Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department with Syncope

From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Syncope:
J. Stephen Huff, MD (Subcommittee Chair)
Wyatt W. Decker, MD
James V. Quinn, MD, MS
Andrew D. Perron, MD
Anthony M. Napoli, MD (EMRA Representative 2004-2006)
Suzanne Peeters, MD (Dutch Society of Emergency Physicians)
Andy S. Jagoda, MD

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INTRODUCTION

Syncope is a symptom complex that is composed of a brief loss of consciousness associated with an inability to maintain postural tone that spontaneously and completely resolves without medical intervention. It is distinct from vertigo, seizures, coma, and states of altered consciousness. Syncope is a common presentation to the emergency department (ED) that accounts for 1% to 1.5% of ED annual visits and up to 6% of hospital admissions.[1,2] The ED evaluation of patients with syncope may be problematic for several reasons. Accurate historical information is often lacking or there may be conflicting historical information from observers. Furthermore, patients are often asymptomatic when they arrive in the ED and may have no recall of the event.

Any process that transiently reduces cerebral perfusion may be the precipitant of syncope. Concerns that well-appearing patients are at risk for sudden death often fuel extensive clinical evaluations or hospital admissions because the large differential diagnosis includes some processes that may be life-threatening. Many studies have demonstrated the low yield of nondirected diagnostic testing.[3-6] From the available literature, it is unclear whether admitting asymptomatic syncope patients for observation and inpatient evaluation affects patient outcome. Additionally, it is estimated that more than $2 billion a year is spent in the United States on hospitalization of patients with syncope.[7] An analysis of the 2001 American College of Emergency Physicians (ACEP) clinical policy on syncope found that by applying the Level B recommendations, all patients with cardiac causes of syncope were identified, and the admission rate would be reduced from 57.5% to 28.5%.[8] These facts must lead to a reassessment of the role of the emergency physician in evaluation of the patient presenting with syncope.

The emergency physician must still identify those relatively few patients with life-threatening processes (eg, dysrhythmias, pulmonary embolism, aortic dissection, subarachnoid hemorrhage, acute coronary syndromes) and other patients who may benefit from intervention (eg, patients with bradycardia, medication-induced orthostatic hypotension). Frequently, however, the ED evaluation of a patient presenting with syncope does not reveal a clear etiology. The emergency physician must then determine which of these patients require further diagnostic evaluation and monitoring and in what setting that should occur. The role of the emergency physician in evaluating the patient with syncope has moved from efforts to determine a specific diagnosis of syncope type to that of risk stratification, similar to the process of chest pain evaluation.

Symptoms and complaints associated with syncope should be fully evaluated. A careful history should be obtained, considering other associated symptoms, whether cardiac, neurologic, abdominal, or respiratory, because it may lead to a diagnosis of an underlying medical condition such as an acute coronary event, aortic dissection, pulmonary embolism, seizure, ectopic pregnancy, or gastrointestinal hemorrhage.

This document does not attempt to outline the evaluation of patients presenting with syncope associated with specific diagnoses but rather focuses on assisting the emergency physician in addressing 3 critical questions:

1. What history and physical examination data help to risk-stratify patients with syncope?
2. What diagnostic testing data help to risk-stratify patients with syncope?
3. Who should be admitted after an episode of syncope of unclear cause?

This policy is an update of the 2001 ACEP clinical policy on syncope.[9] Other professional societies have developed guidelines for evaluation of syncope but this policy is designed to reflect recommendations focused on the practice of emegency medicine.[10,11]

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. MEDLINE searches for articles published between March 1998 and May 2005 were performed using a combination of key words, including "syncope" and variations of "risk," "risk stratification," "admission," "outcomes," "emergency department," "prognosis," "differential diagnosis," "physical examination," and "diagnostic evaluation." Searches were limited to English-language sources. Additional articles were reviewed from the bibliographies of studies cited. Subcommittee members also supplied articles from their own knowledge and files.

The reasons for developing clinical policies in emergency medicine and the approaches used in their development have been enumerated.[12] This policy is a product of the ACEP clinical policy development process and is based on the existing literature; where literature was not available, consensus of emergency physicians was used. Expert review comments were received from individual emergency physicians, individual members of the American College of Cardiology, members of ACEP's Observation Section, Geriatric Section, and Quality and Performance Committee. Their responses were used to further refine and enhance this policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for strength of evidence and classified by the subcommittee members into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic clinical reports respectively (Appendix A). Articles were then graded on 6 dimensions thought to be most relevant to the development of a clinical guideline: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (eg, selection, detection, transfer), external validity (ie, generalizability), and sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula taking into account design and quality of study (Appendix B). Articles with fatal flaws were given an "X" grade and not used in formulating recommendations in this policy. Evidence grading was done with respect to the specific data being extracted, and the specific critical question being reviewed. Thus, the level of evidence for any one study may vary according to the question, and it is possible for a single article to receive different levels of grading as different critical questions are answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of this policy.

Clinical findings and strength of recommendations regarding patient management were then made according to the following criteria:

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

Level C recommendations. Other strategies for patient management that are based on preliminary, inconclusive, or conflicting evidence, or in the absence of any published literature, based on panel consensus.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, strength of prior beliefs, and publication bias, among others, might lead to such a downgrading of recommendations.

This policy is not intended to be a complete manual on the evaluation and management of adult patients with syncope but rather a focused look at critical issues that have particular relevance to the current practice of emergency medicine.

It is the goal of the Clinical Policies Committee to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain enough quality information to answer a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only diagnostic and management options that the emergency physician should consider. ACEP clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the crucial questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in hospital-based EDs.

Inclusion Criteria. This guideline is intended for adult patients presenting to the ED with syncope.

Exclusion Criteria. This guideline is not intended for children or for patients in whom the episode of syncope is thought to be secondary to another disease process. Among the clinical conditions specifically excluded are patients with seizures, chest pain, headache, abdominal pain, dyspnea, hemorrhage, hypotension, or a new neurologic deficit.

CRITICAL QUESTIONS

1. What history and physical examination data help to risk-stratify patients with syncope?

Level A recommendations. Use history or physical examination findings consistent with heart failure to help identify patients at higher risk of an adverse outcome.

Level B recommendations.

1. Consider older age, structural heart disease, or a history of coronary artery disease as risk factors for adverse outcome.
2. Consider younger patients with syncope that is nonexertional, without history or signs of cardiovascular disease, a family history of sudden death, and without comorbidities to be at low risk of adverse events.

Level C recommendations. None specified.

The traditional approach of focusing on establishing an etiology of syncope in the ED is often of limited utility. Multiple studies have demonstrated a diagnostic rate of only 20% to 50% in the initial evaluation of the syncope patient.[1,13,14] Even in subspecialty studies with patients undergoing extensive diagnostic evaluations, 15% to 30% of patients remain without a definitive cause.[15-18] Review of the syncope literature reveals that because of the lack of a criterion standard, the final diagnosis given to a syncope patient is difficult to validate and subject to variability.

Few studies have directly evaluated risk stratification of syncope patients in the ED. In a Class I study, Martin et al[5] studied 252 syncope patients to develop a risk classification system and then tested the system in a validation cohort of 374 patients. Predictors of arrhythmia or 1-year mortality in the validation cohort were found to be: (1) abnormal ECG result, (2) history of ventricular arrhythmia, (3) history of congestive heart failure, or (4) age more than 45 years. The event rate (clinically significant arrhythmia or death) at 1 year in the validation cohort ranged from 0% for those with none of the 4 risk factors to 27% for those with 3 or 4 risk factors. In a similarly designed Class I study from Italy, Colivicchi et al[19] derived risk factors for 1-year mortality (not arrhythmias) in 270 patients and then validated them on 328 patients and found an abnormal ECG result, a history of cardiovascular disease, lack of prodrome, and age older than 65 years to predict all deaths in the 2 cohorts. These studies have determined that age, abnormal ECG result, lack of a prodrome, a history of cardiovascular disease, especially ventricular arrhythmia, and heart failure all appear to have predictive value in assessing 1-year risk of adverse outcomes in patients with syncope.

A Class I study by Quinn et al,[2] the San Francisco Syncope Study, examined short-term serious events in 684 ED patients presenting with syncope. Recursive partitioning techniques identified the following characteristics associated with a higher likelihood of an adverse event within 7 days of ED presentation: abnormal ECG result, shortness of breath, systolic blood pressure less than 90 mm Hg after arrival in the ED, hematocrit level less than 30%, and congestive heart failure by history or examination. This derivation set has now been prospectively

validated.[20] A prospective Class III study by Sarasin et al[21] also found that an abnormal ECG result, history of congestive heart failure, and age more than 65 years were all risk factors for experiencing a serious arrhythmia.

Little literature exists to guide the clinician in cases of exertional syncope in young patients (age <35 years). This is an uncommon occurrence, usually with a very different etiology than syncope in an older patient. Possible etiologies include hypertrophic cardiomyopathy, coronary artery abnormalities, conduction abnormalities (long QT, preexcitation syndromes), and arrythmogenic cellular dysplasias. Cardiology consultation may be considered either as an inpatient or outpatient.

History and Physical Examination Data

History and physical examination are the defining factors in syncope risk stratification. Often the patient may not have accurate recall of the event; thus, eyewitness accounts, are an important part of the history, which includes estimation of duration of loss of consciousness and evidence of seizure activity. Mild, brief, tonic-clonic activity may commonly accompany syncope of any etiology ("convulsive syncope"). Witnesses also may report falls or other trauma during the episode. Postsyncopal history, also best obtained from eyewitnesses, includes duration of confusion or lethargy after the episode or evidence of focal neurologic deficits. After an episode of syncope, patients may briefly appear disoriented or confused, but this resolves within moments and is often shorter than the postictal period associated with generalized seizures. Absent or brief prodrome (less than 5 seconds) may be present with dysrrhythmias, whereas neurally mediated syncope (synonyms include neurocardiogenic syncope and "vasovagal" syncope) may be characterized by longer prodromes and associated nausea or vomiting. Obvious precipitating events or stress with a consistent history may be sufficient to diagnose neurally mediated syncope, which is important because the diagnosis of neurally mediated syncope is consistently associated with a good prognosis.[22] However, it is problematic that prodromal symptoms are subjective, and agreement on the presence of "vagal" symptoms and the eventual diagnosis is inconsistent among physicians.[2] Syncope that occurs while the patient is seated or reclining is more likely to have a cardiac etiology,[23] whereas syncope that occurs within 2 minutes of standing may suggest orthostatic hypotension.[24,25]

Medications and drug interactions may cause syncope. Many drugs prolong the QT interval and are associated with life-threatening dysrhythmias. Vasoactive drugs such as antihypertensive agents, vasodilators used for angina, and those used for erectile dysfunction may lead to syncope. In one study, antihypertensive agents, other cardiovascular drugs, diuretics, and central nervous system agents were most frequently cited as a cause of syncope. Drug-related syncope was especially common in elderly patients taking multiple medications.[26]

Though less well established in the literature, a family history of premature sudden cardiac death should alert the clinician to the possibility of serious congenital conduction abnormalities, including preexcitation syndromes, long QT syndromes, or Brugada syndrome.[27-29]

The demographic variables of age, sex, and race are potential risk factors for cardiovascular disease. Epidemiologic and cohort studies have confirmed the importance of age,[3,5,22] though of course age alone is a marker for increased mortality. Although increasing age is accompanied by an increased risk of poor outcome, there is no single age cutoff but rather a continuum of gradually increasing risk.

Cardiovascular diagnoses and older age do increase the risk of sudden death in patients with syncope. In a prospective cohort study, in patients older than 60 years, those with a cardiovascular diagnosis regardless of age had an increase in sudden death within 2 years.[30] Two Class II studies found cardiovascular risk to be the only predictor of 1-year mortality and also found that cardiovascular risk, not syncope, was the best predictor of mortality and cardiovascular events.[31,32] According to Class I and Class II studies, patients younger than 45 years, in the absence of other symptoms or examination findings, tend to be of lower risk, whereas older patients are at greater risk for adverse outcomes. There is no discrete cutoff age for assessing age-related risk, and the ability to make any firm age-based recommendation about risk stratification is confounded by the arbitrary choice of age thresholds in different studies. Patients with a history of poor left ventricular function, which appears to be best predicted by a diagnosis of heart failure, are consistently at greater risk of sudden death in almost every study assessing risk,[2,5,19,21] which is not just due to the fact that a history of heart failure alone has a poor prognosis. Syncope in the patient with heart failure is a poor prognostic sign. Middlekauff et al[33] showed in a Class II study that even if patients with heart failure are diagnosed with a noncardiac etiology for their syncope, these patients appeared to be at risk of sudden death. Exertional syncope raises special concerns about structural heart lesions producing fixed cardiac output.

Vital signs. Loss of consciousness with syncope is transient, and the hypoperfusion or hypotension usually is transient as well. Persistent hypotension is concerning and should suggest the possiblity of another disease process. Tachycardia and hypotension may represent ongoing hemodynamic instability or volume depletion, and a cause for persistent hypotension (sepsis, hemorrhage, cardiac failure) should be sought.

Orthostatic hypotension is usually defined as a decrease in systolic blood pressure with standing of 20 mm Hg or greater. This finding may identify some patients with syncope related to volume depletion, autonomic insufficiency, or medications. Recurrence of symptoms such as light-headedness or even syncope on standing is more significant than any numeric change in blood pressure. Orthostatic hypotension is common in patients with syncope of unknown etiology, as well as in patients with other documented diagnoses such as cardiac disease, and is detected in most patients within 2 minutes after standing. This finding is also present in up to 40% of asymptomatic patients older than 70 years, and 23% of those

younger than 60 years.[24] Relying on the diagnosis of orthostatic hypotension as a cause of syncope should be symptom-related and a diagnosis of exclusion in otherwise low-risk patients, with the realization that many high-risk patients will have orthostasis.[34]

Cardiopulmonary. Physical examination findings of congestive heart failure are indicators of high risk of sudden death or early mortality after syncope, as shown in a Class I study.[2] Murmurs indicative of valvular heart disease or outflow obstruction should prompt further evaluation for structural heart disease.

Head and face. Tongue biting, particularly if it is lateral, has a high specificity for convulsive seizures. Because of low sensitivity, absence of tongue bites has no diagnostic significance.[35] Head trauma resulting from syncope is not associated with any particular type of syncope or short-term outcome,[2] although syncope and resultant head injury have been associated with 1-year death.[19]

Abdominal. Abdominal pain or tenderness associated with syncope should be investigated. It may be a marker of significant pathology or hemorrhage. Rectal examination with observation and testing for bleeding is recommended if gastrointestinal hemorrhage is suspected.

2. What diagnostic testing data help to risk-stratify patients with syncope?

Level A recommendations. Obtain a standard 12-lead ECG in patients with syncope.

Level B recommendations. None specified.

Level C recommendations. Laboratory testing and advanced investigative testing such as echocardiography or cranial CT scanning need not be routinely performed unless guided by specific findings in the history or physical examination.

Diagnostic Testing Data

In patients for whom a diagnosis of syncope is established, history and physical examination identify the cause in the majority of patients in which an etiology will be established. The yield of the ECG in finding a cause is low (less than 5%),[3,4,36,37] but the test is noninvasive and relatively inexpensive and can occasionally pick up potentially life-threatening conditions such as preexcitation syndromes, prolonged QT syndromes, or Brugada syndrome in otherwise healthy-appearing young adults.[27,28] A patient with a normal ECG result has a low likelihood of dysrhythmias as a cause of syncope.[2,21,38] The definitions of an abnormal ECG vary from study to study and within specialty guidelines. One study defined an abnormal ECG result as any nonsinus rhythm or an ECG with any new changes compared with a previous ECG and found it the most important predictor of serious outcomes.[2] Another study found the presence of an abnormal ECG (defined as any abnormality of rhythm or conduction, ventricular hypertrophy, or evidence of previous myocardial infarction but excluding nonspecific ST-segment and T-wave changes) was a multivariate predictor for arrhythmia or death within 1 year after the syncopal episode.[5]

Cardiac monitoring. Continuous cardiac monitoring in the ED occasionally detects an arrhythmia not evident on a single 12-lead tracing. A strong suspicion of arrhythmias may prompt inpatient or ambulatory monitoring. For most patients, monitoring longer than 24 hours is not likely to increase the detection of significant arrhythmias. One study found 4 factors that identified patients likely to have an abnormality with prolonged monitoring of up to 72 hours: (1) age older than 65 years, (2) male sex, (3) history of heart disease, and (4) nonsinus rhythm on initial ECG. However, none of the patients with arrhythmias detected in the second and third 24-hour periods were symptomatic.[39]

Laboratory testing. In an evaluation of syncope, laboratory tests rarely yield any diagnostically useful information, and their routine use is not recommended.[3,36,37] However, in an unselected group of patients presenting to the ED with syncope from any cause, Quinn et al[2] found hematocrit level less than 30% to be a useful predictor of adverse events.

Advanced tests and imaging. There is no evidence to suggest that routine screening of syncope patients with advanced imaging (such as CT), testing such as functional cardiac echocardiography, or electrophysiologic testing is indicated. In a Class II study on echocardiography and syncope, Sarasin et al[40] found that the only added clinically useful information was in those patients with a history of cardiac disease, an abnormal ECG result, or when aortic stenosis was suspected. The use of advanced testing must be guided by the patient's history and physical examination results, shaping the physician's overall impression of likelihood that any of the rare, life-threatening conditions that can present with syncope might exist.

3. Who should be admitted after an episode of syncope of unclear cause?

Level A recommendations. None specified.

Level B recommendations.

1. Admit patients with syncope and evidence of heart failure or structural heart disease.
2. Admit patients with syncope and other factors that lead to stratification as high-risk for adverse outcome (Figure).

Level C recommendations. None specified.

The primary reason for admitting patients with syncope to an inpatient unit, observation unit, or other monitored area should be that the physician's risk assessment indicates that a patient may be at risk for significant dysrrhythmia or sudden death and that observation might detect that event and enable an intervention. Problematic is the definition of short-term outcome, which is subjective and not clearly defined. Which patients will benefit from a 24- to 48-hour hospital admission or observation unit admission is not adequately described in the medical literature, nor has the value of admission in preventing a later adverse outcome been demonstrated. Endpoints for patients followed up after an episode of syncope are typically

Older age and associated comorbidities*
Abnormal ECG†
Hct <30 (if obtained)
History or presence of heart failure, coronary artery disease, or structural heart disease

*Different studies use different ages as threshold for decisionmaking. Age is likely a continuous variable that reflects the cardiovascular health of the individual rather than an arbitrary value.

†ECG abnormalities, including acute ischemia, dysrhythmias, or significant conduction abnormalities.

Figure. Factors that lead to stratification as high-risk for adverse outcome.

reported at intervals of 6 months to 1 year or even longer. Only the San Francisco Syncope Rule, which used an endpoint of 7 days, has evaluated short-term risk of patients discharged from the ED. Other studies of ED patients have patient numbers that are too small for firm conclusions.[41] The most rational approach to admission is to understand the specific risks for patients as stated in critical question 1, and make the admission decision in light of available literature. High-risk patients require hospital admission. However, one should also realize that the decision to admit patients often takes into consideration other symptoms, other medical problems, and social factors. Admission may also be initiated for additional testing and consultation or for anticipated therapy.

Future Directions

A small number of studies have explored a clinical decision or observation unit, with testing or consultation as an alternative to inpatient admission in patients stratified as neither high-risk nor low-risk for adverse outcomes (ie, intermediate-risk patients). Further studies are needed to identify distinct subgroups that might benefit from this strategy.[42] The distinction between ED evaluation and admission is blurring with the availability of additional diagnostic resources, the opportunity for longer observation periods, and the reality of prolonged ED stays.

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Evidentiary Table.

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Blanc et al[1]	2002	Prospective cohort, observational, with retrospective review of charts	Review of all patients (37,475) presenting to the ED from June 1999 to June 2000; with syncope: 454 had definite syncope	454 (1.2%) were diagnosed as having syncope; for 296 patients, it was the first episode; 169 were discharged from the ED; 285 were admitted; in 76% of patients, a discharge diagnosis was reported but evaluation was inadequate to explain a syncopal episode in 16%	Syncope is a frequent symptom, but its cause often remains unknown partly because of inadequate management	Study looked at the evaluation and diagnostic findings of patients admitted to a hospital in France; definition of syncope not clear in patient notes	III
Quinn et al[2]	2004	Prospective cohort study	Physicians prospectively completed a structured data form when evaluating patients with syncope; serious outcomes were defined at the start of the study; all patients were followed up to determine whether they had experienced a serious outcome within 7 days of their ED visit	684 ED visits for syncope, with 79 of these visits resulting in patients experiencing serious outcomes; of the 50 predictor variables considered, 26 were associated with a serious outcome on univariate analysis	The San Francisco Syncope Rule derived in this cohort of patients appears to be sensitive for identifying patients at risk for short-term serious outcomes	Prospective derivation study of San Francisco Syncope Rule	I
Kapoor et al[3]	1983	Prospective cohort study	Followed 204 patients with syncope to determine how often a cause of syncope could be established and to define the prognosis of patients	A cardiovascular cause was established in 53 patients and a noncardiovascular cause in 54 patients; the cause remained unknown in 97 patients	Patients with syncope can be separated into diagnostic categories that have prognostic importance; patients with a cardiovascular cause have a strikingly higher incidence of sudden death than patients with a noncardiovascular, unknown cause	Study of diagnosis and outcome in 204 syncope patients, demonstrating increased mortality in those with cardiac etiology; correction made for patient subgroups with no change in results	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Martin et al[5]	1997	Prospective studies	Two prospective studies were carried out at a large urban teaching hospital ED; a cohort of 252 patients with syncope presenting to the ED was used to develop the risk classification system; a second cohort of 374 patients with syncope was used to validate the system	Multivariate predictors of arrhythmia or 1-y mortality; arrhythmias or death within 1 y	Historical and ECG factors available at presentation can be used to stratify risk of arrhythmias or mortality within 1 y in ED patients presenting with syncope; multivariate predictors of arrhythmia or 1-y mortality were: an abnormal ED ECG result, history of ventricular arrhythmia, history of CHF, or age >45 y; arrhythmias or death within 1 y occurred in 7.3% (derivation cohort) to 4.4% (validation cohort) of patients without any risk factors and in 80.4% (derivation) to 57.6% (validation) of patients with 3 or 4 risk factors	All potential predictors were included during derivation; the decision rule has been validated in this study; the derivation and validation data are set independent in 2 cohorts; 1 for derivation, 1 for validation; outcomes were defined at the start of the study; more ECG abnormalities/cardiac morbidity in derivation cohort; multivariate regression analysis post-study for subgroups with variables known to have different prognostic value; assessment of outcomes not blinded	I
Crane[13]	2002	Retrospective	Study applied ACP risk stratification/admit guidelines to 208 patients evaluated with syncope; 43% of cohort was not assigned a diagnosis after their assessment in ED; 47 (22%) were placed in ACP group 1; 63 (30%) in ACP group 2; and 100 (48%) in ACP group 3	36% of those in group 1, 14% of those in group 2, and none in group 3 died within a y	It is possible to risk-stratify syncope patients presenting to an ED by using ACP guidelines for managing syncope	Risk stratification successful based on 1-y mortality; no blinding	III (risk stratification)
Kapoor et al[14]	1982	Retrospective	121 patients hospitalized for syncope of uncertain cause	The definitive cause for syncope was diagnosed in only 13 of 121 patients after average hospitalization of 9 days	Findings suggest that an extensive evaluation of syncope of unknown origin is cost-ineffective and that prospective goal-directed approaches should be developed	Low diagnostic yield and high cost of inpatient evaluations were noted findings in patients without evident diagnosis on initial evaluation	III
Ammirati et al[17]	2000	Simplified 2-step diagnostic algorithm was developed and prospectively implemented in 9 community hospitals in Lazio region of Italy	195 consecutive patients presenting with syncopal spells to EDs throughout a 2-mo period	Improvement in clinical decisionmaking rated by percentage of cases remaining as "undiagnosed" after evaluation	The systematic implementation of the proposed diagnostic algorithm resulted in a striking reduction of undiagnosed cases	Study examines the use of a diagnostic algorithm to determine the cause/ diagnosis of syncope; a prior study is used as a "control" group; lack of risk stratification, and no separate derivation (consensus through literature) and validation set of data; it is unclear how diagnoses were reached and how diagnoses were validated	III (risk stratification)

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Sarasin et al[18]	2001	Prospective	Consecutive patients who presented to the ED with syncope as a chief complaint were enrolled	A diagnosis of etiology of syncope or syncope subtype	The diagnostic yield of a standardized evaluation of syncope was 76%, including the use of specialized cardiovascular tests in selected patients	Lack of criterion standard to validate diagnosis	II
Colivicchi et al[19]	2003	Prospective multicenter	270 consecutive patients presenting with syncope to the EDs of 6 community hospitals was used as a derivation cohort for the development of the risk classification system; data from the baseline clinical history, physical examination, and ECG were used to identify independent predictors of total mortality within the first 12 mo after the initial evaluation; risk classification scoring was prospectively confirmed in a validation cohort of 328 consecutive patients	Multivariate predictors of death within 1 y	Clinical and ECG factors available at presentation can be used to stratify risk of mortality within 1 y in patients presenting with syncope	Multivariate analysis showed the following predictors of mortality: (1) age >65 y; (2) cardiovascular disease in clinical history; (3) syncope without prodromes; and (4) abnormal electrocardiogram; mortality increased significantly as the score increased in the derivation cohort (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)	I
Quinn et al[20]	2006	Prospective cohort study to validate previous derivation set	Physicians prospectively completed a structured data form when evaluating patients with syncope; serious outcomes were defined at the start of the study; all patients were followed up to determine whether they had experienced a serious outcome within 7 days of their ED visit	791 visits for syncope; 53 (6.7%) resulted in bad outcomes	The rule was 98% sensitive (95% CI 89%-100%) and 56% specific (95% CI 52%-60%) to predict adverse outcomes; LR (+) 2.2; LR (-) 0.04	Single institution	I

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Sarasin et al[21]	2003	Prospective validation and retrospective derivation	175 patients with unexplained syncope (Geneva, Switzerland) were used to develop and cross-validate the risk score; a second cohort of 269 similar patients (Pittsburgh) was used to validate the system; data from patient's history and 12-lead emergency ECG were used to identify predictors of arrhythmias; risk-score performance was measured by comparing the proportions of patients with arrhythmias at various levels of the score and ROC curves	The prevalence of arrhythmic syncope was 17% in the derivation cohort and 18% in the validation cohort; predictors of arrhythmias were abnormal ECG result, a history of CHF, and age older than 65 y	In patients with unexplained syncope, a risk score based on clinical and ECG factors available in the ED identifies patients at risk for arrhythmias	Derivation group 10 y later than validation group; very selected patient group	III (risk stratification)
Soteriades et al[22]	2002	Retrospective Framingham database 1971-1998		Study evaluating population-based incidence and outcome of syncope	Of 7,812 patients participating in the study, 822 had syncope; incidence 6.2/1,000; 36.6% syncope unknown cause	Those with syncope had higher mortality rates, and even more so when it was cardiogenic syncope; selected population; inclusion criteria of basic study population unclear in this article	II (risk stratification)
Graham and Kenny[25]	2001	Prospective	62 patients with >2 episodes of syncope in the past y referred for additional testing; those who had a positive tilt table test and no other identified cause for syncope were assigned a diagnosis of vasovagal syncope	Tilt-table testing was performed using a standard protocol	Patients identified as vasodepressor syncope by virtue of positive tilt test were given a questionnaire; up to one third lacked traditional symptoms associated with vasodepressor syncope; atypical presentations of vasovagal syncope occur in many patients referred to a tertiary referral center; knowledge of the clinical characteristics of unexplained syncope for which vasovagal syncope was the determined diagnosis should assist in appropriate management of such patients	Selection/referral bias; no true criterion standard for diagnosis	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Oh et al[31]	1999	Prospective cohort	Interview and review of chart to obtain information on 19 symptoms and comorbidities	Arrhythmias, mortality, or recurrent syncope	497 patients enrolled; in 222 cause of syncope established by history and physical examination; in the other 275, the absence of nausea and vomiting or presence of eletrocardiographic abnormalities were predictive of arrhythmic syncope; underlying cardiac disease was the only predictor of 1-y mortality; symptoms were not useful in risk stratification	Selection bias by study population from tertiary syncope center	II
Kapoor and Hanusa[32]	1996	Prospective case control	470 syncope patients and 470 matched patients without syncope	The characteristics of 470 patients with syncope were similar, except that the patients without syncope had more cardiac diseases than those with syncope	Syncope itself is not a risk factor for overall and cardiac mortality or cardiovascular events; underlying heart diseases were risk factors for mortality regardless of whether the patient had syncope or not	For subgroups with important prognostic differences, adjustments were made for these factors; assessment of outcomes was blinded; follow-up was sufficiently long and complete; survival curves are presented	II
Middlekauff et al[33]	1993	Population with advanced heart failure prospectively identified; retrospective review of historical information and diagnostic tests	The relation of syncope to sudden death was evaluated in 491 consecutive patients with advanced heart failure, no history of cardiac arrest, and a mean left ventricular ejection fraction of 0.20±0.07; syncope patients (60) and nonsyncope patients (431) with CHF class III-IV were compared	60 patients (12%) had a history of syncope; syncope had a cardiac origin in 29 (48%) and was due to other causes in 31 (52%); sudden death was primary endpoint	Patients with advanced heart failure are at especially high risk for sudden death regardless of the etiology of syncope	Control group much larger than reference group; all patients in same stage of disease (NYHA 3-4, no history of cardiac arrest and LVEF 0.20±0.07); selected group	II
Sarasin et al[34]	2002	Prospective	Orthostatic blood pressure changes were measured in a standardized fashion for up to 10 min, or until symptoms occurred, in consecutive patients with syncope as a chief complaint	Orthostatic blood pressure changes	According to diagnostic criteria, orthostatic hypotension was considered to be the cause of syncope in 156 patients (24%); 58 patients (37%) had drug-induced hypotension; 33 (21%) had hypovolemia; 19 (12%) had post-prandial hypotension; and 46 (29%) had idiopathic hypotension	788 patients with syncope seen, but because of refusal or incomplete data, only 650 included in the study; 579 (89%) had standardized measurements of systolic blood pressure with other exclusions including inability to stand up	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/ Test(s)/Modality	Outcome Measure/ Criterion Standard	Results	Limitations/Comments	Class
Eagle and Black[36]	1983	Retrospective	100 patients admitted to the hospital for evaluation of syncope		In 39 patients, no etiology for syncope was found, and another 18 were thought to have had a vasovagal episode; 12 patients had arrhythmias as the cause for syncope	Study includes hospital testing but no follow-up beyond initial evaluation; no standard evaluation; difficult to use for risk stratification because of selection bias	III
Sarasin et al[40]	2002	Prospective	650 consecutive patients with syncope and clinical suspicion of an obstructive valvular, or with syncope not explained by history, physical examination, or ECG underwent echocardiography	The causes of syncope were assigned using published diagnostic criteria	Echocardiography was useful only in patients with abnormal ECG results, history of cardiac disease, or symptoms and signs of aortic stenosis	Small sample size of patients with unexplained syncope	II (risk stratification)
Morag et al[41]	2004	Prospective, short-term outcomes study	45 patients met inclusion criteria: nondiagnostic ED evaluation; 67% were hospitalized on monitored bed	Intervention for arrhythmia during hospitalization; interviews at 1 mo	This pilot study suggests that a negative-structured ED evaluation may identify patients ≥50 y of age who may be safely discharged from the ED; none of the patients experienced a life-threatening event or required significant therapeutic interventions during hospitalization; no patient had a new diagnosis relevant to syncope	Study raises question: is hospitalization necessary; however, sample size too small to assess; no control group used; outcomes defined at the start of the study; patients in different stages in their disease	III
Shen et al[42]	2004	Prospective	Patients were randomly allocated to 2 treatment arms: syncope unit evaluation and standard care; 103 consecutive patients entered the study	Presumptive diagnosis, hospitalization rate, and patient hospital days	103 consecutive patients with syncope; 51 patients were randomized to the syncope unit; for syncope unit patients, the presumptive diagnosis was established in 34 (67%) vs 5 (10%) of standard care patients; total patient hospital days were reduced from 140 to 64	Randomized trial for ED observation unit for intermediate risk syncope; small numbers and fairly sophisticated evaluations in the ED limit generalizability; selection bias: selected intermediate risk group	II (risk stratification) III (admission)

ACP, American College of Physicians; *CHF*, congestive heart failure; *ECG*, electrocardiogram; *ED*, emergency department; *LVEF*, left ventricular ejection fraction; *LR*, likelihood ratio; *min*, minute; *mo*, month; *NYHA*, New York Heart Association; *ROC*, receiver operating characteristic; *y*, year.

Appendix A. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analyses of randomized trials	Prospective cohort using a criterion standard	Population prospective cohort
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing ≥2 interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X