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Review

Syncope: Classification and risk stratification

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ABSTRACT

Background: Syncope is one of the most common reasons for emergency department and urgent care clinic visits. The management of syncope continues to be a challenging problem for front-line providers inasmuch as there are a multitude of possible causes for syncope ranging from relatively benign conditions to potentially life-threatening ones. In any event, it is important to identify those syncope patients who are at immediate risk of life-threatening events; these individuals require prompt hospitalization and thorough evaluation. Conversely, it is equally important to avoid unnecessary hospitalization of low-risk patients since unneeded hospital care adds to the healthcare cost burden.

Results: Historically, front-line providers have taken a conservative approach with admission rates as high as 30–50% among syncope patients. A number of studies evaluating both the short- and long-term risk of adverse events in patients with syncope have focused on development of risk-stratification guidelines to assist providers in making a confident and well-informed choice between hospitalization and out-patient referral. In this regard, a much needed consensus on optimal decision-making process has not been developed to date. However, knowledge from various available risk-stratification studies can be helpful.

Conclusion: This review summarizes the findings of various risk-stratification studies and points out key differences between them. While, the existing risk-stratification methods cannot replace critical assessment by an experienced physician, they do provide valuable guidance. In addition, the various risk-assessment schemes highlight the need for careful initial clinical assessment of syncope patients, selective testing, and being mindful of the short- and long-term risks.

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Introduction

Syncope is a syndrome characterized by a transient self-limited episode of loss of consciousness occurring as a result of a brief interruption of oxygen supply to the brain. This interruption of cerebral nutrient flow in a syncopal event is almost always due to transient cessation of blood flow [1,2]. A transient reversible drop in systemic arterial blood pressure to a level below that needed to sustain cerebral perfusion is the most common cause of syncope. Other possibilities are rare, and include acute hypoxemia (e.g. aircraft decompression) or major metabolic disturbance affecting neuronal pathways.

Since transient global cerebral hypoperfusion is the sine qua non of syncope pathophysiology, other causes of loss of consciousness should not be classified as 'syncope'. Thus seizures, concussions, hypoglycemia, and other non-perfusion related disturbances are separate diagnostic issues; these are non-syncope causes of transient loss of consciousness (TLOC) [1,3].

In true syncope, the episode is characterized by a rapid onset of loss of consciousness with or without any warning symptoms. Even when warning symptoms are present before syncope, loss of consciousness usually occurs within 10–20 s of their onset. Recovery is typically prompt and complete without any need for medical intervention and without any new residual neurologic findings.

Classification of syncope

The classification of syncope is mainly based on the underlying mechanisms that lead to the final event of transient global hypoperfusion. The diagnostic classification of the causes of syncope modified from the European Society of Cardiology (ESC) syncope practice guidelines [1] is summarized in Table 1.

Table 1
The diagnostic classification of the causes of syncope modified from the European Society of Cardiology syncope practice guidelines.

Reflex (neurally-mediated) syncope
- Vasovagal:
  - triggered by emotional distress
  - triggered by orthostatic stress
- Situational:
  - cough, sneeze
  - gastrointestinal stimulation
  - micturition
  - others
- Carotid sinus syncope

Orthostatic hypotension syncope
- Volume depletion:
  - inadequate fluid intake (hot weather), diarrhea, vomiting, etc.
- Drug-induced orthostatic hypotension:
  - alcohol, vasodilators, diuretics, beta-adrenergic blockers
- Primary autonomic failure:
  - pure autonomic failure, multiple system atrophy, Parkinson's disease with autonomic failure, Lewy body dementia
- Secondary autonomic failure:
  - diabetes, amyloidosis, spinal cord injuries

Cardiac syncope (cardiovascular)
- Arrhythmia as primary cause:
  - Bradycardia:
    - sinus node dysfunction, atrioventricular conduction system disease
    - implanted device malfunction
  - Tachycardia:
    - supraventricular including atrial fibrillation
    - ventricular (idiopathic secondary to structural heart disease, or due to channelopathies)
- Structural disease:
  - Cardiac: cardiac valvular disease, acute myocardial infarction/ischemia, hypertrophic cardiomyopathy, cardiac masses (atrial myxoma, tumors, etc.), pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valves dysfunction
  - Other cardiovascular: pulmonary embolus/hypertension, acute aortic dissection

Neurally-mediated syncope (also termed neural reflex syncope)

This type of syncope includes a number of conditions. The most important and also the most common within this category is vasovagal syncope. The second most common is carotid sinus syncope (CSS) which mostly occurs in the elderly and primarily in men [3–6]. Carotid sinus hypersensitivity (CSH) is a clinical finding elicited by massaging the carotid sinus. CSH should be distinguished from CSS as the former is a clinical finding and the latter is a clinical manifestation. CSS is only diagnosed if carotid massage causes sufficient bradycardia (usually >6 s) and/or hypotension to cause reproduction of the patients' symptoms.

Situational syncope is a third category of reflex faint; it includes syncope triggered by any of a number of activities such as: micturition, defecation, coughing, or swallowing. The initial event (e.g. micturition) triggers [1,3] either a slow heart rate or depressed vascular tone (or both) that results in sufficient hypotension to cause transient cerebral hypoperfusion and ultimate transient self-limited episode of loss of consciousness. In some cases (e.g. cough syncope, trumpet-blowers syncope), transient venous obstruction due to increased intra-thoracic pressure may contribute to cerebral hypoperfusion.

Orthostatic hypotension

Orthostatic syncope occurs as result of the body's inability to maintain blood pressure adequate for cerebral perfusion when the individual moves to the upright posture, and which in turn results in TLOC [1,7,8]. The change in posture from lying down to an upright position results in shift of as much as 500–1000 mL of blood away from the chest to venous capacitance system below the diaphragm; this shift in turn results in diminished venous return to heart and consequent reduction of cardiac filling pressure and stroke volume leading to hypotension and cerebral hypoperfusion.

The human body has physiological defenses against orthostatic hypotensive episodes. These include a reflex increase in heart rate, reflex arterial and venous vasoconstriction (especially in the splanchnic bed and lower extremities), and neuroendocrine adjustments (activation of renin–angiotensin–aldosterone system) [7]. All of these defenses prevent healthy individuals from having a syncopal event. However, in certain situations these defenses could be undermined. For example, superimposed volume depletion or loss of impaired cardiac response due to chronotropic incompetence, or impaired reflex vasoconstriction due to autonomic dysfunction or medications (e.g. beta-blockers, etc.), or loss of skeletal muscle tone which is common in the elderly, may cause reduced venous return. The individual as a result of syncope will slump to gravitationally neutral position which usually results in prompt resumption of cerebral perfusion. Physical counter pressure maneuvers such as leg-crossing and muscle straining have been found to be helpful in increasing venous return by enhancing muscle pump activity [1].

Syncope due to cardiac arrhythmias

Cerebral hypoperfusion resulting in syncope can occur due to either brady- or tachy-arrhythmias. Bradycardia is the more common; in this category, symptomatic hypotension can occur as a result of sinus pauses, high-grade atrioventricular block or asystole that occurs at the termination of an atrial arrhythmia (particularly at the end of an episode of atrial fibrillation). Cardiac pacemaker placement is helpful in preventing these bradycardiac episodes.

Both supraventricular and ventricular tachyarrhythmias may be responsible for triggering syncope. Neurally-mediated hypotension may also contribute in these patients. Patients with autonomic dysfunction are at greatest risk for arrhythmia-related syncope since protective reflexes that are supposed to be in effect to counter the tachycardic stress are absent or are too sluggish.

The occurrence of syncope due to ventricular tachyarrhythmias in patients with poor left ventricular function or due to channelopathy (i.e. long QT syndrome, catecholaminergic paroxysmal ventricular tachycardia, Brugada syndrome) is predictive of increased risk of mortality due to sudden cardiac death [9]. Therefore, these patients when identified need to be promptly referred to cardiac electrophysiology for further evaluation; most will warrant placement of an implantable cardioverter defibrillator (ICD) and some may be candidates for mapping and ablation therapy.

Syncope due to structural cardiac disease

Although infrequent, syncope can occur as a result of acute myocardial infarction or pulmonary embolism. Reduced stroke volume is the underlying mechanism for cerebral hypoperfusion in these cases, although neural-reflex factors may contribute, especially in the case of acute myocardial ischemia. Valvular/structural heart disease (e.g. severe aortic stenosis, severe mitral stenosis, and large left atrial myxoma) can cause syncope. The cerebral hypoperfusion in these situations is often a result of the direct hemodynamic impact of an anatomical anomaly as well as neurally-mediated reflexes or lack of them. In patients with severe aortic stenosis, inappropriate vasodilatation with exertion is an accepted basis for symptomatic hypotension resulting in syncope [10].

Syncope secondary to cerebrovascular causes

The brain is well protected with multiple blood vessels feeding the Circle of Willis and therefore true syncope almost never occurs as a direct result of cerebrovascular disease alone. However, although rare, a transient ischemic attack in the vertebrobasilar distribution may cause syncope. The presence of posterior circulation symptoms such as loss of balance and vertigo makes these events distinguishable from other causes of syncope.

Steal syndrome associated with subclavian stenosis is another rare condition that can result in symptoms of syncope, dizziness, vertigo, or nystagmus especially with vigorous use of ipsilateral arm muscles. Syncope as a solitary manifestation of this condition is extremely rare [11].

Syncope mimics

TLOC can occur in a variety of situations such as seizures, concussions, or intoxication. However, as noted earlier, these are not true syncopal events as the basis is not cerebral hypoperfusion. They are being mentioned here due to the diagnostic confusion that they may cause.

Psychogenic pseudosyncope (often termed pseudoseizure by neurologists especially if jerky muscle movements accompany the collapse) is the most common condition in the syncope mimics category. It may be difficult to distinguish these 'pseudo' episodes from true syncope. However, pseudosyncope/pseudoseizures most often will occur several times a day which almost never happens in the case of true syncope. Tilt-table testing may be helpful not only in identifying these patients, but also may permit discussing the diagnosis frankly with these patients [12].

TLOC can also occur in cases of cataplexy and certain types of akinetic or minimally kinetic seizures [13]. In elderly people, accidental falls may cause TLOC due to concussion. The diagnostic confusion caused by the above-mentioned conditions can be cleared by careful attention to history taking, but an experienced clinician is usually essential. When uncertainty persists, the placement of external or implantable loop recorders may be helpful to distinguish these conditions from true syncope.

Risk stratification of syncope

Syncope is a challenging symptom for the first contact provider [usually an emergency department (ED) or urgent care physician] to deal with. First, the patient has usually recovered, so there are no clear physical findings to suggest a cause. Second, there are so many possible causes to consider. Third, the patient or witnesses (if any) may have been so surprised by the unexpected event, that detailed historical findings are not clearly recollected. Finally, the time available in an ED to undertake a detailed assessment is limited.

Syncope is not typically a life-threatening condition by itself (although the underlying cause may be). However, syncope may result in untoward consequences such as physical injury and diminished quality of life. Syncope may also be an indicator of potentially life-threatening underlying conditions; for instance, severe structural heart disease with consequent malignant arrhythmias and heart failure.

A confident diagnosis of the cause of a syncope event may or may not be made in ED or clinic. In cases where the cause of TLOC is established with certainty during initial evaluation, the subsequent course of action is clear. However, more often the diagnosis is unclear and the responsible providers are faced with the dilemma of choosing between immediate hospitalization versus timely outpatient evaluation. Physicians historically have favored a conservative course of action resulting in many more patients being admitted to hospital than is warranted.

The ESC Syncope Task Force provided guidelines for front-line providers to use for assessing patients presenting with TLOC/collapse/syncope and thereby arrive at a decision between inpatient versus outpatient evaluation.

Fig. 1 provides an overview of an approach to assessment of a patient who presents with TLOC/collapse based on the ESC Syncope Task Force Guidelines [1].

At the present time, despite tutoring the physicians in ESC guidelines, high admission rates appear to persist (as high as 30–50% per

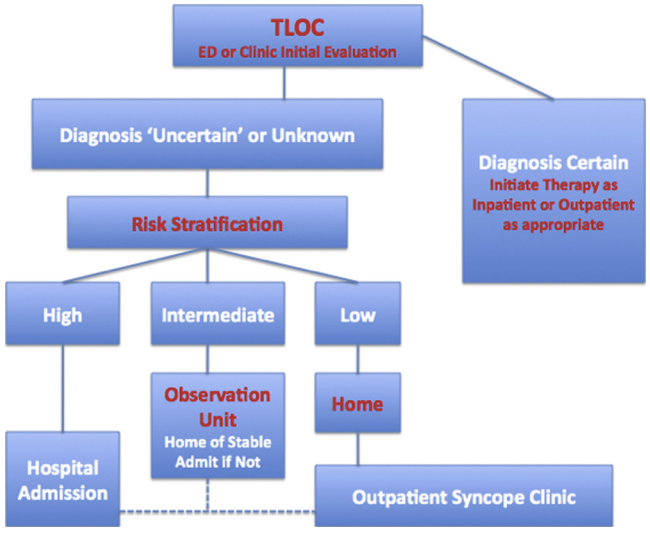

Fig. 1. Flowchart for diagnostic evaluation of patients who present to the emergency department (ED) or clinic with transient loss of consciousness (TLOC)/syncope. Modified after Ref. [1].

various reports). By way of example, Bartoletti et al. [14] examined admission rates among patients referred to ED with syncope. The study was based on ESC guidelines for management of syncope [1]. A total of 1124 patients were evaluated and 400 (39.1%) of them met at least one criterion for admission per ESC guidelines and 680 (60.9%) did not meet any criteria. The actual admission rates were 89.3% among patients with indication and 25.3% among those without any indication. The high admission rates among the low-risk patients are indicative of physician concern for patient safety after discharge. Similar findings were noted in EGSYS 2 study [15] where the admission rate was noted to be as high as 39% despite providing expert online assistance to the front-line physicians. The unnecessary inpatient admission of low-risk patients not only adds to the cost of care but also may not improve patient safety or diagnostic outcomes.

Risk stratification of TLOC/syncope patients has been the subject of several recent trials with the objective being able to derive effective criteria to help choose between inpatient admission and outpatient syncope clinic referral [16]. The most important objectives of risk-stratification studies are to assess the immediate or short-term (1 week to 1 month) and longer-term (approximately 1 year) risk of:

1) Death or life-threatening events.
2) Recurrence of syncopal events, which in turn may lead to physical injury, disability, or diminished quality of life.

Although a consensus risk-stratification tool is not yet available, such a tool-set would hopefully help ED or clinic physicians determine the immediate risk of adverse events and if risk is deemed to be high, it should prompt the physician to admit to the hospital for further evaluation [16]. In cases where the risk is felt to be intermediate, one should consider placement of the patient in a syncope observation unit if available, as was done in the SEEDS study [17]. In the absence of immediate or short-term risk based on such a tool, the patients may be referred for outpatient evaluation preferably in a clinic dedicated for evaluation of patients with syncope or TLOC. In some situations, the presence of risk factors for increased long-term risk of life-threatening events, patients may need hospitalization for further assessment. Several clinical studies focus on assessment of short-term and long-term risk factors to provide the needed guidance.

Short-term or immediate risk

The short-term or immediate risk of adverse events in the subsequent 30 days after initial presentation has been the focus of several clinical studies (Table 2). The findings are summarized briefly here and in Table 2.

1) San Francisco rule
   The risk factors identified to be predictive of increased risk of adverse events within the 7 days included [18]:
   1) An abnormal electrocardiogram (ECG) (i.e. new rhythm changes or non-sinus rhythm).
   2) Systolic blood pressure <90 mmHg.
   3) Hematocrit <30%.
   4) Congestive heart failure (CHF) (either present at the time of initial presentation or a history of CHF).

   The adverse events included the occurrence of death, myocardial infarction, malignant arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, significant hemorrhage or other serious events which required return to ED and subsequent hospitalization.
2) The Rose rule
   This was an ED-based single center study from Edinburgh UK that was designed to identify the risk factors predictive of an adverse event within 1-month after initial presentation to ED with syncope [19]. The adverse events were defined as the occurrence of death, acute myocardial infarction, life-threatening arrhythmia, being diagnosed with any arrhythmia which required implantation of a cardiac pacemaker or defibrillator within one month, pulmonary embolism, cerebrovascular accident, hemorrhage or profound anemia requiring blood transfusion, and any returns to ED within one month which required urgent surgical or endoscopic intervention. The findings that predicted the likelihood of above-mentioned adverse outcomes included:
   1) Brain natriuretic peptide >300 pg/mL.
   2) Stool positive for occult blood.
   3) Oxygen saturation <94% on room air on initial presentation.
   4) Hemoglobin <90 g/L.
   5) Chest pain at the time of syncope.
   6) Bradycardia (heart rate <50 beats per minute).

   Of the study population, 7.1% met with an endpoint at the end of one month. The sensitivity and specificity of Rose rule were estimated to be 87.2% and 65.5%, respectively.
3) The Boston study
   This study included a total of 293 patients who were followed for 30 days after their initial presentation to ED with syncope, looking for occurrence of adverse outcomes such as death, serious illness that required hospitalization or acute interventions [20].

   Sixty-eight (23%) patients met with an adverse outcome. The risk factors identified in this study that predicted the likelihood of an adverse event included the following:
   1) Acute coronary syndrome (ACS).
   2) Conduction system disease.
   3) History of cardiac disease.
   4) Valvular heart disease.
   5) Family history of sudden death.
   6) Abnormal vital signs in ED.
   7) Volume depletion.
   8) Primary central nervous system event.

   The sensitivity and specificity of this study are 97% and 62%, respectively.
4) STePS study
   A total of 676 patients were included in this study after screening a total of 2700 patients with presumed syncope [21]. The adverse outcomes within 10 days of initial presentation with syncope were assessed. The statistically significant risk factors predictive of adverse outcomes were:
   1) Age >65 years.
   2) Male gender.
   3) Structural heart disease.
   4) Heart failure.
   5) Trauma.
   6) Absence of symptoms of impending syncope.
   7) Abnormal ECG.

   The study, however, had a low positive predictive value of only 11–14% due to a low rate of adverse events.

Table 2
Short-term risk (1 week to 1 month).

Study	Clinical markers
San Francisco [18]	Abnormal ECG, low blood pressure, CHF, SOB, hematocrit <30%
Rose rule [19]	Abnormal ECG, elevated BNP, chest pain, fecal blood
STePS [21]	Abnormal ECG, trauma, no warning, male gender

ECG, echocardiography; CHF, congestive heart failure; SOB, shortness of breath; BNP, brain natriuretic peptide.

The above-mentioned studies tried to identify the risk factors that predicted the likelihood of an adverse outcome. The risk factors identified in these studies tended to have a high sensitivity but not specificity. However, to identify the high-risk patients who will need prompt hospitalization upon initial evaluation, the knowledge from these studies can be summarized as follows.

High-risk markers of short-term adverse outcomes

The following risk factors were noted to be consistently associated with increased risk of adverse outcomes in all the studies and when identified as part of the initial evaluation almost always result in hospitalization of the patient.

1) ACS or symptoms suggestive of ACS associated with syncope i.e. chest pain or shortness of breath.
2) Evidence of CHF at the time of presentation or a history of it.
3) History of structural heart disease.
4) Abnormal ECG.
5) Anemia.
6) Hemodynamic instability.

The ESC guidelines on management of syncope listed the criteria for hospitalization of patients presenting with syncope. Hospitalization of patients is a decision that should be made carefully as one should be mindful of not only patient inconvenience and anxiety but also a high level of avoidable healthcare expenditure.

Long-term risk

Long-term risk is defined as the risk of an adverse event in one year or longer after initial presentation with syncope. Several studies have attempted to establish the long-term risk factors; several of these are summarized below. Table 3 summarizes the findings from these studies.

1) Martin et al.
   This prospective cohort study from the University of Pittsburgh consisted of two groups [22]. The first group included 252 patients with syncope who were made a part of a risk-assessment scheme (derivation cohort). In this group, the data from the patient's history, physical examination, and ECG done in the ED were used to identify predictors of arrhythmias or mortality within the first year. The second group consisted of 374 patients with syncope in order to validate the system (validation cohort). The objective was to identify the predictors of adverse outcomes (death or serious arrhythmias) at 1-year follow-up. Four multivariate risk factors were identified in this study:
   1) Abnormal ECG [odds ratio (OR) 3.2, 1.6–6.4] defined as rhythm abnormalities, conduction disorders, hypertrophy, old myocardial infarction, or atrioventricular block.
   2) History of ventricular arrhythmia (OR 4.8, 1.7–13.9).
   3) History of congestive heart failure (OR 3.1, 1.3–7.4).
   4) Age >45 years (OR 3.2, 1.3–8.1).

Table 3
Longer-term.

Study	Clinical markers
Martin et al. [22]	Abnormal ECG, CHF, SOB, ventricular arrhythmia, age >45 years
OESIL score [23]	Abnormal ECG, age >65 years, history of cardiovascular disease, no warning
EGSYS [24]	Palpitation before event, abnormal ECG or heart disease, syncope during effort, syncope supine

ECG, echocardiography; CHF, congestive heart failure; SOB, shortness of breath.

   In patients without any risk factors, adverse events which are defined as death or arrhythmias occurred in 7.3% of patients in the derivation cohort and 4.4% in the validation cohort. In patients with three to four risk factors, the above-mentioned adverse events occurred in 80.4% of patients in the derivation cohort and 57.6% in the validation cohort.
2) STePS study
   A total of 676 patients were included in this study [21]. Long-term adverse outcomes were defined as death or the need for major therapeutic procedures. Adverse outcomes occurred in 9.3% of the study population which included 40 (6%) deaths and 22 patients requiring major therapeutic procedures.
   Five risk factors identified through a multivariate analysis were associated with adverse outcomes in this study, which included:
   1) Age >65 years.
   2) History of neoplasm.
   3) Cerebrovascular disease.
   4) Structural heart disease.
   5) Ventricular arrhythmia.
   Mortality was noted to be higher ($p < 0.05$) at 1 year in patients who were admitted to the hospital (14.7%) compared to the patients who were discharged (1.8%).
3) OESIL study
   The risk factors identified to be predictive of 1-year mortality in this study [23] included:
   1) Age >65 years.
   2) History of cardiovascular disease.
   3) Lack of prodromes.
   4) Abnormal ECG defined as rhythm abnormalities, conduction disorders, hypertrophy, old myocardial infarction, possible acute ischemia, or atrioventricular block.
   One-year mortality in this study increased progressively from 0% in patients with none of the above-mentioned risk factors, to approximately 57% in patients with 4 risk factors.
4) EGSYS score
   The six risk factors identified in the EGSYS study that were predictive of adverse outcomes [24] are:
   1) History or evidence of ischemic heart disease.
   2) Valvular heart disease.
   3) Cardiomyopathy.
   4) Congenital heart disease.
   5) CHF.
   6) Abnormal ECG (sinus bradycardia, atrioventricular block greater than first degree, bundle branch block, acute or old myocardial infarction, supraventricular or ventricular tachycardia, evidence of left or right ventricular hypertrophy, ventricular preexcitation, long QT, or Brugada pattern).
   The mortality at 2 years was noted to be 2% in patients with a score <3 and 21% for a score >3.

Risk stratification based on cardiac versus non-cardiac causes of syncope

Syncope from a cardiac cause has been noted to be associated with both short- and long-term risk of adverse outcomes. The comparison of morbidity and mortality in patients with cardiac syncope and non-cardiac syncope has been the subject of several studies.

1) Soteriades et al.
   A total of 7814 patients were included in this study which evaluated the incidence and prognosis among participants in the Framingham heart study from 1971 to 1998 [25]. Syncope occurred in 822 patients. Cardiac cause was considered by the

investigators to be the etiology in 9.4% and vasovagal in 21.2%. In 36.6% the cause of syncope remained unknown. The multivariate hazard ratios for mortality from any cause and stroke were noted to be significantly higher in patients with presumed cardiac cause of syncope when compared to patients with syncope from other causes. The study, however, had inherent weakness of its diagnostic classification mainly due to the limited nature of collected clinical information.

2) Kapoor et al.

This study assessed the morbidity and mortality at the end of 5 years in a total of 433 patients who presented with syncope [26]. Initial history, physical examination, ECG, and prolonged cardiac monitoring were helpful in assigning the cause of syncope, but only in 22% of the study population. The mortality at the end of 5 years was noted to be significantly higher (50.5%) in patients with cardiac cause of syncope when compared to patients with non-cardiac or unknown cause of syncope (24.1%). In addition, the incidence of sudden cardiac death was noted to be significantly higher (33.1%) in patients with cardiac cause of syncope when compared to non-cardiac (4.9%) or unknown cause (8.5%).

3) Ungar et al.

This recent study which included a relatively older set of patients (age 66 + 20 years) examined the risk of cardiovascular mortality among the patients enrolled in Evaluation of Guidelines in Syncope Study 2 (EGSYS 2) study [27]. A total of 380 patients were included in this study which examined both short-term (1 month) and long-term (2 years) mortality. A total of 35 (9.2%) deaths occurred at the end of 2 years. The deaths were significantly higher (82%) in patients who were older and who had cardiac risk factors, abnormal ECG or a history of structural heart disease and sustained injuries related to syncope when compared to patients without abnormal ECG or structural heart disease (3%).

4) Numeroso et al.

In this recent study a total of 200 patients presenting with syncope were followed to evaluate incidence of both short-term (1 month) and long-term (1 year) adverse events which were defined as death, recurrence of syncope, cardiovascular events, and major procedures [28]. Cardiac syncope was associated with both greater short- and long-term occurrence of at least one adverse event.

Is syncope a marker of increased risk of cardiovascular morbidity and mortality?

This important question remains unresolved. A large recent population-based study from Denmark [29] suggested that the occurrence of syncope in patients without any prior history of co-morbidities may confer an increased risk of cardiovascular morbidity and mortality. A total of 37,017 (median age 47 years) patients admitted to hospital with a first syncope event between 2001 and 2009 were identified from nationwide registries and approximately five times the number (n = 185,085) were chosen from the Danish population as control subjects (without syncope) who were matched for age and sex. Multivariable Cox regression analysis demonstrated a significantly higher all-cause mortality and cardiovascular hospitalization and event rate (recurrent syncope, stroke, and placement of ICD or pacemaker) in patients with syncope when compared to the control subjects without syncope. The study did have a major limitation in that the study population was hospitalized patients with syncope and the other causes necessitating hospitalization were not controlled. The findings in this study however do emphasize the importance of careful initial evaluation of all patients with syncope and the need for diligent risk stratification.

Table 4
Criteria for hospitalization or intensive evaluation based on European Society of Cardiology 2009 guidelines.

Severe structural heart disease or coronary heart disease:
- Heart failure
- Low left ventricular ejection fraction
- Previous myocardial infarction

Clinical features suggestive of arrhythmic syncope:
- Syncope in supine position
- Syncope during exertion
- Palpitations associated with syncope
- Family history of sudden cardiac death

Electrocardiographic findings suggesting arrhythmic syncope:
- Nonsustained ventricular tachycardia
- Bifascicular block (left bundle branch block or right bundle branch block combined with left anterior of posterior fascicular block)
- Other intraventricular conduction abnormalities with QRS complex duration >120 ms
- Inadequate sinus bradycardia (<50 bpm) or sinoatrial block in absence of negative chronotropic medications (e.g. beta-blockers or nondihydropyridine calcium channel blockers) or physiologic bradycardia associated with physical training
- Pre-excited QRS complex
- Prolonged or short QT interval
- Right bundle branch block pattern with ST elevation in leads V1–V3 (Brugada pattern)
- Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of arrhythmogenic right ventricular dysplasia

Important co-morbidities:
- Severe anemia
- Electrolyte abnormalities

Conclusion

Understanding the various causes of syncope and differentiating syncope from other causes of TLOC are critical elements in the assessment of patients who present with 'collapse'. In addition, risk stratification is an indispensable part of the initial evaluation of patients presenting with syncope as it provides an opportunity to identify and protect the patients at immediate risk of life-threatening events by prompt hospitalization. Risk stratification, when optimal, also offers the opportunity to avoid unnecessary hospitalization of low-risk patients, thereby reducing the healthcare expenditure. Consequently, the need to develop optimal risk assessment tools and train front-line providers in their use cannot be over-emphasized.

At the present time, while a consensus risk-stratification instrument remains in evolution, short-term risk stratification studies provide compelling evidence to hospitalize syncope patients with a suspected cardiac cause (structural or arrhythmic). All the long-term studies unequivocally emphasize the need for careful evaluation and management of underlying heart disease in these patients.

Currently, the 2009 ESC Task Force Guidelines for management of syncope provide a useful and relatively up-to-date summary of current criteria for hospitalization [1] (Table 4). These guidelines strongly encourage the development within major medical centers of dedicated 'syncope clinics,' staffed by a multidisciplinary team of interested medical professionals (cardiology, neurology, internal medicine, psychiatry). Such units may act as a resource for accelerating effective assessment of in-hospital patients, but even more importantly provide a readily accessible site for timely outpatient evaluations of syncope/collapse patients who did not require urgent hospitalization.

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