal. The results of a urine pregnancy test are positive.

- What are the causes of syncope?

The causes of syncope are varied, ranging from benign to life-threatening. Syncope can best be classified as cardiac or noncardiac in etiology (Table 2). Despite thorough evaluation, 30% to 50% of syncope cases seen in the ED are of unexplained etiology [4,11].

Noncardiac Causes

The most commonly identified etiology of syncope is vasovagal or neurocardiogenic syncope. Vasovagal syncope is characterized by a prodrome lasting more than 5 seconds [12,13]
and is associated with precipitating events or stresses [13,14]. Common stresses include unexpected pain, fear, unpleasant sight, sound or smell, and prolonged standing at attention. Situational syncope is also vagally mediated and is characterized by episodes occurring during or immediately after micturition, defecation, cough, or swallowing [15]. Carotid-sinus syncope is another variety of neurally mediated or vasovagal syncope.

Hypovolemia due to dehydration, medication, or hemorrhaging is another common cause of syncope [9]. A hypovolemic etiology of syncope is often manifested as orthostatic hypotension, which is defined as a decrease in systolic blood pressure of 20 mm Hg or greater or an increase in heart rate of 15 bpm within 2 minutes of standing. In contrast, general tachycardia or hypotension is nonspecific for hemodynamic instability or volume depletion. The presence of orthostatic hypotension can therefore aid in correctly attributing a syncopal episode to volume depletion, autonomic insufficiency, or medications. Orthostatic hypotension is commonly seen in patients who suffer from recurring episodes of syncope or lightheadedness and is a common finding in pregnancy. Orthostatic hypotension is present in up to 40% of asymptomatic patients older than 70 years and 23% of patients who are younger than 60 years [16].

Medications causing syncope include most antihypertensive and cardiovascular agents, such as diuretics and vasodilators. Drugs that prolong the QT interval are associated with life-threatening arrhythmias. The geriatric patient taking multiple medications is especially at risk for medication-induced syncope [17].

Generalized anxiety and panic disorders as well as major depression have been associated with vasovagal syncope [18]. Fainting is a known manifestation of somatization disorder [18].

**Cardiac Causes**

Cardiac syncope is characterized by an absent or brief prodrome (less than 5 seconds), palpitations, and brief loss of consciousness. Cardiac syncope often occurs while the patient is seated or reclining; however, neurologic syncope also may occur in the seated or reclined position [13].

Syncope of cardiac etiology can be classified into mechanical or obstructive causes and dysrhythmic or electrical causes. These range from aortic stenosis and cardiac tamponade to paroxysmal ventricular tachycardia and a conduction system disease. These types of underlying medical conditions are more easily diagnosed in the presence of associated respiratory or neurologic symptoms or chest pain. A patient with a history of cardiac disease will likely have a cardiac cause of syncope. A history of ventricular arrhythmia or congestive heart failure is predictive for an adverse outcome [2,7,11]. Patients who experience cardiac syncope and who also have poor left ventricular function have a higher risk of sudden death [19,20].

Syncope following exertion may indicate structural heart disease, such as with obstruction of left ventricular outflow due to fixed (aortic stenosis) or dynamic (hypertrophic cardiomyopathy) causes [21]. Young patients who present with syncope following exercise and who have a family history of syncope, sudden death, or arrhythmias should be scrupulously evaluated for a cardiac etiology [22]. Careful attention should be paid to prolonged QT intervals or evidence of hypertrophic cardiomyopathy [22].

**Table 2. Etiology of Syncope**

<table>
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<tr>
<th>Etiology of Syncope</th>
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<tr>
<td>Vasovagal/neurocardiogenic</td>
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<td>Hypovolemic</td>
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<td>Medication</td>
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<td>Hemorrhage</td>
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<td>Cardiac</td>
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<td>Dysrhythmic or electrical</td>
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<tr>
<td>Mechanical or obstructive</td>
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<td>Unexplained syncope</td>
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**Does diagnosis of syncope differ by age-group?**

In patients younger than 65 years, noncardiac causes make up approximately 40% of syncope cases, while 20% may be attributed to cardiac abnormalities. In those aged 65 years or older, cardiac causes comprise up to 40% of cases, while noncardiac causes comprise only 20% [23]. In general, syncope in children and adolescents is a benign event. However, syncope that occurs during exercise can be indicative of a potentially fatal condition [16,22]. In younger individuals, syncope is most often associated with a single, isolated disease process [24,25].

Women and individuals younger than 55 years of age are more likely to experience neurally mediated hypotension. These episodes often last longer than 5 seconds and occur while the person is standing or emotionally upset. Symptoms that accompany this form of syncope include palpitations, blurred vision, and nausea [15]. Frequently recurring syncope in young patients with no heart disease may be due to psychiatric disorders [18].

Syncope in elderly patients is more difficult to diagnose and is associated with a higher level of morbidity and mortality, particularly due to trauma associated with falls following
Table 3. Approach to Diagnostic Testing in Syncope

<table>
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<tr>
<th>Likely arrhythmic cause:</th>
<th>Consider electrophysiologic testing</th>
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<tbody>
<tr>
<td>Cardiac-associated chest pain or ECG signs of ischemia:</td>
<td>Serial cardiac enzymes</td>
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<td>Valvular disease by physical exam:</td>
<td>Echocardiography</td>
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<td>Possible cardiac etiology:</td>
<td>Holter or continuous-loop monitoring</td>
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<tr>
<td>Unexplained recurrent syncope:</td>
<td>Consider tilt-table testing</td>
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<tr>
<td>Unexplained syncope in patient older than age 40 years:</td>
<td>Carotid sinus massage</td>
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<tr>
<td>Women of childbearing age:</td>
<td>Pregnancy test</td>
</tr>
<tr>
<td>Possible neurologic etiology:</td>
<td>Head CT and EEG</td>
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<tr>
<td>Possible psychiatric etiology:</td>
<td>Psychiatric evaluation</td>
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CT = computed tomography; ECG = electrocardiogram; EEG = electroencephalogram.

• What diagnostic measures should be considered in evaluating the syncope patient?

The history and the physical examination identify a cause of syncope in 45% of patients [27]. While the diagnostic yield of an ECG in syncope is only 5% [7,26], a standard 12-lead ECG should be used for patients in whom there is a possibility of cardiac disease to help identify myocardial infarction or life-threatening dysrhythmias. Martin et al found that an abnormal ECG is a multivariate predictor for arrhythmia or death for 1 year following an episode of syncope [28]. An ECG may also aid in identifying prolonged QT intervals as the cause of the syncope [29].

In patients in whom a diagnosis cannot be made after history, physical examination, and ECG, targeted diagnostic testing should be undertaken (Table 3). In syncope, there is no gold standard against which the results of diagnostic tests can be measured. Hence, it remains difficult to ascertain sensitivity and specificity of these tests [27,30].

If the presence of a significant arrhythmia is suspected, prolonged cardiac monitoring of up to 72 hours may be warranted. This includes patients who are male, older than 65 years, have a history of heart disease, and have an abnormal rhythm on initial ECG. However, many arrhythmias discovered in a 24- to 72-hour window of monitoring are asymptomatic [31]. Holter monitoring in patients with syncope suggestive of a cardiac cause or in patients with unexplained syncope may demonstrate symptoms in conjunction with arrhythmias in 4% of patients and symptoms without arrhythmias in 17% [32]. In utilizing continuous-loop recorders in patients with frequently recurring syncope, arrhythmias were found during syncope in 8% to 20%, and normal rhythm was found during symptoms in 12% to 27% [33]. Implantable subcutaneous continuous-loop recorders may increase the yield slightly [34]. The diagnostic yield of longer-term monitoring is higher and thus its utilization is justified predicated on the clinical suspicion of an arrhythmia as the etiology of a syncopal event. Longer-term monitoring may also be of benefit in patients with recurrent syncope of unknown etiology.

History, physical examination, and ECG are often sufficient to identify the presence of heart disease [9]. Only when the presence or absence of underlying cardiac disease cannot be determined clinically is an echocardiogram helpful as echocardiograms rarely reveal unsuspected abnormalities and generally do not lead to the diagnosis of a cause [35].

The European Society of Cardiology recommends carotid sinus massage in patients older than 40 years with syncope of unknown etiology, and it also should be considered in patients with spontaneous symptoms suggestive of carotid sinus syncope, such as syncope while shaving or while turning the head [36]. However, in patients with a history of carotid artery disease, this maneuver should be avoided.

Passive upright tilt-table testing at 60 degrees for 45 minutes may be appropriate in patients with unexplained recurrent syncope in whom cardiac causes of syncope, including arrhythmias, have been excluded [30]. In patients with negative results on a passive tilt-table test who have a high pretest probability of neurally mediated syncope, such as 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 [30].

Electrophysiologic testing is indicated when initial evaluation suggests an arrhythmic cause of syncope, such as patients with abnormal ECG and/or structural heart disease, palpitations, or family history of sudden death [27,35]. Electrophysiologic testing may be helpful in guiding therapy in patients with syncope and a high-risk profession such as airline pilots [36]. Single-averaged ECG is not diagnostic of the cause of syncope but may be useful in selecting patients for electrophysiologic studies when coronary artery disease is present and ventricular tachycardia is suspected [30,36].
Further Testing and Diagnosis

Despite the positive pregnancy test, which may indicate a benign etiology of syncope, the ED physician decides to admit the patient based on a concern for valvular heart disease. The patient undergoes an echocardiogram, and the presence of a bicuspid aortic valve and mild aortic stenosis is noted. The patient is informed that the murmur is congenital and, given the current mild nature of her aortic stenosis, there is no immediate cause for concern. Nevertheless, she will need to be followed closely by a cardiologist for serial heart examinations and echocardiography. Additionally, the patient is told that the syncopal episode can be explained by increased demands of cardiac output due to her pregnancy. Physiologic changes during pregnancy affect hemodynamic balance controlled by blood volume and myocardial contractility and therefore may make the patient more prone to syncope [43].

- What are the outcomes of syncope patients?

Despite established guidelines on management of syncope, there is little available medical literature discussing short-term outcomes of syncope patients following discharge from the ED. Most literature has studied outcomes of patients at 6-month and 1-year intervals. However, one study determined 4 predictors of adverse outcomes at 72 hours. These factors include a history of ventricular arrhythmias, an abnormal ECG in the ED, age greater than 45 years, and a history of congestive heart failure [44]. In patients with none of these risk factors, there was no risk of cardiac mortality but a 0.7% risk of an arrhythmia [44].

Martin identified predictors of arrhythmias within 1 year of presentation of the syncope patient to the ED; these included age greater than 45 years, male sex, and nonwhite race [28]. In patients with 3 or more of these risk factors, there was at least a 57.6% risk of 1-year all-cause mortality or significant arrhythmia [28]. Other studies have shown that patients older than 60 years as well as patients of any age having a cardiovascular diagnosis have an increase in sudden death within 2 years [41].

The San Francisco Syncope Rule may be helpful as a means of predicting patients with serious outcomes at 1 week. Supporting data suggest that age greater than 75 years, an abnormal ECG, hematocrit less than 30, a complaint of shortness of breath, and a history of CHF are all significant risk factors for poor outcome at 1 week [45].

The 1-year mortality differs in patients with cardiac syncope versus noncardiac or unexplained syncope. Cardiac syncope patients have 18% to 33% mortality in contrast to 3% to 4% in noncardiac or unexplained syncope [25].

- Which patients with syncope should be admitted to the hospital?

The cost of care per hospital admission for syncope has been estimated at approximately $5300 per stay for a total cost of over $1 billion per year nationally [1,38]. Although in current practice there is a liberal policy toward hospital admission, no study proves that hospital admission improves outcome for patients with syncope of undetermined etiology [41]. The American College of Emergency Physicians recommends admitting syncope patients with any of the following [41]:

1. A history of congestive heart failure or ventricular arrhythmias
2. Associated chest pain or other symptoms compatible with acute coronary syndrome
3. Evidence of significant congestive heart failure or valvular heart disease on physical examination
4. ECG findings of ischemia, arrhythmia, prolonged QT interval, or bundle branch block

In addition, admission should be considered for patients who are older than 60 years, have a history of coronary heart disease or congenital heart disease, or have a family history of sudden death [41]. These recommendations have been tested and validated in a recent prospective trial [42].

Neurologic testing is useful only in patients who have focal neurologic findings or a history consistent with a seizure [27,36]. An electroencephalogram provides diagnostic information in less than 2% of cases of syncope [37]. Computed tomography scans of the head provide new diagnostic information in 4% of cases [38]. Psychiatric evaluation should be considered in patients with known psychiatric illness, no organic heart disease, and recurrent syncope [9].

Blood tests are commonly ordered but are often unnecessary since they do not yield diagnostically useful information [7,12,39]. In patients in whom seizure rather than syncope is suspected, serum glucose and bicarbonate levels may be helpful [6]. If blood loss is suspected, examination for the presence of blood in the stool may be more useful than checking hematocrit or hemoglobin since they may be normal in early stages of blood loss [40]. In addition, a pregnancy test should be considered in women of childbearing age who experience syncope. However, a physician should not mechanically interpret a pregnancy as the sole cause of a syncopal episode. Rather, a complete evaluation of the patient should be done to fully identify the etiology [41].
addition, cardiac syncope is an independent predictor of mortality when taking into account baseline cardiac conditions such as past congestive heart failure or myocardial infarction [38].

One prospective cohort study showed that patients older than 60 years and those with a cardiovascular diagnosis regardless of age had an increase in sudden death within 2 years. The study also found that the elderly were more likely to have severe trauma from falls related to syncope [25]. There have been additional studies that have correlated short-term mortality after a syncopal episode with advanced age [3,4]. Thirty percent of non-institutionalized elderly patients over age 75 years will experience a repeat syncopal episode within 2 years [38].

Summary

Despite increasing emphasis on evidence-based medicine, efforts to reduce unnecessary and expensive medical testing, and concerns over the rapidly rising costs of medical care, syncope remains a frequent cause for medical admission and expensive clinical workup. More often than not no definitive diagnosis or intervention is made. Further studies focusing on outcome of patients with syncope will be helpful in future management of these patients in the ED setting. Ultimately, the role of the physician in distinguishing potentially life-threatening causes of syncope from benign ones is crucial in assuring the well-being of these patients.

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<th>Statement</th>
<th>Strongly Agree</th>
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Additional comments:

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Part 2. Please complete the following sentence.

As a result of reading this case study, I . . .

☐ see no need to change my practice.
☐ will seek more information before modifying my practice.
☐ intend to change the following aspect(s) of my practice: (Briefly describe)

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Signature: ___________________________ Date: ___________________________

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