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Syncope: Assessment of risk and an approach to evaluation in the emergency department and urgent care clinic[☆]

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ABSTRACT

Syncope is among the most frequent forms of transient loss of consciousness (TLOC), and is characterized by a relatively brief and self-limited loss of consciousness that by definition is triggered by transient cerebral hypoperfusion. Most often, syncope is caused by a temporary drop of systemic arterial pressure below that required to maintain cerebral function, but brief enough not to cause permanent structural brain injury. Currently, approximately one-third of syncope/collapse patients seen in the emergency department (ED) or urgent care clinic are admitted to hospital for evaluation. The primary objective of developing syncope/TLOC risk stratification schemes is to provide guidance regarding the immediate prognostic risk of syncope patients presenting to the ED or clinic; thereafter, based on that risk assessment physicians may be better equipped to determine which patients can be safely evaluated as outpatients, and which require hospital care. In general, the need for hospitalization is determined by several key issues: i) the patient's immediate (usually considered 1 week to 1 month) mortality risk and risk for physical injury (e.g., falls risk), ii) the patient's ability to care for him/herself, and iii) whether certain treatments inherently require in-hospital initiation (e.g., pacemaker implantation). However, at present no single risk assessment protocol appears to be satisfactory for universal application, and development of a consensus recommendation is an essential next step.

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Introduction

Transient loss of consciousness (TLOC) is a common cause of emergency department (ED) or urgent clinic visits, and is an important source of falls and injury, especially in the elderly. Syncope is among the most frequent forms of TLOC, and is characterized by a relatively brief and self-limited loss of consciousness that by definition is triggered by transient cerebral hypoperfusion. Most often, syncope is caused by a temporary drop of systemic arterial pressure below that required to maintain cerebral function, but brief enough not to cause permanent structural brain injury [1–4]. In terms of frequency, the combination of ‘syncope and collapse’ is listed among the top 10 discharge diagnoses for ED visits based on the most recently available 2011 U.S. National Hospital Ambulatory Medical Care Survey (NHAMCS) [5]. Syncope is associated with high direct clinical and indirect social costs. Among syncope patients seen in the emergency department (ED) approximately 40% are hospitalized [6].

Apart from being a common problem, syncope tends to be both a disconcerting experience for patients and their families, and a difficult condition to evaluate in the ED or clinic. Since the patient has generally fully recovered by the time they are seen, the physician often has little in the way of observable abnormalities to rely upon, and often reports from eye-witnesses are inadequate. Consequently, given the resulting uncertainties regarding the cause of the problem, many of these patients (on average about one-third) are admitted to hospital for observation and further testing. However, even when admitted, almost one-half of patients are discharged without a convincing diagnosis having been established.

The primary objective of developing syncope/TLOC risk stratification algorithms is to provide guidance regarding the immediate prognostic risk of syncope patients presenting to the ED or clinic; thereafter, based on that risk assessment physicians may be better equipped to determine which patients can be safely evaluated as outpatients, and which should be admitted to hospital (Fig. 1). In many cases, if risk assessment methods were more widely applied, a substantial number of hospital admissions would be avoided thereby reducing cost of care. Those individuals not admitted could be safely and economically evaluated in specialized multidisciplinary outpatient syncope clinics [1,7–12].

This review focuses on improving understanding of clinical and laboratory features that are useful for determining whether a patient with suspected syncope is best admitted to hospital, or could be safely evaluated as an

outpatient. The ultimate goal is improved assessment of prognostic risk at the time of initial patient presentation, leading to more efficient and cost-effective subsequent management.

Syncope classification

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

Syncope evaluation

ED or clinic assessment of patients who present with presumed syncope may be challenging for several reasons. First, the affected individual is usually asymptomatic on arrival and as a result the physician is without direct ‘observation’ of the episode and be sure. Second, the patient (especially if elderly) may not be able to provide a detailed history. Third, even if the event(s) have been witnessed, the observer may not be able to recollect sufficient detail. Nevertheless, careful evaluation of apparent syncope whether in the ED or a specialized syncope clinic is crucial; only by identifying the specific cause can an effective preventive treatment strategy be initiated. In this regard, it is understood that most often, syncope is not an immediately life-threatening condition, but one that may nonetheless substantially diminish quality of life and lead to physical injury.

Risk of death and life-threatening events

Many syncope patients, especially young healthy individuals with a normal ECG and without heart disease, do not represent a worrisome prognostic subgroup and if further evaluation is needed this can be undertaken in the outpatient setting. Typically the large majority of these individuals have one of the neurally-mediated reflex syncope syndromes (i.e., vasovagal faint, post-micturition syncope, etc.). In such cases mortality risk is low, but syncope recurrence leading to injury and diminished quality-of-life issues may be important considerations, along with potential adverse impact on employment status and driving privileges. On the other hand, even in apparently healthy individuals, the prognosis of syncope is not always benign; this is especially the case in

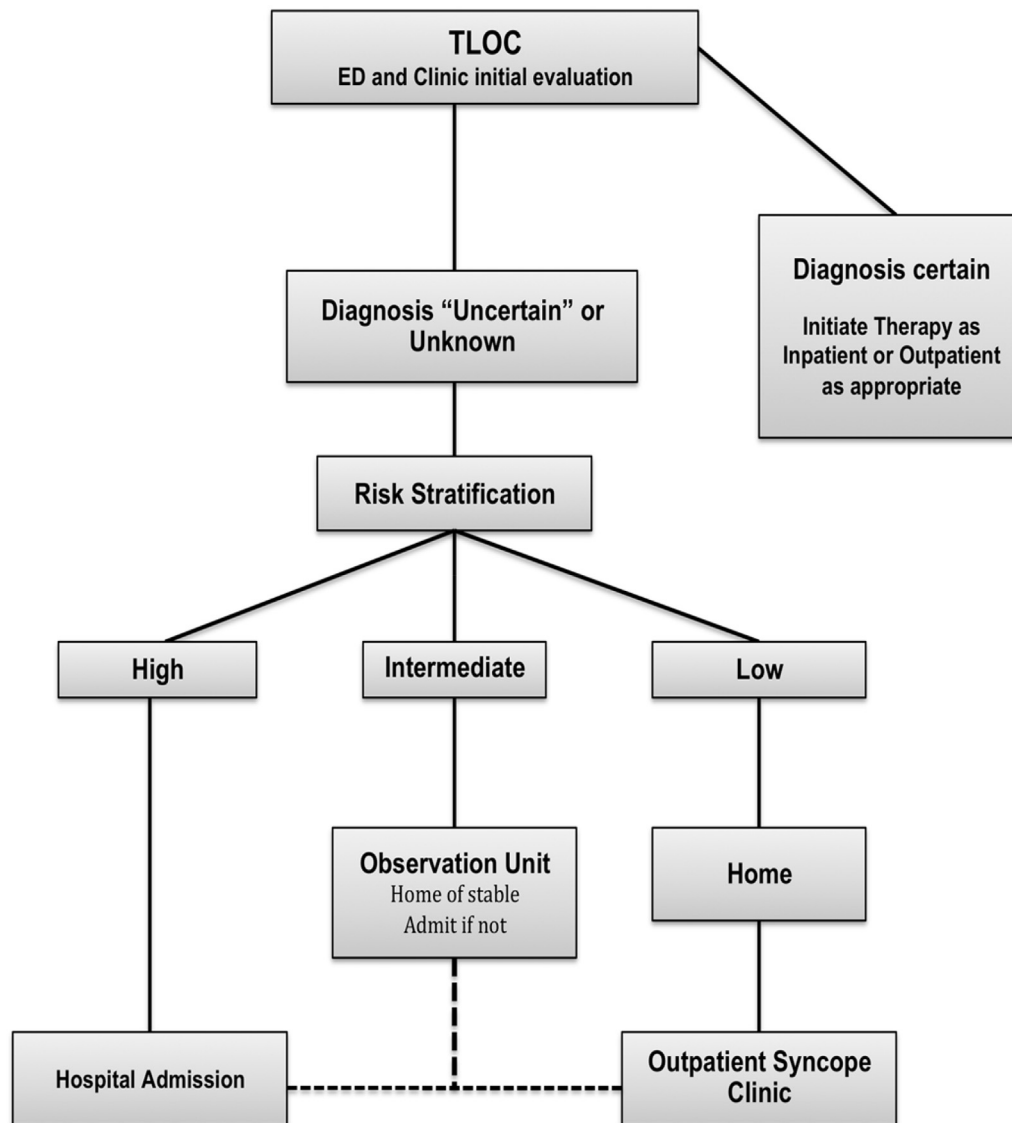


Fig. 1 – Flow chart for diagnostic evaluation of patients who present to the emergency department (ED) or clinic with transient loss of consciousness (TLOC)/syncope. Modified after Ref. [1].

Table 1 – A classification of the causes of syncope. VVS = vasovagal syncope, CSS = carotis sinus syndrome, ANS = autonomic nervous system, AV = atrioventricular, VT = ventricular tachycardia, SVT = supraventricular tachycardia, ICM = ischemic cardiomyopathy, NICM = non-ischemic cardiomyopathy, HCM = hypertrophic cardiomyopathy, ARVC: arrhythmogenic right ventricular cardiomyopathy.

Syncope: classification and principal causes

Neural reflex	Orthostatic	Cardiac arrhythmia	Structural CV
<ul style="list-style-type: none"> - VVS - CSS - Situational - Cough - post micturition etc, 	<ul style="list-style-type: none"> - Drug induced - ANS failure - Primary - Secondary 	<ul style="list-style-type: none"> - Bradycardia - Sick sinus - AV block - Tachycardia - VT - SVT - Channelopathies 	<ul style="list-style-type: none"> - Aortic valvular stenosis - ICM, NICM - HCM, ARVC - Pulmonary hypertension - Aortic dissection - Subclavian steal
≈ 60%	≈ 15%	≈ 10%	≈ 5%
Unknown ≈ 10%			

the presence of certain subtle cardiac diseases (e.g., anomalous coronary arteries, early stage cardiomyopathy) or channelopathies (i.e., long QT syndrome [LQTS], Brugada syndrome).

The presence and severity of co-existing structural heart disease are the most important predictors of mortality risk in syncope patients. In the European Evaluation of Syncope Guidelines 2 Study and EGSYS-2 [13,14], among 398 patients seen in the EDs of 11 Italian general hospitals, death of any cause occurred in 9.2% patients over a mean follow-up of 614 days. Among all deaths, 82% of patients had an abnormal ECG and/or heart disease. On the other hand, only 6 (3%) deaths occurred in patients without abnormal ECG and/or heart disease (i.e., negative predictive value, 97%).

Key clinical factors favoring cardiac causes of syncope or death were [13]: age >45 years, history of congestive heart failure, history of ventricular arrhythmias, and abnormal ECG (other than nonspecific ST changes). Arrhythmias or death within 1 year occurred in 4–7% of patients without any risk factors and progressively increased to 58–80% in patients with three or more factors. The 1-year mortality of patients with cardiac syncope is consistently higher (18–33%) than patients with non-cardiac causes (0–12%) or unexplained syncope (6%) [13,14].

In the Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL) study [15], the 4 patient characteristics that were associated with adverse outcome: age >65 years, a clinical history of cardiovascular disease, syncope without apparent warning symptoms, and an abnormal ECG [10]. In this study a risk score was proposed to assist assessment of the medical ‘urgency’ associated with the patient’s presentation, with each characteristic scoring one point. One-year mortality increased with increasing score (0% for a score of 0; 0.8% for 1 point; 19.6% for 2 points; 34.7% for 3 points; 57.1% for 4 points; $p < 0.0001$ for trend).

While patients with cardiac syncope have higher mortality rates compared to patients with syncope of non-cardiac or unknown causes, cardiac syncope patients do not necessarily exhibit a higher mortality compared with patients having similar degrees of heart disease [16–20]. Thus, for the most part, it is the severity of structural heart disease that counts, albeit with some important exceptions, including:

- i. severe aortic stenosis (average survival without valve replacement of 2 years),
- ii. hypertrophic cardiomyopathy in which syncope is a predictor of increased sudden death risk,
- iii. heart failure and severe left ventricular dysfunction, and
- iv. syncope in the setting of one of the channelopathies (e.g., Brugada syndrome, long QT syndrome [LQTS]), or in the presence of arrhythmogenic right ventricular cardiomyopathy (ARVC).

Older age, and associated frailty also contribute importantly to increased risks accompanying syncope. Falls and orthopedic complications substantially increase mortality. Thus, orthostatic hypotension, a condition more prevalent in the elderly than in the young, is associated with a 2-fold higher risk of death compared with the general population.

In part associated co-morbidities may be contributing, but in addition complications of falls such as major limb fractures are associated with substantial mortality in the elderly.

Short-term risk

The risk of life-threatening conditions in the few days or weeks after syncope is the main trigger for immediate hospital admission. In many cases, admission might be avoided by careful risk assessment at the time of presentation. The presumption that an immediate in-hospital evaluation improves long-term clinical outcome has never been demonstrated, and admission to units not experienced in the syncope evaluation is likely to be accompanied by the high costs associated with excessive use of low yield tests (e.g., head CT/MR, EEG, conventional Holter monitor). Alternative strategies such as referral to a specialized outpatient ‘blackout’ or syncope clinic may be superior especially if immediate high mortality risk is excluded by careful risk assessment.

Several studies have evaluated the short-term risk of death (usually defined as <1 month), injury, or syncope recurrence after initial presentation (Table 2).

i) San Francisco Syncope Rule [21]

An abnormal ECG (i.e., new changes or non-sinus rhythm), shortness of breath, systolic blood pressure ≤ 90 mm Hg, hematocrit $\leq 30\%$ and congestive heart failure (by history or examination) predicted the likelihood of a serious adverse event within 7 days of ED evaluation. Serious adverse events were defined as death, myocardial infarction, arrhythmia, pulmonary embolism, stroke, subarachnoid hemorrhage, significant hemorrhage, or any condition causing a return ED visit and hospitalization for a related event. The rule was determined to exhibit a sensitivity of 98% and a specificity of 56%. However, these results could be only partially confirmed by 3 validation studies that showed a high rate of both false positive and false negative results.

ii) ROSE rule [22]

The ROSE rule was a single center (Edinburgh, UK) study designed to derive and validate clinical decision rules for syncope assessment; specifically these rules consisted of: medical history, physical findings, ECG, and biochemical markers. Brain natriuretic peptide (BNP) ≥ 300 pg/mL, positive fecal occult blood, hemoglobin ≤ 90 g/L, oxygen saturation $\leq 94\%$, Q wave on ECG, chest pain at the time of syncope and bradycardia <50 bpm predicted the likelihood of serious adverse event within one month of ED evaluation. Serious adverse events were defined as death, acute myocardial infarction, life-threatening arrhythmia, decision to implant a pacemaker or cardiac defibrillator within one month, pulmonary embolus, cerebrovascular accident, hemorrhage requiring a blood transfusion, acute surgical procedure or endoscopic intervention. At one month, 7.1% of validation cohort met an end-point, with ROSE rule sensitivity and specificity being 87.2% and 65.5% respectively.

Table 2 – Principal short-term syncope risk stratification studies. ECG = electrocardiography, BP = blood pressure, CHF = congestive heart failure, SOB = shortness of breath, BNP = brain natriuretic peptide, ED = emergency department, CNS = central nervous system.

Study (N)	Markers	Follow up & adverse outcomes, frequency
San Francisco Rule (Derivation, 684)	- Abnormal ECG - Low BP - CHF, SOB - Hematocrit <30	7 days 79, 11.5%
Rose Rule (Derivation, 550) Validation, 550)	- Elevated BNP - Chest pain - Abnormal ECG - Fecal blood	1 month Derivation, 40, 7.3% Validation, 39, 7.1%
STePs (N = 676)	- Abnormal ECG - Trauma - No warning, Male gender	10 days 41, 6.1%
Boston (N = 293)	- Acute coronary syndrome - Conduction system disease - Cardiac disease history - Family history of sudden death - Volume depletion - Persistent abnormal vital signs in ED - Primary CNS event	1 month 68, 23%

iii) STePS study [23]

The STePS study screened over 2700 patients with presumed syncope at 4 general hospitals in the Milan region of northern Italy during the first half of 2004. A total of 676 patients were included in the study. Statistically significant independent risk factors for short-term (within 10 days) adverse outcomes (defined as cardiopulmonary resuscitation, pacemaker or defibrillator implant, intensive care unit admittance and early readmission to hospital) were: Age >65 years, male gender, structural heart disease, heart failure, trauma, absence of symptoms of impending syncope, and an abnormal ECG. However, owing to the relative low rate of events, the clinical utility was hampered by a very low positive predictive value that ranged from 11% to 14%.

iv) Boston study [24]

The Boston study utilized a pre-determined decision rule to assess risk in consecutive adult patients presenting to the ED with syncope. The clinical rule deemed to increase the ≤ 30 day risk of an adverse outcome or critical intervention comprised any one of the following clinical factors: 1) Acute coronary syndrome, 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 CNS event. Follow-up was complete in 293 patients. Adverse outcomes or interventions occurred in

68 (23%) patients. The rule identified 66/68 patients with an end-point (sensitivity 97%, specificity 62%).

Based on the findings derived from the studies mentioned above, the risk factors noted to be consistently associated with adverse outcomes are:

- i. Acute coronary syndrome associated with syncope
- ii. Evidence or history of CHF
- iii. History of structural heart disease
- iv. Abnormal ECG
- v. Anemia
- vi. Hemodynamic instability

Longer-term risk

The risk of an adverse outcome one-year or more after a syncope event has been the subject of a number of risk assessment reports (Table 3).

i) Martin et al. [25]

Martin et al. examined in a prospective fashion two sets of patients attending an urban University medical center ED in Pittsburgh, Pennsylvania. The first group of 252 syncope patients was used to derive a risk assessment scheme, and the second set (n = 374) was used as a validation cohort. The objective was to identify predictors of arrhythmia or mortality at 1-year follow-up. Four risk factors were identified following multivariate analysis: 1) abnormal ECG (odds ratio [OR] 3.2, 1.6–6.4) defined as rhythm abnormalities, conduction disorders, hypertrophy, old myocardial infarction, or atrioventricular [AV] 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), or 4) age >45 years (OR 3.2, 1.3–8.1). These risk factors were found to be predictors of severe arrhythmia (sustained ventricular tachycardia, symptomatic supraventricular tachycardia, pauses >3 s, AV block, pacemaker malfunction) or 1-year mortality. Arrhythmias or death at <1 year occurred in 7.3% (derivation cohort) to 4.4% (validation cohort) without any risk factors, versus 80.4% (derivation cohort) to 57.6% (validation cohort) with three or four risk factors.

ii) STePS study [23]

The one-year mortality in the STePS cohort was 6% with the cause of most deaths being undetermined. An additional 3.3% of the population exhibited other adverse outcomes. By multivariable analysis, long-term adverse outcome was associated with age >65 years, history of neoplasm, cerebrovascular disease, structural heart disease, or ventricular arrhythmia.

iii) OESIL study [15]

The one-year predictors for mortality in OESIL were age >65 years, history of cardiovascular disease, lack of prodrome and an abnormal ECG defined as rhythm abnormalities, conduction

Table 3 – Principal studies of Longer-term Syncope Risk Stratification ECG = electrocardiography, CHF = congestive heart failure, SOB = shortness of breath, CV = cardiovascular.

Study	Risk markers
Martin et al.	- Abnormal ECG, - CHF, SOB - Ventricular arrhythmia
OESIL score	- Age > 45 - Abnormal ECG, - Age > 65 - History of CV disease - No warning
EGSYS	Palpitation before event Abnormal ECG Heart disease Syncope during effort Syncope supine (2 pts)

disorders, hypertrophy, old myocardial infarction, possible acute ischemia or AV block. In the OESIL risk assessment, mortality within one year increased progressively from 0% for no factor, to approximately 57% for 4 factors.

iv) EGSYS score [13]

Six predictive factors were identified. Heart disease was deemed to be present if there was a history of or evidence for ischemic heart disease, valvular dysfunction, myocardio-pathies, congenital heart disease or congestive heart failure. The ECG was considered abnormal if there was sinus bradycardia, AV block greater than first degree, bundle branch block, acute or old myocardial infarction, supraventricular or ventricular tachycardia, left or right ventricular hypertrophy, ventricular preexcitation, long QT or Brugada pattern. The EGSYS score predicted a 2-year mortality of 2% in those with a score <3, and 21% for a score ≥3.

Limitations of current risk stratification schemes

Despite the considerable effort that has been directed toward devising the various syncope risk stratification methods, none has as yet been met by consensus approval and none can replace a comprehensive history obtained and interpreted by an experienced clinician. In some instances, the proposed risk stratification tool is too broad a brush and ‘defines’ an excessively large and non-specific patient population at risk (e.g., an abnormal ECG, age >65 years). In other instances the proposed risk stratification tool is not readily available on short notice (e.g., echocardiography, BNP measurement), or in other instances the tool may predict mortality of other cause unrelated to syncope (e.g., history of neoplasm).

Given the ongoing uncertainty facing ED and urgent care clinic physicians when encountering patients with presumed syncope, certain recommendations may be worthy of consideration:

1. Detailed training in key aspects of medical history taking required for assessment of syncope patients, and in appropriate selection of laboratory testing,

2. Provision of observation units in the ED or hospital where patients may remain until seen promptly by a syncope/TLOC consultation team. The latter may be a subset of another service particularly interested in syncope/TLOC such as Cardiology, Neurology, Geriatrics or Internal Medicine. In addition, these specialties may work together resulting in a multidisciplinary approach to the patient (i.e., a virtual ‘Syncope Management Unit’, SMU),
3. Initiation of an outpatient syncope/TLOC clinic for rapid follow-up assessment discharged from the ED. This same service might additionally provide prompt consultation in the ED during daytime hours.

Summary

Syncope has many possible causes ranging from relatively benign to potentially life-threatening; sorting through the possibilities may not be feasible given time limitations in an urgent care setting. Therefore, the physician almost always must determine whether the affected individual needs in-hospital evaluation or can be safely referred to an outpatient syncope evaluation clinic. In general, several key issues determine the need for hospitalization:

- i. the patient's immediate mortality risk and risk potential for physical injury (e.g., falls risk) based on the risk stratification steps outlined above,
- ii. the patient's ability to care for him/herself (e.g., risk of falls and injury), and
- iii. whether certain treatments inherently require in-hospital initiation (e.g., pacemaker implantation).

In instances when the etiology of syncope has been diagnosed with confidence at the initial clinical evaluation in the urgent care setting, these questions are readily addressed and the appropriateness of hospitalization versus timely outpatient evaluation is clear. Thus, for example, patients with accompanying complete heart block, ventricular tachycardia, acute aortic dissection, hypertrophic cardiomyopathy, evident or suspected channelopathy (e.g., long QT syndrome, Brugada syndrome) or pulmonary embolism, should be admitted, whereas most vasovagal fainters (which comprise more than half of all cases) can be sent home after careful discussion of the nature of the problem and simple preventative maneuvers (e.g., hydration, avoidance of hot crowded environments, etc.), and if necessary clinic follow-up is arranged. In those cases in which the diagnosis is uncertain, risk stratification schemes such as those summarized above become more essential. In this regard, increasing age, abnormal ECG, and a history of cardiovascular disease (especially ventricular arrhythmia or heart failure), appear to be relatively consistent predictors of increased susceptibility to worrisome sustained arrhythmia and/or mortality. Other factors that also seem to be relevant include syncope occurring without apparent warning or during effort (i.e., ‘in full flight’) or while the patient was supine (suggests a severe arrhythmia). Further, most deaths and serious outcomes seem to be correlated to the severity

of underlying disease rather than to syncope per se. However, as noted earlier, at present no single risk assessment protocol appears to be satisfactory for universal application, and the development of a consensus recommendation is an essential next step [7].

REFERENCES

- [1] Moya A, Sutton R, Ammirati F, Blanc JJ, Brignole M, Dahm JB, et al. Guidelines for the diagnosis and management of syncope (version 2009): the Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). *Eur Heart J* 2009;30:2631–71.
- [2] Blanc JJ, L'Her C, Touiza A, Garo B, L'Her E, Mansourati J. Prospective evaluation and outcome of patients admitted for syncope over a 1 year period. *Eur Heart J* 2002;23:815–20.
- [3] Sarasin FP, Louis-Simonet M, Carballo D, Slama S, Rajeswaran A, Metzger JT, et al. Prospective evaluation of patients with syncope: a population-based study. *Am J Med* 2001;111:177–84.
- [4] Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, Benjamin EJ, et al. Incidence and prognosis of syncope. *N Engl J Med* 2002;347:878–85.
- [5] Ambulatory and Hospital Care Statistics Branch of the Centers for Disease Control and Prevention's National Center for Health Statistics website http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2011.ed_web_tables.pdf.
- [6] Grubb BP. Clinical practice. Neurocardiogenic syncope. *N Engl J Med* 2005;352:1004–10.
- [7] Benditt DG, Can I. Initial evaluation of “syncope and collapse” the need for a risk stratification consensus. *J Am Coll Cardiol* 2010;55:722–4.
- [8] Brignole M, Ungar A, Casagrande I, Gulizia M, Lunati M, Ammirati F, et al. Prospective multicentre systematic guideline-based management of patients referred to the syncope units of general hospitals. *Europace* 2010;12:109–18.
- [9] Shen WK, Decker WW, Smars PA, Goyal DG, Walker AE, Hodge DO, et al. Syncope Evaluation in the Emergency Department Study (SEEDS). A multidisciplinary approach to syncope management. *Circulation* 2004;110:3636–45.
- [10] Youde J, Ruse C, Parker S, Fotherby M. A high diagnostic rate in older patients attending an integrated syncope clinic. *J Am Geriatr Soc* 2000;48:783–7.
- [11] Petkar S, Bell W, Rice N, Iddon P, Cooper P, McKee D, et al. Initial experience with a rapid access blackouts triage clinic. *Clin Med* 2011;11:11–6.
- [12] Sutton R, Brignole M, Benditt DG. Syncope: a focused review of key current management challenges. *Nat Cardiol* 2012;9:590–8.
- [13] Del Rosso A, Ungar A, Maggi R, Giada F, Petix NR, De Santo T, et al. Clinical predictors of cardiac syncope at initial evaluation in patients referred urgently to general hospital: the EGSYS score. *Heart* 2008;94:1690–8.
- [14] Ungar A, Del Rosso A, Giada F, Bartoletti A, Furlan R, Quartieri F, et al. Early and late outcome of treated patients referred for syncope to emergency department. The EGSYS 2 follow-up study. *Eur Heart J* 2010;31:2021–6.
- [15] Colivicchi F, Ammirati F, Melina D, Guido V, Imperoli G, Santini M, et al. Development and prospective validation of a risk stratification system for patients with syncope in the emergency department: the OESIL risk score. *Eur Heart J* 2003;24:811–9.
- [16] Pires LA, May LM, Ravi S, Parry JT, Lal VR, Nino CL. Comparison of event rates and survival in patients with unexplained syncope without documented ventricular tachyarrhythmias versus patients with documented sustained ventricular tachyarrhythmias both treated with implantable cardioverter-defibrillators. *Am J Cardiol* Mar 15 2000;85(6):725–8.
- [17] Olshansky B, Hahn EA, Hartz VL, Prater SP, Mason JW. Clinical significance of syncope in the electrophysiologic study versus electrocardiographic monitoring (ESVEM) trial. The ESVEM Investigators. *Am Heart J* 1999;137(5):878–86.
- [18] Steinberg JS, Beckman K, Greene HL, Marinchak R, Klein RC, Greer SG, et al. Follow-up of patients with unexplained syncope and inducible ventricular tachyarrhythmias: analysis of the AVID registry and an AVID substudy. Antiarrhythmics versus implantable defibrillators. *J Cardiovasc Electrophysiol* 2001;12(9):996–1001.
- [19] Knight BP, Goyal R, Pelosi F, Flemming M, Horwood L, Morady F, et al. Outcome of patients with nonischemic dilated cardiomyopathy and unexplained syncope treated with an implantable defibrillator. *J Am Coll Cardiol* 1999;33:1964–70.
- [20] Olshansky B, Poole JE, Johnson G, Anderson J, Hellkamp AS, Packer D, et al. Syncope predicts the outcome of cardiomyopathy patients: analysis of the SCD-HeFT study. *J Am Coll Cardiol* 2008;51:1277–82.
- [21] Quinn JV, Stiell IG, McDermott DA, Sellers KL, Kohn MA, Wells GA. Derivation of the San Francisco Syncope Rule to predict patients with short-term serious outcomes. *Ann Emerg Med* 2004;43:224–32.
- [22] Reed MJ, Newby DE, Coull AJ, Prescott RJ, Jacques KG, Gray AJ. The ROSE (risk stratification of syncope in the emergency department) study. *J Am Coll Cardiol* 2010;55:713–21.
- [23] Costantino G, Perego F, Dipaola F, Borella M, Galli A, Cantoni G, et al. Short- and long-term prognosis of syncope, risk factors, and role of hospital admission: results from the STePS (short-term prognosis of syncope) study. *J Am Coll Cardiol* 2008;51:276–83.
- [24] Grossman SA, Fischer C, Lipsitz LA, Mottley L, Sands K, Thompson S, et al. Predicting adverse outcomes in syncope. *J Emerg Med* 2007;33:233–9.
- [25] Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. *Ann Emerg Med* 1997;29:459–66.