Critical Questions in Syncope: Risk Stratification in the Emergency Department

Case Study and Commentary, Matthew J. Reed

Abstract
• Objective: To review the management of syncope, with a focus on evaluation, diagnosis, and risk stratification in the emergency department (ED).
• Methods: Review of the literature and authoritative guidelines.
• Results: Syncope is a transient loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. A prolonged postictal phase is the best discriminator between a true syncopal event with an anoxic seizure and a likely neurological seizure. Sudden onset syncope without pre-warning symptoms may be indicative of syncope of cardiac origin and must be taken seriously. Initial ED evaluation with a detailed history, complete physical examination, and 12-lead ECG will suggest the cause of syncope in about 40% of patients. For these patients, management should focus on treating the underlying condition. For unstable patients in whom a diagnosis is unclear, the focus should be on resuscitation and further investigation. For stable patients in whom there is no obvious underlying cause, risk stratification should be done to assess whether the patient is at high risk of a serious cardiovascular event or death.
• Conclusion: In patients with syncope, it is important for the clinician to take a detailed history, perform a focused examination, and be aware of the potential pitfalls that may lead to failure to recognize a potentially fatal condition.

Syncope is a common presenting complaint to the emergency department (ED) [1], accounting for 750,000 ED visits per year in the United States (0.77% of all visits). It may be the main presenting feature of a significant life-threatening condition or secondary to a benign cause. Patients may have fully recovered and may appear well once in the ED, thus it is important to take a detailed history, perform a focused examination, and be aware of the potential pitfalls that may lead to failure to recognize a potentially fatal condition.

Case Study

Initial Presentation

A 64-year-old man, JS, presents to the ED with his wife via emergency ambulance. She describes talking to him while he was sitting at home on the sofa. He became unresponsive for 30 seconds and then had a 5-second generalised tonic-clonic seizure, regaining consciousness shortly afterwards and quickly becoming lucid.

• What is the initial approach to assessment in a patient presenting to the ED with syncope?

In a patient presenting to the ED with syncope, the initial evaluation should answer 3 key questions [2]:

1. Is it a syncope?
2. If so, is there an obvious diagnosis? If present, management should focus on treating this underlying condition.
3. If there is no obvious underlying condition, is the patient at high risk of a serious cardiovascular event or death?

• What is the definition of syncope?

Syncope is a transient loss of consciousness (TLOC) due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery [2]. The term transient loss of consciousness encompasses syncope as well as neurological seizure, and the distinction between the two is not always immediately apparent in the ED. Commonly, the term TLOC is used until the patient has had further investigations and a cause of the TLOC is identified (Figure 1).

From the Department of Emergency Medicine, Royal Infirmary of Edinburgh, Edinburgh, UK.
While confusion may be present immediately after true syncope, this should not last for more than several minutes [2]. A prolonged post-ictal phase is the best discriminator between a true syncopal event with an anoxic seizure and a likely neurological seizure (Table 1) [3]. Other discriminators such as tonic-clonic activity, incontinence, and tongue biting may help but do not in isolation rule out true syncope if a period of cerebral anoxia has occurred [4]. Seizure activity that is thought to be neurogenic should not be classified as syncope.

There are other syndromes that can mimic syncope such as neurological seizure, pre-syncope/lightheadedness, vertigo, disequilibrium, mechanical fall, and collapse query cause. Pre-syncope and lightheadedness are sensations of fainting and are not associated with loss of consciousness; vertigo is an illusion of motion that suggests a disturbance of the vestibular system, either central or peripheral in origin; disequilibrium is a sense of postural instability that is generally described as involving the legs and trunk without a sensation in the head; and collapse query cause usually results from generalized weakness from 1 or several underlying conditions, commonly in more elderly patients, and is not associated with loss of consciousness [5].

- What are the common causes of syncope that present to the ED?

The main 3 diagnostic categories for patients with syncope are (1) reflex/neurocardiogenic/vasovagal (vaso-depressor, cardio-inhibitory or mixed), (2) cardiac (either arrhythmic or structural), and (3) syncope secondary to orthostatic hypotension (either due to volume depletion, venous pooling, or autonomic failure from a variety of causes) [2]. Reflex syncope makes up
about 40% of cases, cardiac syncope 11%, orthostatic hypotension 25%, and the remaining 24% are unexplained [6].

**History**

In the ED, JS denies any pre-warning symptoms and has no recollection of the events that occurred. Following the episode, the first thing he can recall is the journey to hospital in the ambulance. He denies any chest pain, palpitations, or breathlessness prior to the collapse. He says that he suffers from mild hypertension and takes aspirin and bendroflumethazide. He denies any previous similar episodes.

- What aspects of the history are associated with a serious outcome?

Sudden onset syncope without pre-warning symptoms may be indicative of syncope of cardiac origin and must be taken seriously. A brief or absent pre-syncopeal period may be associated with syncope of a cardiac nature, especially an arrhythmia [7]. An average length of pre-syncopeal symptoms of 3 seconds has been reported [8]. Syncope associated with neurocardiogenic (vasovagal) syncope has been reported to last an average of 2½ minutes [2,7].

Most patients do not remember their syncopeal episode. Some patients can recall the event as it may terminate just prior to the loss of consciousness (“pre-syncope”). The presence of pre-syncopeal symptoms such as nausea, diaphoresis, dizziness and a feeling of warmth may suggest vasovagal syncope [7–9]. Precipitant factors (ie, micturition and coughing) may suggest situational syncope, and a positional aspect (ie, syncope precipitated by rising from a sitting position) may suggest orthostatic syncope. Other important symptoms prior to the syncopeal event include chest pain, sudden onset of headache or dyspnea, palpitations, back pain, or focal neurological deficits. The presence of any of these may suggest an alternative serious cause.

<table>
<thead>
<tr>
<th>Table 1. Historical Findings that Help Distinguish Seizure from Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seizure Likely</strong></td>
</tr>
<tr>
<td><strong>Symptoms before the event</strong></td>
</tr>
<tr>
<td>Aura (such as funny smell)</td>
</tr>
<tr>
<td>Nausea, vomiting, abdominal discomfort, feeling of cold, sweating (neurally mediated)</td>
</tr>
<tr>
<td>Lightheadedness, blurring of vision</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Symptoms after the event</strong></td>
</tr>
<tr>
<td>Prolonged confusion</td>
</tr>
<tr>
<td>Aching muscles</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Adapted from reference 7.
A witness history should be sought and a drug history taken to identify the use of antihypertensive or other cardiac medication or drugs that cause bradycardia or hypotension or prolong the QT interval (ie, erythromycin, quinine, and major tranquilizers). Nitrate use immediately prior to the syncopal episode is associated with glyceryl trinitrate syncope. A menstrual history should be taken in women of childbearing age, as syncope can be a presentation of ectopic pregnancy [10]. In addition, neurocardiogenic syncope is relatively common in early pregnancy. Some patients presenting with syncope may be under the influence of alcohol or recreational drugs, making history-taking difficult. While these substances may lead to collapse, syncope is unlikely to occur as a direct consequence of either alcohol or recreational drugs. These patients should be assessed at the time of presentation with a thorough examination and electrocardiogram (ECG); however, subsequent assessment of risk and additional investigations may need to wait until the patient is more compliant.

Finally, a family history of cardiac disease or sudden unexplained family death or history of syncope precipitated by exercise raise the possibility of hypertrophic cardiomyopathy, Brugada’s syndrome, or pre-excitation disorders such as congenital long QT syndrome and arrhythmogenic right ventricular dysplasia, which can be precipitated by a sympathetic surge.

### Physical Examination

On examination, JS’s vital signs are recorded as follows: heart rate 50, blood pressure 140/80 mm Hg, near patient capillary blood glucose 5.7 mmol/L, oxygen saturation on room air 97%, and respiratory rate 12. On detailed physical examination his chest is clear, his heart sounds are normal, and his apex is nondisplaced. He has no carotid bruits and has a jugular venous pressure just visible 1 cm above the clavicle. His abdomen is soft with no palpable masses, and he has a normal neurological examination.

### What is the approach to clinical examination?

The cardiovascular system should be specifically examined looking for a postural drop (a fall of 20 mm Hg or more, or a fall to < 90 mm Hg after standing for at least 3 minutes), a displaced apex, valve lesions, the presence of cardiac failure, carotid bruits, or a ventricular pause of greater than 3 seconds precipitated by carotid sinus massage. Carotid sinus massage should be examined for in patients over age 40 if the history is suggestive for carotid sinus hypersensitivity and once a carotid bruit has been excluded. This test is diagnostic for carotid sinus hypersensitivity and should be performed if syncope may have been precipitated by neck movements or pressure on the neck. It is important to first exclude the presence of a carotid bruit and to be aware of the risk of precipitating a prolonged sinus pause or an episode of hypotension. Patients should also have intravenous access and be in an area where resuscitation equipment is available if required.

### What key investigation should be performed in every syncopal or seizure patient?

A standard 12-lead ECG must be performed in every syncopal or seizure patient who presents to the ED. This initial ECG is normal in most patients with syncope [11–15]. The ECG may be diagnostic in only 2% to 6% of patients. Martin et al found that the presence of an abnormal ECG (defined as any abnormality of rhythm or conduction, ventricular hypertrophy, or evidence of prior myocardial infarction, but excluding nonspecific ST-segment and T-wave changes) was a multivariate predictor for arrhythmia or death within 1 year of syncope [16]. A further study showed that an abnormal ECG was a predictor for arrhythmic syncope [17]. Equally, a normal ECG is associated with negative electrophysiology studies and a low risk for syncope secondary to a cardiovascular cause. The ECG also allows assessment of the QT interval and may suggest disorders such as Wolff-Parkinson-White syndrome.

The current European Society of Cardiology syncope guidelines [2] document the ECG abnormalities that increase the risk of a syncope secondary to arrhythmia as:

- Bifascicular block
- QRS > 0.12 seconds
- Mobitz second-degree AV block
- Sinus bradycardia (< 50 bpm), sinoatrial block, sinus pause > 3 seconds
• Pre-excited QRS complexes

• Prolonged QT interval

• Signs of Brugada’s syndrome (right bundle branch block, ST segment elevation in leads V1–V3)

• Arrhythmogenic right ventricular dysplasia (epsilon wave or localised QRS > 110 msecs in V1–V3, or inverted T waves in V2 and V3 without right bundle branch block)

• Q-waves suggesting myocardial infarction.

It is suggested that patients with these abnormalities be admitted for monitoring and be investigated for arrhythmic syncope. There is no evidence that any of these findings is associated with an early adverse outcome and no studies have been powered to assess the prognostic value of individual ECG abnormalities. All patients considered at risk of having an arrhythmic cause for their syncope should be admitted for monitoring and be investigated with longer ECG assessment in the form of 24-hour tape monitoring and loop recording on either an inpatient or outpatient basis. These investigations have good sensitivity; however, patients suffering arrhythmias may not demonstrate abnormalities during the monitoring period. While arrhythmias demonstrated during routine ED monitoring are obviously diagnostic, more prolonged monitoring does not form part of the ED investigation. Echocardiogram should also be performed when there is known or suspected structural heart disease.

**Evaluation**

An ECG performed in the ED shows a sinus rhythm of 60 bpm with T wave inversion in lead III, but no other abnormalities.

**What laboratory tests would be useful?**

A urine β-HCG should be considered in all women of childbearing age to rule out an ectopic pregnancy. While complete blood count and urea and electrolyte estimation may seem reasonable investigations in syncope, except for hemoglobin or hematocrit, laboratory investigations and plain radiographs have not been shown to discriminate in the management of syncope and current guidelines do not recommend routine testing [2]. In one study of syncopal patients, 2 of 134 patients were found to be hypoglycemic, and one later diagnosed with diuretic-induced orthostatic hypotension was hyponatremic. Four in 134 patients with syncope secondary to gastrointestinal hemorrhage had an abnormal hematocrit that dropped with rehydration; however, on each occasion the diagnosis was suspected on clinical grounds [7].

In the absence of chest pain or ECG signs of acute myocardial infarction (AMI), patients do not require an AMI rule out. The routine measurement of cardiac markers in adult patients presenting to the ED with syncope has a diagnostic yield for AMI of less than 1% [18–21]. This may be higher in elderly patients, who are more likely to present with atypical symptoms of AMI such as syncope. Even in this group, the number of patients who do not have other features suggestive of AMI is small [19]. B-type natriuretic peptide (BNP), which is secreted in response to an increase in ventricular volume and pressure load, is known to be an excellent marker of prognosis in patients with heart failure or cardiac disease [22]. There is some evidence that it may be of use in syncope [23–25].

**Follow-up**

JS seems to have made a full recovery and the physician wonders whether it is safe to send him home. He is aware of some clinical decision rules that exist to risk stratify patients who present to the ED with syncope and wonders whether they may be helpful.

**What clinical decision rules are available for ED risk stratification?**

Initial ED evaluation with a detailed history, complete physical examination, and 12-lead ECG will suggest the cause of syncope in about 40% of patients. For these patients, management should focus on treating the underlying condition. This condition may be an unstable condition such as massive pulmonary embolus, requiring resuscitation and thrombolysis, or something more benign such as postural hypotension. For unstable patients in whom a diagnosis is unclear, the focus should be on resuscitation and further investigation. For stable patients in whom there is no obvious underlying cause, risk stratification should be done to assess whether the patient is at high risk of a serious cardiovascular event or death.

In 1983, Kapoor et al [13] published the first prospective risk stratification study of 204 syncopal patients. Mortality was 30% in the patients in whom a cardiovascular cause had been identified. More recently Soteriades et al [26] studied 7814 participants of the Framingham Heart Study. A cardiac cause for syncope, found in 9.5%, was associated with a 6-month mortality rate exceeding 10%. Colivicchi et al [27] performed a 6-center study that recruited 270 patients into a derivation study and 328 into a validation group. They de-
SYNCOPE

developed a risk score (OESIL score) based on 4 characteristics, with each factor scoring 1 point:

- Age > 65
- Clinical history of cardiovascular disease
- Syncope without prodromal symptoms
- Abnormal ECG

The authors found that 1-year mortality increased with increasing risk score [27].

There have been other risk scores derived for longer-term outcome such as the EGSYS score [28], which predicts risk of 2-year mortality based on the scoring of 6 characteristics of the clinical history. The EGSYS score can also be used to predict whether the syncope is of cardiac cause. Del Rosso et al assigned a score from + 4 to − 1 to the following factors that were found to be predictors: abnormal ECG and/or heart disease (+ 3), palpitations before syncope (+ 4), syncope during effort (+ 3) or in supine position (+ 2), autonomic pro-
dromes (− 1) and predisposing and/or precipitating factors (− 1). A score ≥ 3 identified cardiac syncope with a sensitivity of 95%/92% and a specificity of 61%/69% in the derivation and validation cohorts, respectively.

There are only 3 studies that have looked at shorter-term outcome, which is more relevant and amenable to intervention by the ED physician. Two of these are clinical decision rules and the other (STePS study) [29] looked at 676 subjects presenting to the ED with syncope who did not have a condition likely to require hospital admission. It found the following factors associated with poor short-term outcome:

- Abnormal ECG (atrial fibrillation/tachycardia, sinus pause > 2 seconds, sinus bradycardia, conduction disorders (bundle branch block, second-degree Mobitz I atioventricular block), signs of previous myocardial infarction or ventricular hypertrophy or multiple premature ventricular contractions).
- Concomitant trauma
- Absence of symptoms of impending syncope
- Male gender

Long-term poor outcomes occurred in 9.3% and included 40 deaths (6.0%). Long-term poor outcome was correlated with age > 65 years and a history of neoplasm, cerebrovascular disease, structural heart disease and ventricular arrhythmia [29].

The San Francisco Syncope Rule [30,31] uses 5 risk factors to predict 1-month outcome, suggesting admission if any 1 is present:

- Abnormal ECG
- Anemia (hematocrit < 30%)
- Shortness of breath
- Systolic hypotension (< 90 mm Hg)
- History of congestive cardiac failure.

The ROSE rule [23] utilizes 7 risk factors to predict 1-month outcome, also suggesting admission if any 1 is present:

- B-type natriuretic peptide ≥ 300 pg/mL
- Bradycardia ≤ 50 in ED or pre-hospital
- Rectal examination showing fecal occult blood (if suspicion of gastrointestinal bleed)
- Anemia (hemoglobin ≤ 90 g/L)
- Chest pain associated with syncope
- ECG showing Q wave (not in lead III)
- Oxygen saturation ≤ 94% on room air

The San Francisco Syncope Rule has not performed well in external validation and the ROSE rule has not yet been externally validated outside the environment in which it was derived, and therefore both should not yet be used routinely.

- What guidelines are available to aid in ED risk stratification of syncope?

The most commonly used guidelines [32] are those of the European Society of Cardiology [2], developed with the input of representatives from many different specialities and disciplines. The American College of Emergency Physicians (ACEP) guidelines [33], while similarly addressing questions of history, examination, and appropriate investigation, focus specifically on aspects of emergency medicine practice and suggest criteria for admission. According to the ACEP guidelines, patients with syncope and evidence of heart failure or structural heart disease should be admitted to the hospital, as should patients with
Case-Based Review

Syncopal events are often undiagnosed, and are classified as high-risk for adverse outcome. These factors are:

- Older age and associated comorbidities
- ECG abnormalities, including acute ischemia, dysrhythmias, or significant conduction abnormalities
- Hematocrit < 30
- History or presence of heart failure, coronary artery disease, or structural heart disease

It is unclear whether either the application of guidelines to syncope management, or the practice of admitting patients with syncope to hospital, has any impact on patient outcome. No such benefits have ever been demonstrated. Presently there is also no consensus as to which clinical decision rule should be used and none have gone through the entire process a clinical decision rule should do prior to recommendation for universal use. For this reason, our ED has produced a simplified ED-focused guideline to aid syncope admission decision-making; our guideline incorporates aspects of the ESC and ACEP guidelines and several clinical decision rules (Table 2).

### Table 2. Syncope Guideline of the Royal Infirmary of Edinburgh Based on the ESC [2] and ACEP Guidelines and Several Clinical Decision Rules [33]

<table>
<thead>
<tr>
<th>HIGH RISK (Admit)</th>
<th>MEDIUM RISK (Consider discharge with early outpatient review)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History findings</strong></td>
<td><strong>History findings</strong></td>
</tr>
<tr>
<td>Palpitations related to syncope</td>
<td>Age &gt; 60 yr</td>
</tr>
<tr>
<td>Associated chest pain</td>
<td>No prodromal symptoms</td>
</tr>
<tr>
<td>Associated headache</td>
<td>Previous myocardial infarct</td>
</tr>
<tr>
<td>Related to exertion</td>
<td>Known history of valvular heart disease</td>
</tr>
<tr>
<td>Family history of sudden death age &lt; 60 yr</td>
<td>Known angina / coronary artery disease</td>
</tr>
<tr>
<td>Previous history of VT/VF/cardiac arrest</td>
<td>Known history of congestive cardiac failure</td>
</tr>
<tr>
<td><strong>Examination findings</strong></td>
<td><strong>Examination findings</strong></td>
</tr>
<tr>
<td>Systolic heart murmur heard</td>
<td>&gt; 20 mm Hg drop on standing</td>
</tr>
<tr>
<td>Signs of heart failure present</td>
<td>Diastolic heart murmur heard</td>
</tr>
<tr>
<td>Systolic BP &lt; 90 mm Hg</td>
<td>Ventricular pause &gt; 3 seconds on carotid sinus massage</td>
</tr>
<tr>
<td>Suspicion of pulmonary embolism</td>
<td>Trauma associated with collapse</td>
</tr>
<tr>
<td>AAA detected</td>
<td><strong>ECG findings</strong></td>
</tr>
<tr>
<td>New neurological signs on examination</td>
<td>Right bundle branch block</td>
</tr>
<tr>
<td>Suspicion of CVA or SAH</td>
<td>QRS duration &gt; 120 msecs</td>
</tr>
<tr>
<td>FOB present on PR exam</td>
<td>OLD T wave / ST segment changes</td>
</tr>
<tr>
<td>Other suspicions of GI bleed</td>
<td>Frequent pre-excited QRC complexes</td>
</tr>
<tr>
<td><strong>ECG findings</strong></td>
<td>Q-waves unchanged from old ECG</td>
</tr>
<tr>
<td>Mobitz type II heart block</td>
<td>Atrial fibrillation or flutter</td>
</tr>
<tr>
<td>Wenckebach’s type II heart block</td>
<td>PR &gt; 200 msecs (1st degree heart block)</td>
</tr>
<tr>
<td>Bilascicular block</td>
<td><strong>LOW RISK (Consider discharge)</strong></td>
</tr>
<tr>
<td>Complete heart block</td>
<td>None of the above characteristics</td>
</tr>
<tr>
<td>Sinus pause &gt; 3 seconds</td>
<td><strong>Sinus pause &gt; 3 seconds</strong></td>
</tr>
<tr>
<td>NEW ST elevation</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>Sinus bradycardia &lt; 50</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>Sino-atrial block</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>QTc &gt; 450 msecs</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>NEW T wave / ST segment changes</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>Brugadas (ST segment elevation V1–V3)</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
<tr>
<td>Arrhythmogenic right ventricular dysplasia</td>
<td><strong>NEW ST elevation</strong></td>
</tr>
</tbody>
</table>
Case Conclusion

According to the European Society of Cardiology guidelines, JS is not at high risk; however, he has some moderate risk factors on account of the lack of pre-warning symptoms and his age. He may be suitable for discharge with outpatient follow-up. While this is being arranged, JS has a second episode of syncope. He was being monitored at the time, and an ECG showing a 10-second period of asystole with some preserved P wave activity was recorded during the episode (Figure 2). He is transferred to the coronary care unit where a temporary pacing wire is placed prior to a formal definitive implantable pacemaker. He is discharged home 2 days after his initial presentation.

Figure 2. JS’s ECG showing a 10-second period of asystole with some preserved P wave activity.

References


Corresponding author: Matthew J. Reed, Dept. of Emergency Medicine, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, UK, matthew.reed@luht.scot.nhs.uk.

Financial disclosures: None