

# Syncope: Overview and approach to management

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## Introduction

Syncope is a common, important medical problem caused by many conditions, ranging from benign and self-limiting to chronic, recurrent, and potentially fatal causes. Unfortunately, differentiation between benign and malignant causes can be difficult and challenging. Even with knowledge of common syndromes and conditions that cause syncope, and guidelines [1], an effective approach to the problem requires careful integration of clues provided in the history and physical examination combined with keen clinical acumen. Management of this baffling problem can be frustrating, confusing, and often unrewarding. Treatment can be impossible to prescribe without a clear understanding of the cause, and treatments may be directed to risk as well as symptom reduction.

Fortunately, experienced, astute, circumspect clinicians can deliver effective care when careful attention is paid to detail. This chapter considers a general overview of the problem of syncope and provides guidelines on how to approach management. Reference is given to other chapters in this book that provide more detail on specific topics.

## Definitions

Syncope is often considered with several more vague symptoms that are manifestations of many clinical conditions. “Spells,” transient confusion or weakness, dizziness, loss of memory, lightheadedness, near loss of consciousness (“presyncope” or

“near-syncope”), falling episodes, and coma are often confused with, and inappropriately labeled as, “true” syncope. Distinction between sleeping, confusion, intoxication, and fainting may not be completely clear. To make matters more difficult, an elderly patient, already confused, may fall and pass out with only vague recall of the event. Such a patient may even think he or she passed out when nothing of the sort occurred. This diverse collection of clinical presentations perplexes the patient and the physician. Episodes can be difficult to define even with careful observation, and the mechanism may be confusing even with extensive monitoring.

True syncope is an abrupt but transient loss of consciousness associated with absence of postural tone followed by rapid, usually complete, recovery without the need for intervention to stop the episode. A prodrome may be present. While alarming, this *symptom* is non-specific. It is generally triggered by a process that results in abrupt, transient (5–20 s) interruption of cerebral blood flow, specifically to the reticular activating system.

Collapse, associated with syncope, can be misinterpreted. In one study of 121 patients admitted to the emergency room with “collapse” as the admitting diagnosis, 19 had cardiac arrest, four were brought in dead and one was asleep [2]. Only 15 were ultimately diagnosed as having fainted. The final diagnosis in eight was still “collapse.” Primary neurological or metabolic derangements can also mimic, but rarely cause, true syncope. Also, syncope can mimic a seizure or a metabolic derangement.

## Importance of syncope

*“The only difference between syncope and sudden death is that in one you wake up.”*

[3] (vive la différence) [4]

*Syncope can be the premonitory sign of a serious cardiac problem including cardiac arrest.* Generally, syncope is benign and self-limited but it can mimic a cardiac arrest and even be its precursor. Several causes for syncope, generally cardiac, are potentially fatal. When syncope is caused by hemodynamic collapse from critical aortic stenosis, ventricular tachycardia, AV block, dissecting aortic aneurysm, or pulmonary embolus, an aggressive evaluation and treatment regimen is needed to forestall death. A potentially lethal cause should always be suspected, especially in elderly patients, or it will be missed [5,6]. While less common, even younger individuals with syncope can be at risk of death [7]. For this age group, the congenital long QT interval syndrome, hypertrophic cardiomyopathy, right ventricular dysplasia, Brugada syndrome, polymorphic ventricular tachycardia with associated short or normal QT interval, congenital aortic stenosis, among other causes, must be considered. Even apparently healthy individuals can die suddenly after a syncopal episode (consider the death of basketball star Reggie Lewis [8]).

*Syncope can have a major impact on lifestyle.* Patients’ reactions to syncope can vary from complete lack of recognition and concern, to fear and difficulty returning to previous level of activities with complete disability. Even if syncope is benign, it can have a major impact on quality of life and may change lifestyle dramatically, independent of physicians’ concerns and recommendations. The degree of functional impairment from syncope can match that of other chronic diseases, including rheumatoid arthritis, chronic back pain, or chronic obstructive lung disease [9]. Patients can have fear of recurrence and excessive fear of dying. There can be imposed limitations on driving and work (see Chapter 20). Restrictions can be self-imposed, imposed by the family, by the physician, or by legal constraints (see Chapter 21). Up to 76% of patients will change some activities of daily living, 64% will restrict their driving, and 39% will change their

employment [9]. Seventy-three percent become anxious or depressed, especially if a cause is not found and treated [10,11].

*Syncope can cause injuries.* Injuries from syncope occur in 17–35% of patients [12–16]. When injuries occur, syncope is often suspected to be caused by a serious, life-threatening, or cardiac cause, but data conflict [16,17]. Sudden, *unexpected* loss of consciousness (sometimes referred to as “Stokes–Adams” attacks) can have many causes. The circumstances that surround the episode and absence of a warning prodrome cause most injuries. Injury itself does not necessarily indicate a life-threatening, cardiac, or arrhythmic cause for syncope, although sudden collapse with injury has been associated with an arrhythmic cause. While an arrhythmic cause is often suspected when serious injury results from syncope, few compelling data support the need for a more aggressive approach to evaluate or to treat syncope in injured patients. Minor injuries occur in 10–29%, fractures occur in 5–7% (more severe in the elderly), and traffic accidents in 1–5% of syncope patients [18,19].

*Syncope is expensive.* Up to one million patients annually are evaluated for syncope in the USA, with 500,000 new cases each year. Approximately 3–5% of emergency room visits are to evaluate syncope [14,20], emergency room visits leading to hospital admission [13]. Between 1 and 6% of acute hospital admissions are for syncope. The cost to evaluate and treat syncope exceeds \$750 million/year. The cost for the average admission is more than \$5500 [20] and hospitalization is helpful in only 10% of patients admitted in whom the etiology was not clear by the admitting history, physical examination, and electrocardiogram (ECG). The cost expended to determine one syncope diagnosis in patients diagnosed in 1982 was \$23,000 [20] after a mean hospital stay of 9.1 days. When vasodepressor syncope is not recognized, evaluations can lead to tremendous expense [21]. The costs per diagnosis can be as high as \$78,000, depending on the tests performed and the diagnostic accuracy. The average patient with syncope makes 10.2 visits/year to a physician and sees an average of 3.2 specialists for the problem [22].

Approximately 10% of falls in the elderly are

caused by syncope [23]. Serious injury is more frequent when syncope precedes the fall [24–30]. Falls occur in 20% of the population over 65 years old. The cost to treat falls in the elderly exceeds \$7 billion/year in the USA [23]. It is a common cause for disability.

## Epidemiology

The frequency of syncope and its associated mortality varies with age, gender, and cause. In one large series, 60% of syncope patients were women [14], but in the Framingham study more younger syncope patients were women while more elderly syncope patients were men [24]. In the Framingham study, syncope had occurred in 3% of men and 3.5% of women, based on biannual examinations [24], with the highest frequency in the elderly. In the Framingham population, the annual incidence of syncope for those over 75 years old was 6% and the prevalence of syncope in the elderly was 5.6%, compared with a low of 0.7% in the 35–44-year-old male population [24]. The elderly are most likely to have syncope, to be injured from syncope, to seek medical advice, and to be admitted to a hospital [31,32] (see Chapter 18).

Of 3000 US Air Force personnel queried (mean age 29.1 years), 2.7% (82 of 3000) had at least one episode of syncope [33]. Other retrospective studies of healthy individuals suggest that up to 40% will pass out [34,35]. The population evaluated (outpatients, emergency room patients, hospitalized patients, the elderly), the definition of syncope, and the criteria for diagnosis (by examination or questionnaire), contribute to wide variations in published data. Probably, 20–30% of the population will pass out sometime in their lifetime [14,36,37]. Most individuals with syncope do not seek medical advice but the actual percentage of those who do is unknown. It is suspected that most individuals who do not seek medical attention have a low recurrence rate and probably have an excellent long-term survival. Outpatients evaluated or never admitted for their episodes *may* also be at lower risk for recurrence and *may* have a more benign long-term prognosis. Patients in these subgroups probably have neurocardiogenic syncope or some other autonomically mediated or situational cause for collapse.

Forty to eighty-five percent of those who come for evaluation of syncope will not have a recurrence [38]. Isolated episodes are common: 90% will have only one episode in 2 years, yet 54% with two episodes have recurrence over the same time period [39]. The recurrence rate of syncope remains similar despite widely different suspected causes (severe cardiovascular disease or not) and despite apparently effective treatment [38]. The fact that syncope is frequently an isolated occurrence can make it difficult to diagnose and difficult to assess the need for treatment (it may or may not recur). An apparent therapeutic effect of any intervention may instead be related to the sporadic nature of the symptom and not to treatment of the underlying process [38,40,41]. An older report suggested that tonsillar enlargement caused tachycardia and syncope [42]. Following tonsillectomy, syncope did not recur. Therefore, tonsillectomy was assumed to prevent recurrent syncope. While ludicrous, it is important to recognize the similarity to modern thinking on this same topic.

Even without treatment, syncope can remain dormant for a protracted period or “respond” to the apparent effect of the evaluation itself. Indeed, many benign forms of syncope seem to be heavily influenced by placebo. However, the goal of therapy, to reduce the frequency and severity of episodes, is achievable. It appears that syncope is less likely to recur when its cause is diagnosed properly and treated effectively [43–45].

## The differential diagnosis

With so many potential causes for syncope, it is difficult, if not impossible, to provide a complete reference list of all common and uncommon causes (Tables 1.1 and 1.2). New and creative ways to pass out are always possible [46–53], and some syncope is not really syncope at all [54–56]. Syncope has its fads [57–62]; consider the “mess trick” (the fainting lark [61,62]) of the Valsalva maneuver during hyperventilation. This rarely causes syncope now but mass fainting at rock concerts is possible [59]. Syncope has even been reported with sushi ingestion [63].

An old, retrospective study [57], representing a large collection of patients with syncope, provides insight into the most common causes and myths

**Table 1.1** Common causes for syncope.

<i>Cardiovascular disease</i>	<i>Non-cardiovascular disease</i>	<i>Other</i>
Arrhythmic	Reflex mechanisms	Syncope of unknown origin
AV block with bradycardia	Vasodepressor “neurocardiogenic”	About 50% of all syncope patients
Sinus pauses/bradycardia	Micturition	Undiagnosed seizures
Ventricular tachycardia and structural heart disease	Deglutition	Improperly diagnosed syncope
Non-arrhythmic – hemodynamic	Orthostatic hypotension	Confusional states due to hypoglycemia, stroke, etc.
Hypertrophic cardiomyopathy	Dysautonomia	Drug induced
Aortic stenosis	Fluid depletion	Alcohol
	Illness, bed rest	Illicit drugs
	Drugs	Prescribed drugs (esp. the elderly)
	Psychogenic	
	Hysterical	
	Panic disorder	
	Anxiety disorder	

**Table 1.2** Uncommon causes for syncope.

<i>Cardiovascular disease</i>	<i>Non-cardiovascular disease</i>
Arrhythmic etiology	Reflexes
Supraventricular tachycardia	Post-tussive
Long QT interval syndrome	Defecation
Brugada syndrome	Glossopharyngeal
Arrhythmogenic right ventricular cardiomyopathy	Postprandial
Idiopathic ventricular tachycardia(s)	Carotid sinus hypersensitivity
Myocardial infarction (and bradycardia/tachycardia)	Hyperventilation
Non-arrhythmic etiology	Migraine
Pulmonary embolus	Carcinoid syndrome
Pulmonary hypertension	Systemic mastocytosis
Dissecting aortic aneurysm	Metabolic
Subclavian steal	Hypoglycemia
Atrial myxoma	Hypoxia
Cardiac tamponade	Multivessel cerebrovascular disease

regarding syncope. Between 1945 and 1957, of a total cohort of approximately 1000 syncope patients, data from 510 patients were evaluated [57]. The remaining patient charts were “unsatisfactory for analysis.” In contrast to more recent data, a cause for syncope was diagnosed in nearly all (96%) of the patients (Table 1.3). Is this amazing clinical acumen? Perhaps. More likely, though, the diagnoses were a “best guess” with few, if any, confirmatory data.

Data from the Framingham study provide new insights into the differential diagnosis of syncope in the modern era and provide the outcome of these

patients [64]. Of 727 patients with syncope, the cause was vasovagal in 21%, orthostatic hypotension in 9.4%, cardiac causes in 9.5%, seizures in 4.9%, stroke or transient ischemic attack in 4.1%, medication related in 6.8%, and other in 7.5%. Of importance, even with modern methods to assess cause, syncope was a result of an unknown cause in 36.6% (31% of men and 41% of women) [64].

In a report of five pooled studies, the etiology of syncope was vasovagal in 18%, situational in 5%, orthostatic in 8%, cardiac in 18%, medication related in 3%, psychiatric in 2%, neurological in 10%, carotid sinus hypersensitivity related in 1%, and

**Table 1.3** Breakdown of various causes of syncope in an older retrospective study of 510 patients. Although an accurate cause for syncope may not be diagnosed from the data, interesting conclusions may be drawn. (Data from [57].)

<i>Presumed cause for syncope</i>	<i>Number</i>
Vasovagal	298
Orthostatic hypotension	28
Epilepsy	26
Cerebrovascular disease	24
Unknown etiology	23
Postmicturition	17
Stokes–Adams attacks	17
Hyperventilation	15
Hypersensitive carotid sinus	15
Tussive	13
Aortic stenosis	9
Paroxysmal tachycardia	8
Angina	4
Hysteria	4
Myocardial infarction	3
Pulmonary hypertension	2
Migraine	2
Hypertensive encephalopathy	2

unknown in 34% [65,66]. The presence of cardiac disease does not indicate the cause for syncope is cardiac or is even known [67].

## Common causes for syncope

### Neurocardiogenic (vasovagal) syncope

A vasovagal episode is the most common cause for syncope [57,64,66] (Table 1.3). Vasovagal (neurocardiogenic) mechanisms may account for, or contribute to (in the presence of other clinical conditions), 30–80% of all syncopal episodes [13,15,33,35,37,68–71]. Recent data from several studies confirm that neurocardiogenic syncope is the most common etiology of syncope.

Neurocardiogenic syncope can be caused by, or provoked by, several inciting, often noxious, stimuli. The specific stimulus can be difficult to characterize, can be highly individualized, and can vary by physical and emotional state [3]. Emotional stresses alone (danger, real or perceived, fear, or anxiety) are common triggers [3,72] and distinctly human [73]. The responsible reflex causing syncope can be “normal” and may be self-limited.

When a specific set of conditions initiates syncope, it is termed “situational syncope” [71]. For example, the vasovagal (neurocardiogenic) reflex can occur with severe volume loss resulting from diarrhea or blood loss and may never recur. Complete evaluation and long-term drug therapy is indicated only when episodes recur frequently and cannot be explained by a precipitating cause (see Chapter 2). Sometimes it is difficult to discover an initiating factor responsible for the complex vasovagal reflex so that the diagnosis is not clear. This may explain, in part, the wide variation in the frequency of the diagnosis of neurocardiogenic syncope between reports.

While neurocardiogenic causes for syncope are generally benign, a syndrome of “malignant” vasovagal syncope has been used to describe patients who have frequent and recurrent episodes, who have episodes without obvious prodrome, who have prolonged asystole, and/or who have spells without an apparent triggering stimulus [74–78]. The specific implications of having this form of neurocardiogenic syncope are unclear regarding prognosis and treatment but these patients do not necessarily require more aggressive therapy [79,80]. Testing the response to orthostatic stress (tilt table testing) can secure the diagnosis for these individuals [81] (see Chapters 2, 7 and 13). An even more malignant, poorly understood, vasovagal reflex might also (rarely) cause death by asystole in some patients with severely impaired left ventricular function [6,82] and in others [83].

### Orthostatic hypotension

The second most common cause of syncope is orthostatic hypotension [57] (Table 1.3). This problem is often overlooked, underdiagnosed, and incompletely evaluated. Orthostatic hypotension [84–92] has many etiologies (see Chapters 3 and 13) but is generally caused by a dysautonomic syndrome, drugs, volume depletion (e.g., blood loss), or a combination of factors each of which, alone, would have no effect. Peripheral autonomic (sympathetic) denervation, resulting from systemic diseases including diabetes and amyloidosis [93,94], can prevent needed peripheral vasoconstriction with standing. Additional specific disease states besides, most commonly diabetes [95], that can cause this condition include Parkinsonism [96], Addison’s disease [97],

porphyria [98], tabes dorsalis [99], syringomyelia [100], spinal cord transection [101], Guillain-Barré syndrome [102], Riley-Day syndrome [103], surgically induced sympathectomy [104], pheochromocytoma [105], multisystem atrophy [106], Bradbury-Eggleston syndrome [107], and the Shy-Drager syndrome (also known as idiopathic orthostatic hypotension) [108–113]. It can even occur with anorexia nervosa [114].

The elderly are most susceptible to conditions that test the resiliency of their response to orthostatic stress [115–117], particularly if there is another trigger (such as a non-sustained tachyarrhythmia or a vasodilator, even if the patient is otherwise hypertensive). Elderly patients frequently have difficulty with effective autoregulation of peripheral and cerebral blood flow and are highly susceptible to symptomatic orthostatic hypotension [85, 118–123]. The elderly tend to have slower heart rates at baseline [122,124] and they tend to be more hypertension at night [125]. Orthostatic hypotension and its treatment are discussed in Chapters 3 and 13.

Medications can cause syncope by a variety of mechanisms, including, commonly, orthostatic hypotension. Nearly 13% of syncopal and pre-syncopal spells in patients who presented to an ambulatory clinic were caused by an adverse drug reaction [126]. Vasodilators (hydralazine, nitrates, angiotensin-converting enzyme inhibitors),  $\alpha_1$ - and  $\beta$ -adrenergic blockers and  $\alpha_2$ -adrenergic stimulants, diuretics, tricyclic antidepressants and phenothiazines, and others, can cause orthostatic hypotension [126]. Nitrates can also trigger a hypotensive, vagal, or other autonomic response [127–129]; to wit, they may be used in the tilt table laboratory. Non-steroidal anti-inflammatory drugs can decrease peripheral vascular resistance and its response to orthostatic stress [126,130]. Hypokalemia can impair reactivity of vascular smooth muscle and limit increase in peripheral vascular resistance.

Volume depletion from blood loss or diuretic use commonly causes orthostatic hypotension. Prolonged bed rest or chronic illness can provoke or exacerbate transient orthostatic hypotension in vulnerable patients, such as the elderly or those with diabetes. Even normal individuals at prolonged bed rest, especially if volume depleted, may

pass out abruptly on rising. Water ingestion or even eating a meal can help by several mechanisms including, but not limited to, fluid repletion [131–133]. Rarely, inherent circulating vasodilators present in a vasoactive intestinal peptide tumor (VIPoma), the carcinoid syndrome, a prolactinoma, or systemic mastocytosis can cause orthostatic hypotension and, rarely, syncope [134–141]. Of note, prolactin levels can be elevated after syncope or a seizure [142,143].

The response to changes in position can be immediate or delayed. As part of the physical examination, orthostatic signs should always be obtained but change in blood pressure may be seen soon after standing in fluid depletion, or may require several minutes of standing for dysautonomic conditions. An orthostatic change (lowering) in blood pressure, without a compensatory change (increase) in heart rate, suggests an autonomic neuropathy.

### Arrhythmic causes

Surprisingly, “paroxysmal tachycardia” and “Stokes-Adams attacks” were suspected as a rare cause for syncope in older studies [57] (Table 1.3). Cardiac and cardiac arrhythmic causes are now suspected to be more common [64]. However, Donzelot described syncope resulting from ventricular tachycardia in 1914 [144] and Barnes [42] described cerebral symptoms of paroxysmal tachycardia in 1926. Cardiac rhythm disturbances, bradycardias, and tachycardias are now well known to be a common cause for syncope [44]. The arrhythmias can be benign (not associated with death) or malignant (associated with increased risk of death). In earlier studies, techniques to detect cardiac arrhythmias were lacking [57]. Now, with more sophisticated diagnostic tools (prolonged monitoring techniques and electrophysiologic tests), a primary arrhythmic etiology can be more easily identified. Common rhythm disturbances associated with syncope include paroxysms of ventricular tachycardia, AV block associated with bradycardia, and marked sinus bradycardia (sick sinus syndrome and tachy-brady syndrome).

Organic heart disease, especially in association with impaired left ventricular function, a bundle branch block, a long QT interval, or pre-excitation (Wolff-Parkinson-White syndrome) should raise suspicions of an arrhythmic etiology for syncope.

Arrhythmic syncope, caused by AV block (generally second or third degree) or ventricular tachycardia, tends to have an abrupt onset with no prodrome (“Stokes–Adams” attack, not *specific* for arrhythmic etiology for syncope). It may have a malignant course (associated with cardiac arrest) and be distinguishable from neurocardiogenic syncope [145], or mimic other causes for syncope.

Supraventricular tachycardia (AV nodal re-entry or AV reciprocating tachycardia), atrial flutter, and fibrillation, while generally benign, can occasionally cause syncope but there is usually a history of palpitations or tachycardia [146]. Up to 15% of patients with supraventricular tachycardia will have syncope or near-syncope brought about by the tachycardia [147].

Atrial fibrillation rarely causes syncope unless the ventricular rate is excessively fast or slow. Slow rates tend to occur in the elderly because of autonomic changes [120–124] or AV nodal dysfunction, whereas fast rates can occur in younger patients with Wolff–Parkinson–White syndrome or with enhanced AV nodal conduction [148].

There are special subgroups of arrhythmias that are important to consider. Short paroxysms of asymptomatic, non-sustained, ventricular tachycardia can be problematic and, while sometimes ascribed to be the cause for syncope [15], the two may be unrelated. Sinus arrest can cause syncope. While generally resulting from intrinsic sinus node disease causing sick sinus syndrome or tachybrady syndrome, it can be difficult to distinguish intrinsic sinus node disease from accentuated vagal tone. Ventricular bigeminy can be associated with hypotension and a slow pulse but almost never with syncope. Ventricular pacing may cause dizziness and weakness but rarely loss of consciousness [149]. However, patients with pacemakers may have syncope from abrupt pacemaker failure or other, unrelated causes, including malignant neurocardiogenic syncope [149–151].

A special subgroup includes patients who have implanted defibrillators. When a patient with an implanted cardioverter defibrillator (ICD) passes out, a recurrent ventricular arrhythmia must be suspected. Careful assessment of the functioning of the ICD and of the underlying rhythm is required. There may be a need to restrict the patient with an ICD if the syncope is caused by an arrhythmia.

Physiologically, tachycardias are less well tolerated hemodynamically than bradycardias, whether or not AV synchrony is present. The *abrupt onset* of the arrhythmia, even when otherwise tolerated, can cause syncope [152,153]. Ventricular tachycardia is usually less well tolerated than supraventricular tachycardia, even at the same heart rate, but hemodynamics worsen with increasing rates [154]. Syncope, however, is most directly related to an abrupt change in the rate, caused by lack of effective reflex peripheral vascular vasoconstriction and ineffective accommodation of cerebral blood flow [42,152].

Chronic sinus bradycardia is much less of a problem than is sinus rhythm with abrupt sinus arrest. Persistent atrial flutter or ventricular tachycardia is less likely to cause syncope than is a paroxysm of the same tachycardia, even at the same rate. It is common for the blood pressure to drop at the onset of tachycardia causing syncope but, over several seconds, the blood pressure can rise and syncope can resolve despite continuation of tachycardia [155–157], resulting from reflex vasoconstriction and elevation in catecholamine levels. Ventricular function, body position, and medications all influence the hemodynamic response to and presence of changes in heart rate, and the presence and length of syncope [158]. The presence of sustained ventricular tachycardia alone does not always explain syncope because it does not always cause syncope. In one series, only 15% of patients who presented to an emergency room with sustained ventricular tachycardia had syncope associated with tachycardia [40].

An arrhythmia present at the time of syncope may be a secondary phenomenon or unrelated and may not be explanatory. Treatment of the arrhythmia would therefore not treat syncope effectively. An example is a patient with a vasovagal spell who develops a “relative” bradycardia after hypotension and after syncope had already started. Treating the bradycardia (with a pacemaker) would not be expected to correct a primary peripheral hemodynamic or central nervous system problem but each case must be considered individually [159]. In neurocardiogenic syncope, when bradycardia is a secondary issue, it is not surprising that its treatment may not help syncope recurrence.

*Case 1*

A 50-year-old avid bicyclist has recurrent syncope at rest (after exercise) with associated AV block and > 8-s pauses but the sinus rate did not slow. Carotid sinus massage was negative. A tilt table test was positive for hypotension and relative. On the treadmill, his heart rate exceeded  $180 \text{ b min}^{-1}$ . He refused to stop exercising. The cause for his AV block was unclear but may have been autonomically mediated.

*Therapy.* A permanent dual chamber pacemaker was placed with complete improvement in symptoms.

*Case 2*

A 45-year-old woman has recurrent syncope and on a Holter monitor had 8-s pauses resulting from sinus arrest. A permanent pacemaker was placed but she continued to pass out. A tilt table test was subsequently positive for hypotension and syncope despite AV pacing.

**Seizures**

Seizures can be mistaken for syncope and vice versa [57,160–167] (Table 1.3). Generally, it is not difficult to distinguish seizures from syncope [166]. When there is confusion, it is most likely that neurocardiogenic syncope is confused with seizures (“convulsive syncope”). A possible exception to this rule is akinetic seizures. The episodes are manifest by abrupt loss of consciousness and dropping to the ground. The episodes may be so violent that the patient appears to be thrown to the ground. As opposed to generalized seizures, at the end of an episode, the patient appears normal and has no postictal drowsiness. The seizures themselves are quite brief but their sudden and unpredictable nature may lead to injury. Myoclonic jerks may precede the attacks and the episodes tend to occur while going to sleep at night or on awakening in the morning. This type of seizure is most common in the 2–5 year pediatric age range but cases have been observed in older children. The electroencephalogram (EEG) is usually markedly abnormal, demonstrating either generalized or multifocal epileptiform discharges. This form of seizure is exceedingly difficult to treat. The usual antiseizure medications are often ineffective, although some patients may respond to valproic acid or a benzodiazepine. Some authors have recommended section

of the corpus callosum in patients with medically intractable seizures that result in repeated injury [168], but this is controversial. Some patients have responded to a medium-chain triglyceride (MCT 3) variant of the ketogenic diet [169].

The incidence of seizure diagnoses as cause for syncope varies widely between reports [13,16]. Hofnagels *et al.* [162] noted that only 31% of physicians caring for patients with “spells” could agree whether or not seizure was the cause. The distinction can be especially difficult if seizures are atypical or episodes are unwitnessed. This problem is compounded by the lack of sensitivity and specificity of the EEG as it is generally performed.

An EEG, by itself, cannot be relied upon to diagnose a seizure disorder. Up to 50% of patients who have a seizure focus will have a negative EEG unless sleep deprivation is used or unless nasopharyngeal leads or deep brainstem leads are placed [161,170–173] (see Chapter 9). To complicate matters, up to 40% of asymptomatic elderly individuals will have asymptomatic electroencephalographic abnormalities. These abnormalities do not imply seizure is the cause for the episode. Nevertheless, seizures likely account for 10–15% of apparent syncopal episodes [16,57]. However, patients with seizures rarely have episodes with sudden onset and abrupt, rapid recovery. Instead, the postictal state is slow and lingering. The tilt table test may be useful to distinguish seizure from syncope [160] and creatine kinase measurements may also be helpful [174].

Alternatively, syncope, with loss of cerebral blood flow, can cause tonic–clonic movements and can mimic a seizure [175]. This apparent seizure activity is associated with slowing of the brain waves not with epileptiform spikes on the EEG. Sometimes, a video EEG is required to determine if a seizure is indeed present.

*Case 3*

A 27-year-old woman with primary pulmonary hypertension has prolonged and frequent episodes of loss of consciousness. Tonic–clonic movements are noted and recovery is prolonged. A video EEG showed a flat recording during an episode. During combined hemodynamic and video EEG recordings, it was discovered that she has apnea, hypotension followed by sinus tachycardia, and asystole with an episode. The “seizure” is syncope. This is a

fairly typical autonomic response for a patient with this condition.

Temporal lobe epilepsy can rarely trigger neurocardiogenic syncope [176]. Also, asystole can masquerade as temporal lobe epilepsy [177].

### **Micturition syncope and syncope resulting from other autonomic causes**

Micturition syncope is one of several variations of autonomically mediated syncope which include deglutition syncope, carotid sinus hypersensitivity, post-tussive syncope, defecation syncope, and trumpet player's syncope [33,57,178]. The mechanism for these forms of syncope are related to abrupt changes in autonomic tone, in intravascular volume, and in cerebrospinal fluid pressure. Specifically, micturition syncope is a result of an abrupt change in position combined with a strong vagal stimulus. Micturition syncope can occur in either sex. Kapoor *et al.* [179] reported that women (in contrast to previous studies suggesting a clear male predominance) have a higher incidence of syncope caused by evening micturition.

While the exact mechanisms for these entities may not be identical, the autonomic nervous system appears to be critically involved in the initiation of the episode. Generally, all causes for syncope appear to involve a poorly tolerated hemodynamic response to specific autonomic cardiovascular reflexes. Autonomic reflexes are often critical in the initiation and termination of syncope, or the presence of the pre-existing problems would allow patients to lose consciousness continuously.

#### *Case 4* [56]

A 72-year-old man passes out after drinking cold, carbonated beverages. Syncope causes a major motor vehicle accident. He has a complete evaluation by cardiologists and internists, including a cardiac catheterization, tilt table test, treadmill test, EEG, and magnetic resonance imaging (MRI) of the brain. The diagnosis was secured by observing him and his heart rhythm while he drank a cold can of soda.

*Diagnosis.* Deglutition syncope resulting from cold, carbonated beverages.

*Therapy.* Avoidance of cold, carbonated beverages eliminated the problem.

#### *Case 5*

A 52-year-old man with reactive airways disease and chronic aspiration caused by gastroesophageal reflux has recurrent syncope after prolonged episodes of coughing. Syncope resolved after effective therapy for his pulmonary problems.

*Diagnosis.* Post-tussive syncope.

#### *Case 6*

A 58-year-old man became asystolic during abdominal surgery during peritoneal manipulation. He gives a history of syncope when he drinks cold liquids and was noted to become asystolic (AV block and sinus arrest are both noted on different occasions) while drinking iced water. Carotid massage caused 7 s of symptomatic asystole. Temporary ventricular pacing during carotid massage was associated with hypotension, but with dual chamber pacing the blood pressure remained above 100 mmHg systolic.

*Diagnosis.* Deglutition syncope.

*Therapy.* With permanent pacing, he remained asymptomatic for 7 years.

#### *Case 7*

An 85-year-old man with a history of coronary artery disease and benign prostatic hypertrophy has taken furosemide, digoxin, and captopril for mild congestive heart failure. He passed out suddenly when awakening to urinate. There was a 15-mmHg drop in blood pressure with standing.

*Diagnosis.* Micturition syncope.

*Therapy.* The patient was warned to arise slowly before urinating in the evening and to sit when urinating.

### **Uncommon, but important, causes for syncope** **Cerebrovascular disease**

Cerebrovascular disease is an uncommon and probably overdiagnosed cause for syncope. Stroke and transient ischemic attacks tend to cause focal neurologic deficits from which recovery is slow and incomplete. If posterior cerebral circulation is

impaired, symptoms such as nausea or dizziness are more likely than transient loss of consciousness. If the anterior circulation is impaired, a focal neurologic defect will occur. Severe, obstructive, multi-vessel cerebrovascular disease can cause syncope but other neurologic findings will likely occur first and will likely persist after syncope.

### **Myocardial ischemia and myocardial infarction**

Syncope is often suspected to be caused by myocardial infarction or ischemia, thus resulting in hospital admission to “rule out” myocardial infarction and assess ischemia. This process is usually unnecessary and unwarranted because myocardial infarction rarely causes syncope [57,180]. If myocardial infarction or ischemia is the cause for syncope, there are generally obvious clues from the history and from the ECG [180]. One potential cause for syncope is bradycardia and hypotension from the Bezold–Jarisch reflex [181], but other arrhythmic and non-arrhythmic causes related to ischemia and infarction are possible.

### **Other cardiac causes for syncope**

Obstructive valvular lesions, such as aortic stenosis and hypertrophic cardiomyopathy, are well-recognized but relatively rare causes of syncope [13,16,182–184]. Other obstructive valvular lesions, such as atrial myxoma and atrial ball valve thrombus, are even rarer. Obstructive lesions such as aortic stenosis tend to cause an exaggerated and malignant form of an exercise-induced vasovagal response leading to syncope and perhaps even death [185]. Other forms of syncope can be confused with obstructive hemodynamic problems [186]. The obstruction itself may not be the direct cause for collapse. When aortic stenosis causes syncope, the episodes tend to be markedly prolonged. Episodes can be triggered by exertion.

### **Metabolic causes**

Syncope, characterized by abrupt onset and complete, brisk recovery, is rarely a result of a toxic or metabolic cause. Hypoglycemia, hypoxia, meningitis, encephalitis, and sepsis can cause coma, stupor, and confusion, but rarely syncope [187]. Hypoxia can, however, influence vascular tone [188]. If a patient does not recall the history surrounding the

event or if the event was unwitnessed, coma and syncope can be hard to distinguish.

### **Neurologic and psychiatric causes**

Neurally mediated (neurocardiogenic) syncope can mimic transient ischemic attacks [189]. Psychiatric causes for syncope can mimic neurocardiogenic syncope [190]. There are several neurologic and psychiatric causes for syncope, which are discussed in detail in Chapters 9 and 12 [191,192].

#### *Case 8*

A 32-year-old woman was referred for a tilt table test for recurrent episodes of loss of consciousness associated with a prodrome of nausea and vomiting. Upon further questioning, the patient described quadriparesis with near-blindness after the episode while awake.

*Diagnosis.* Migraine headaches.

### **Syncope of unknown origin**

In older studies, hardly any patients had syncope of unknown origin (SUO) [57]. In contrast, most contemporary data would indicate that in nearly 50% of patients presenting with syncope (even evaluated by a meticulous history, physical examination, and proper diagnostic testing), no cause will be found, making this a critically important and large patient subgroup [13–16,64,67]. The marked discrepancy between different studies relates partly to the level of certainty tolerated for a diagnosis. Perhaps a low degree of accuracy or “clinical judgment” alone was sufficient to clinch the diagnosis in an older, retrospective analysis. Differences may also be related to selection bias, to inclusion and exclusion criteria, and to physicians’ assumptions made in diagnosing the causes for syncope [193].

Thus, the assumed cause for syncope is often based on flawed methods and incorrect assumptions. It may only be possible to know the definite cause for syncope if the episode is witnessed with an ECG, arterial line, oximeter, and EEG attached to the patient. Even then, the causal mechanism may not be clear. Therefore, even in the best of circumstances, the diagnosis of syncope is often a “leap of faith.”

Various definitions exist for SUO but perhaps the best accepted is syncope without an apparent cause despite a meticulous history and physical

examination and monitoring but no involved diagnostic testing. In reality, *all* patients have SUO, even if testing shows possible causes, as long as the relationship between the abnormality and the episode is not proven.

Because almost all diagnoses are presumptive, SUO has been used to describe different types of patients. This is important when considering diagnostic evaluation and assessment of the prognosis of these patients. Those who undergo electrophysiologic testing for syncope, for example, do not have a cause diagnosed although an arrhythmic cause for syncope is usually suspected. If the tests show induced ventricular tachycardia, did ventricular tachycardia cause syncope or is the cause still unknown? If there are episodes of asymptomatic, non-sustained ventricular tachycardia on Holter monitoring, is this enough evidence to consider that it caused syncope [13]? If all testing is unrevealing, and the patient has no obvious underlying disease, it is likely that syncope under these circumstances results from a neurocardiogenic or dysautonomic origin.

#### Case 9

A 45-year-old woman develops abdominal pain, and severe nausea and vomiting. She develops gross hematemesis and passes out at home. The paramedics are called.

*Presumed diagnosis.* Gastrointestinal bleed or vagal-induced bradycardia/hypotension.

*Actual diagnosis.* In the ambulance she is noted to have long runs of hemodynamically intolerable wide QRS complex tachycardia causing recurrent syncope.

#### Case 10: Is it really syncope?

A 52-year-old Cambodian man collapsed three times at home while working in his garden and standing in the kitchen. He injured himself. On monitoring at night he had 5-s pauses but he also had sleep apnea. On evaluation, he complained of generalized weakness, edema, cold intolerance, difficulty swallowing, changes in his voice, and weight gain. He had bradycardia and a slightly prolonged QT interval. The thyroid-stimulating hormone level was markedly elevated at 55 uIU/ml. The creatine kinase was markedly elevated.

Myxedema explained his “collapse”; it mimicked syncope. The sinus pauses were “red herrings.”

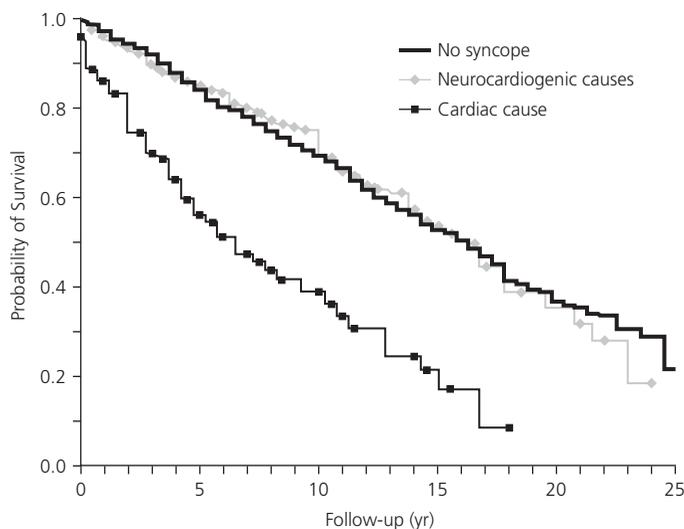
## Classification

Based on a long differential diagnostic list of potential causes, it has become fashionable to subclassify the etiology of syncope into three broad categories: cardiovascular, non-cardiovascular, and unknown [13,14,68,184]. Several contemporary reports have lent support to this approach. Considering patients who are admitted to hospitals or are seen in emergency rooms, approximately 30% will have a cardiovascular cause for syncope found [13,14,68]. Approximately 50% of patients with suspected cardiovascular disease will have an arrhythmia diagnosed, although it may not be the cause of syncope [14].

There is a high sudden and total death rate, despite therapy, for patients with underlying cardiovascular disease, even if the presumed problem responsible is corrected [14]. The 5-year mortality in patients with syncope and a diagnosed cardiovascular cause approaches 50%, with a 30% incidence of death in the first year [14,15]. When a cardiovascular cause is diagnosed, treatment, including specific treatment of hemodynamically unstable and life-threatening arrhythmias, can improve the long-term outcome. Perhaps the treatment that prevents death also prevents recurrent syncope. This becomes difficult to determine because, in comparative trials, the recurrence rate of syncope is similar whether or not a cardiovascular cause was found and treated [38].

Twenty to thirty percent of patients have a non-cardiovascular cause for syncope [14,15]: neurologic causes (see Chapter 9), vasodepressor syncope (see Chapter 2), and orthostatic hypotension (see Chapters 3 and 13). Although the mortality in this group is lower (less than 10% in 1 year, and 30% over a 5-year period), there is nevertheless a substantial risk to the welfare of the patient [13,14].

In nearly half of the patients with syncope, a cause is suspected but not diagnosed, despite a complete evaluation [14,15]. These patients with SUO generally have a benign course, with a low (6 to < 10%) 3-year risk and a modest 5-year risk (24%) of death at one center [14,15], but not all agree that SUO has such a benign prognosis [16].



**Fig. 1.1** Syncope: Outcome by condition. (Adapted from [64].)

**Table 1.4** Common causes of syncope by patient age.

Young (< 35 years)	Middle-aged (35–65 years)	Elderly (> 65 years)
Neurocardiogenic	Neurocardiogenic	Multifactorial
Situational	Cardiac	Cardiac
Psychiatric	Arrhythmic	Mechanical/obstructive
(Undiagnosed seizures)	Mechanical/obstructive	Arrhythmic
(Long QT syndrome)		Orthostatic hypotension
(Wolff–Parkinson–White syndrome, other SVT)		Drug-induced
(Hypertrophy cardiomyopathy)		Neurally mediated
		(Neurocardiogenic)

Less common, but important and potentially life-threatening causes are in brackets.

SVT, supraventricular tachycardia.

It *appears* helpful to consider the simple subclassification of syncope into three main causes: cardiovascular, non-cardiovascular, or unknown origin. The advantage of patient categorization is that it allows clinical assessment of the prognostic meaning of syncope. Recent data from the Framingham Study indicates mortality by cause for syncope [64] (Fig. 1.1). Classification by patient age may also be helpful (Table 1.4). The elderly are at highest risk of death, with a 2-year mortality of 27% compared with 8% in the younger age group, but the presence of syncope has not been shown to influence mortality independently in the elderly [31,32,194,195].

There are, nevertheless, several caveats concerning this classification. The non-cardiovascular group is not really totally non-cardiovascular. Vasodepressor syncope, often considered a non-cardiovascular

cause, is actually a cardiovascular reflex that could just as well be considered a cardiovascular cause for syncope. If this entity were considered to be a cardiovascular cause for syncope, the prognostic categorization would lose its meaning, because most episodes of vasovagal syncope have a benign prognosis. Pulmonary emboli and dissecting aortic aneurysms, often considered to be cardiovascular causes, could actually be considered non-cardiac. If these were considered non-cardiovascular, the prognostic value of this subclassification would change [196]. Also, the presence or absence of a cardiovascular cause did not influence survival of patients admitted with syncope [197].

Syncope is not always related to the cause of death. Syncope patients with dissecting aortic aneurysm, aortic stenosis, ventricular tachycardia, or pulmonary emboli have a high risk of dying even

if syncope is not present. Syncope is not clearly an *independent* predictor of death, although for specific conditions, such as dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, congenital long QT interval syndrome, and Brugada syndrome, it may be. For patients with syncope caused by, or associated with, structural heart disease, the incidence of sudden and total death may be high. It remains unclear whether syncope itself augments the risk of death further [198,199]. It is not surprising that syncope patients with cardiovascular disease have a higher mortality than syncope patients without cardiovascular disease. The subgroups, cardiovascular and non-cardiovascular, are not comparable by age, underlying disease, or prognosis otherwise. The long-term prognosis may be related more to the underlying cardiac disease than to syncope.

To evaluate this further, Silverstein *et al.* [200] stratified patients with and without syncope who were admitted to an intensive care unit. He found that the prognosis was independent of syncope but depended on the severity of the underlying disease. Similarly, the Framingham study did not indicate that patients with cardiovascular disease and syncope were any more likely to die than those with cardiovascular disease without syncope [24]. Others have found a similar result [201]. Even when the cause for syncope is diagnosed and treated in patients with cardiovascular disease, the mortality remains higher than in patients without known cardiovascular disease [14,15].

Patients admitted to hospital with syncope, especially if cardiovascular disease is diagnosed, tend to be sicker and older, and tend to have a higher mortality independent of syncope or its cause. Syncope does not place an extremely elderly (or even young) patient at higher risk of death than other individuals of the same age [32,121,194]. Syncope is probably not a prognostic indicator for patients with the Wolff–Parkinson–White syndrome [202,203] or hypertrophic cardiomyopathy [203,204] (although this is debated), even in younger patients. The presence or absence of a cardiovascular cause for syncope does not necessarily predict long-term survival.

Patients with syncope with an arrhythmic or hemodynamic cause may have a high mortality. It is an especially important prognostic indicator if impaired left ventricular function, ventricular ectopy, and induced ventricular tachycardia at

electrophysiologic testing are all present [17,35,43–45,206–215]. Such patients have a prognosis as poor as those who have had a cardiac arrest or sustained ventricular tachycardia [197]. Other examples include syncope associated with the hereditary long QT interval syndrome (see Chapters 8 and 11), aortic stenosis [216] (even if syncope is caused by alteration in autonomic response [217]), or an atrial myxoma [218]. Treatment of these conditions can improve prognosis and prevent recurrence of syncope. Similarly, repair of an aortic valve for aortic stenosis or removal of an atrial tumor will improve long-term prognosis and *may* treat the cause of syncope [219].

Middlekauff *et al.* [220,221] and Tchou *et al.* [222] found syncope to be an important prognostic predictor for specific patient subgroups: those with impaired left ventricular function and congestive heart failure. In patients with advanced heart failure and syncope, the 1-year mortality was 45% compared with 12% without syncope [220,221]. Patients with idiopathic dilated cardiomyopathy have a 56% 4-year mortality in contrast with a 4% 4-year mortality in patients with dilated cardiomyopathy who do not have syncope [222]. Using electrophysiologic testing, several investigators have shown in separate studies that the mortality in patients with induced ventricular tachycardia was lowered if the tachycardia was treated properly [44,45,197]. Another report using electrophysiologic testing showed that there was a 5% recurrence rate of syncope for treated patients versus a 24% recurrence rate in those with untreated syncope [43].

The prognostic impact of syncope is clearly disease-specific but prompt, aggressive treatment of syncope in patients with malignant ventricular arrhythmias is required and can be life-saving. For other conditions, including various cardiovascular etiologies, the cause of death and syncope are not clearly directly linked. In this regard, categorization into cardiovascular, non-cardiovascular, and unknown etiologies, while potentially useful, represents an oversimplification of an extraordinarily complex issue.

It is possible that syncope and mortality are unrelated. Further, treatment can alter mortality and syncope recurrence but this is disease dependent. The two are not necessarily linked. For example, an ICD may prevent cardiac arrest in a patient with the

congenital long QT interval syndrome but it may not prevent syncope. Repair of an aortic valve may prevent syncope but the patient may still have a significant cardiovascular mortality resulting from associated conditions.

### Initial approach to the patient with syncope

The proper diagnostic and therapeutic approach requires careful analysis of the symptoms and clinical findings, and integration of all the clues in the history, from the patient and others present. No specific battery of tests is ever indicated or is always useful. Extensive diagnostic evaluation is generally unnecessary, expensive, and risky. Repeated evaluation and hospital admission after an initial negative assessment tends to be unrewarding. If this point is reached, consider exploring the history in more detail with the patient, witnesses, and family.

With present technology it is clearly impractical to monitor all episodes of syncope to arrive at a diagnosis, although it is useful to implant and electrocardiographically monitor selected patients [223] (see Chapter 19). Clinicians must base their decisions on historical features, with the presumption that the description of the episode is accurate and complete [14,16,20,36,57,224–226].

*Diagnostic evaluation must be guided from the history.* Common sense cannot be underestimated, even if it is difficult to describe [56]. Listen to the patient. The proper evaluation requires a balance of the judicious use of inpatient and outpatient diagnostic modalities. The expense and risk of the procedures and hospitalization are intensified by the possibility of causing iatrogenic harm from a diagnostic or therapeutic mishap.

*The location of the evaluation is important.* In the emergency room, immediate decisions are crucial concerning the need for admission, assessment of risk, and the need for restriction and follow-up. For the hospitalized patient, early decisions are encouraged concerning types of inpatient management approach. Discharge planning for further outpatient evaluation, if necessary, should begin early in the hospitalization. Surprisingly few patients admitted with syncope, without some kind of plan

before admission, will benefit from hospitalization. Arguably, patients admitted are their own subgroup and have a different, perhaps higher risk of death [197]. The outpatient with a vague or distant history of syncope can be evaluated more leisurely, in contrast to the patient hospitalized in the intensive care unit with impaired left ventricular function. For each circumstance, the cause for and prognosis of syncope will differ and the approach to diagnosis and therapy will differ concomitantly.

Various clinical algorithms have been developed but, because of the diverse nature of syncope, it becomes impossible to implement an evaluation stratagem that will succeed in all circumstances and for all patients. Indeed, algorithms can confuse more than clarify. Consider the complexity of one such algorithm published in a neurology text (Fig. 1.2). Such an approach, even if understandable, or readable, has not been shown to improve outcome.

### The history

To evaluate syncope, sound clinical decisions are based on a carefully performed history with great attention to detail. The history, with its proper interpretation, and a directed physical examination are the only appropriate ways to guide further diagnostic evaluation. The history and physical examination alone can be diagnostic in 25–35% of patients [13,14,16,20,67,200,226] (Table 1.5). Of those for whom a cause is found, the history and physical examination alone were sufficient in 75–85% of patients [13]. If the history does not provide diagnostic clues, it is much more likely that no diagnosis will be reached even with an extensive battery of tests.

Symptoms and several historical features, summarized in Tables 1.6 and 1.7, can help to direct further diagnostic procedures. Specific attention should be directed toward:

- 1 characteristics and length of the episode;
- 2 patient's and witnesses' accounts;
- 3 patient age;
- 4 concomitant (especially cardiac) disease;
- 5 associated, temporally related, symptoms (e.g., neurologic symptoms, angina, palpitations, and heart failure);
- 6 premonitory (prodromal) symptoms;
- 7 symptoms on awakening (postsyncope symptoms);

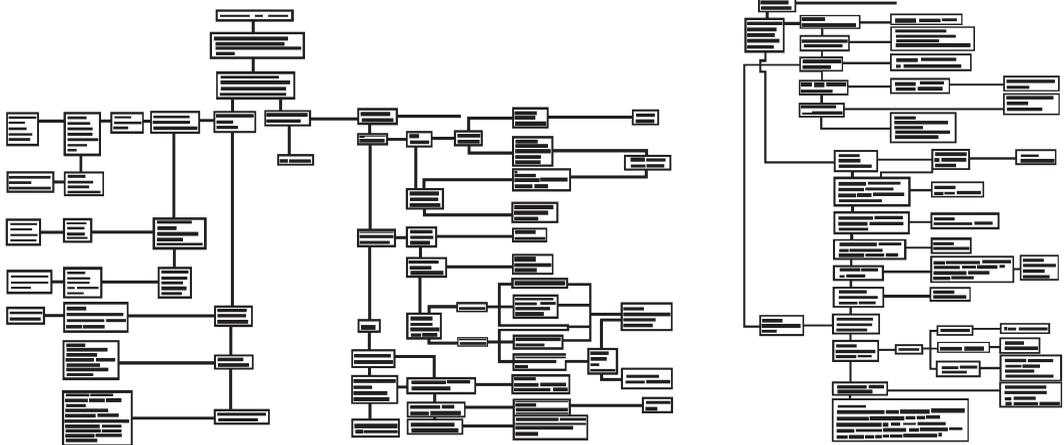


Fig. 1.2 An algorithm for management of syncope. This may confuse more than help.

Table 1.5 Evaluation of syncope. How often is the cause found by history and physical? (Modified from [209].)

	Patient type	Patient number	Diagnosis "found"	History and physical helped
Kapoor [20]	Admitted (SUO)	121	13	—
Day [13]	ER	198	173	147
Silverstein [200]	MICU	108	57	42
Kapoor [14]	All comers	204	107	52
Eagle [16]	Admitted	100	61	52
Martin [226]	ER	170	106	90

History and physical will provide clues to the diagnosis in 30–75% of patients. Diagnosis based on history and physical may be (and often is) inaccurate. ER, emergency room; MICU, medical intensive care unit; SUO, syncope of unknown origin.

8 circumstances, situations surrounding the episode;

9 exercise, body position, posture, and emotional state;

10 number, frequency, and timing of previous syncopal episodes;

11 medications;

12 family history.

As part of the initial assessment, early determination of the presence of heart disease is especially crucial because these patients are at highest risk of death. Make sure that it is indeed syncope that has occurred. Obtain information from other hospitals and doctors, talk with others who have cared for the patient, and to family members.

Consider characteristics of the event itself, the patient, and length of the episodes. One reason for the differ-

ent outcomes for syncope patients relates to the nature of the episodes. Contrast an elderly male who has had a series of syncopal attacks, spaced by short episodes of recovery, to a young woman with multiple episodes spaced over several years. Based on this information alone, the woman is likely to have neurocardiogenic syncope and the man an arrhythmic or orthostatic cause. A patient who is witnessed to collapse and then noted to be pulseless, apneic, and *appears* to require cardiopulmonary resuscitation is probably at higher risk for a malignant arrhythmia or a cardiac cause for syncope. Sudden unexpected collapse (“Stokes–Adams attacks”) suggests, but does not prove, an arrhythmic cause for syncope.

The patient may not remember events surrounding the episode, have retrograde amnesia, or otherwise be incapable of providing an adequate history

**Table 1.6** History: symptoms related to syncopal spell.

<i>Symptom</i>	<i>Probable cause</i>
Nausea, diaphoresis, fear	Neurocardiogenic
Aura	Seizure
Palpitations	Tachycardia (non-specific finding)
Exercise-related	Ventricular or supraventricular tachycardia, hypotension/bradycardia
Posture-related	Orthostatic hypotension, volume depletion, dysautonomia
Urination, defecation, eating, coughing	Vagal-induced hypotension, bradycardia
Diarrhea, vomiting	Hypovolemia, hypokalemic-induced arrhythmia, vagal-induced hypotension, bradycardia
Melena	Gastrointestinal bleed
Visual change, neurologic abnormality	Stroke (unlikely presentation), seizure, migraine
Headaches	Migraine, intracerebral bleed
Chest pain	Ischemia-induced arrhythmia
Dyspnea	Pulmonary embolus, pneumothorax, hyperventilation (hysteria)
Abdominal pain	Aortic aneurysm, gastrointestinal bleed, peritonitis acute abdomen, trauma
Back pain	Dissecting aneurysm, trauma
Flushing	Carcinoid syndrome
Prolonged syncope	Aortic stenosis, seizure, neurologic or metabolic cause
Slow recovery	Seizure, drug, ethanol intoxication, hypoglycemia, sepsis
Injury	Arrhythmia, cardiac cause, neurocardiogenic
Confusion	Stroke, transient ischemic attack, intoxication, hypoglycemia
Prolonged weakness	Neurocardiogenic syncope
Skin color	Pallor – neurocardiogenic; blue – cardiac; red – carbon monoxide

**Table 1.7** History: important data to obtain.

Witnesses	The entire event from multiple viewpoints
Situation	Was there a “trigger”?
Age elderly (> 65 years)	Multifactorial – rule out heart disease. Consider medications
Age young (< 40 years)	Neurocardiogenic most likely cause
Heart disease	Could indicate a poor long-term prognosis
Family history of sudden death	Increased predisposition for malignant arrhythmia or cardiac cause
Number of episodes	< 3, possibly malignant and life-threatening > 3, more likely to be benign and a continued problem
Previous evaluation	Obtain results from previous evaluation
Medications	Possible proarrhythmia, bradycardia, hypotension

[227,228]. Therefore, witnesses’ accounts are of major importance but, while often heavily relied upon, may be inaccurate. The pulse appearing to be absent may not have been properly taken; there are also several reasons why a patient may be (or appears) pulseless. Inherent biases are always possible by the historian and those listening to the story.

*Try to define the episodes as completely as possible.* The patient may remember very little of the episode, deny it, or remember it inaccurately. Always

suspect that aspects of the history reported by the patient or witnesses are incomplete, misinterpreted, or are overblown because of the startling nature of the symptom. Paramedics may ignore witnesses’ accounts and misinterpret the responses of an individual who appears healthy, alert, and talking by the time they arrive. The importance of a serious problem can be under- or overestimated.

*Consider events that trigger the episodes.* Emotions can trigger syncope by a variety of mechanisms

[3,229]. An emotional trigger raises the suspicion of neurocardiogenic syncope; it also may indicate a psychiatric cause. Chest pain can indicate the presence of ischemic heart disease or coronary vasospasm. Abrupt collapse, without premonitory symptoms, may indicate a cardiac arrhythmia, but triggers can be misleading and may be non-specific. Fatigue may be associated with neurocardiogenic syncope [230]. Other associated symptoms with neurocardiogenic syncope include pallor and diaphoresis. Other triggers for neurocardiogenic collapse include coughing [231], exercise [232], cold, carbonated beverages [56], but no history related to these issues is specific.

*Consider situations surrounding and preceding syncope.* Syncope is often related to the situation in which it occurs. Vasovagal (neurocardiogenic) episodes are often provoked by noxious stimuli such as a strong emotional outburst, blood loss, or pain. If the trigger is situational, episodes may be avoided by simply avoiding the situation.

Sometimes it is difficult, if not impossible, to discover the initiating factor. Slow recovery from symptoms is common in neurocardiogenic syncope, as it is after a seizure. Slow recovery is not common in orthostatic hypotension or after a long sinus pause. Consider that patients may try to explain circumstances, such as a motor vehicle accident, with syncope, when in fact they did not pass out.

*Consider specific aspects of the history.* Upper extremity exercise preceding syncope suggests subclavian steal. Back pain raises the suspicion of a dissecting aortic aneurysm. Dyspnea may indicate a cardiac or pulmonary cause. Pulmonary emboli can cause syncope but only with a large embolus. Associated tachypnea, cyanosis, hypotension, and acute right heart failure clarify the diagnosis. Similarly, the presence of angina may indicate the presence of an ischemically mediated arrhythmia or the Bezold–Jarisch reflex (bradycardia and hypotension from inferior wall ischemia) [181].

*Assess the relationship to meals, alcohol, and drugs.* A large meal can cause peripheral vasodilation and hypotension and syncope by a vagal or dysautonomic mechanism [118]. When episodes begin with

slow onset and gradual recovery, consider a toxic or metabolic cause such as hypoglycemia, hyperventilation, alcohol, or drugs (illicit or prescribed). Alcohol and illicit drugs can cause syncope by several mechanisms including exacerbation of a supraventricular or ventricular tachyarrhythmia. Alcohol can also trigger syncope by abrupt change in hemodynamics and other mechanisms [233–239]. Alternatively, what might appear to be syncope from alcohol may instead be intoxication. In such a case, syncope can be used by a patient as a ready explanation for a motor vehicle accident or other adverse consequences related directly to the drinking itself.

*Consider the relation to exercise, position, posture, and events.* If the episode begins after a coughing bout, consider post-tussive syncope. In this case, there is a Valsalva physiology, associated increased intracerebral pressure, and a vagal response. If the episodes occur after awakening to urinate, consider micturition syncope. If the episode occurs during athletic competition or immediately after exercise, it may be completely explained by a neurocardiogenic response, but be careful not to ignore a potentially more severe, underlying cause [3,232,240–242]. Even in a young patient, consider potentially malignant causes: hypertrophic cardiomyopathy, congenital aortic valve disease, or even exercise-induced, idiopathic, right ventricular, left ventricular or bi-directional ventricular tachycardia [243,244]. Exercise-induced supraventricular tachycardias, atrial flutter, or atrial fibrillation rarely cause syncope but when they do, there is usually a history of palpitations or tachycardia. Seizures are often associated with muscular jerks, incontinence, and tongue biting, and there may be postictal confusion or a preictal aura.

If syncope occurs on abrupt rise from a prone position, consider orthostatic hypotension. Even if there is no evidence on examination, orthostatic hypotension may still be a possible cause of syncope if other precipitating contributors are considered. Orthostatic hypotension should be suspected in the elderly and in those with diabetes, if there is prolonged bed rest, and even when the patient is euvolemic. If the episodes occur after intense exposure to heat, consider heat syncope. If there are paresthesias, lip tingling, and anxiety, consider

hyperventilation. If loud noises precede the episode, consider an autonomic mechanism or an arrhythmia resulting from long QT interval syndrome [245].

*Prodromal symptoms can help secure a diagnosis.* Premonitory (prodromal) symptoms including diaphoresis, cold sweat, nausea, anxiety, dizziness, lightheadedness, impending doom, and pallor are common in vasovagal (neurocardiogenic) syncope. Yawning, pallor, nausea, visual blurring, darkening of the vision, sweating, and weakness are also consistent with vagal cause (neurocardiogenic syncope). If the episode is associated with a strong emotional reaction, nausea, diaphoresis, and sense of impending doom, a neurocardiogenic cause is highly likely. These symptoms may also occur independent of syncope but be neurocardiogenic in origin.

If palpitations precede the episode, suspect an arrhythmic etiology. Unfortunately, palpitations are vague and non-specific, and do not diagnose a specific etiology. Palpitations are of several types: sustained rapid, irregular, or pounding. Each type may provide some clues regarding a possible arrhythmic cause for syncope. By themselves, palpitations are unreliable but suggestive for further evaluation.

An aura immediately preceding the episodes is consistent with a seizure. If the episode begins during exercise consider aortic stenosis, hypertrophic cardiomyopathy, or an exercise-induced arrhythmia. If the episode begins after exercise, consider a strong vagal response to exercise.

*Symptoms on awakening (postsyncope symptoms) can be helpful.* The recovery phase from the syncopal episode can also provide important diagnostic clues. If there is confusion, headache, or dizziness, consider migraines, seizure, or another neurologic cause.

*Consider the number and frequency of episodes.* The frequency of occurrence of syncope at initial presentation can be used to assess risk. Patients with recurrent episodes are unlikely to have a malignant arrhythmia as the cause, particularly if the episodes are distributed over several months to years. Patients with multiple syncope recurrences, especially if they are spread out over a long time period, are at

lower risk of cardiac mortality [246]. These episodes are most likely neurocardiogenic, autonomically mediated, or resulting from a psychiatric cause (see Chapters 2, 3 and 12). In contrast, patients with isolated episodes (less than three) of syncope or with a short history of recurrence are at risk for a cardiac death [210,246]. Even if only one episode is present, it can presage a cardiac arrest. Patients with new-onset syncope, even if multiple episodes over a short time period, may have an underlying new cardiovascular cause for syncope that could be a serious premonitory sign.

*Consider cardiac history.* The most worrisome patient is one with left ventricular dysfunction and coronary artery disease. If such a patient presents for evaluation of syncope for which no other cause is obvious, immediate admission should be arranged for further inpatient evaluation. However, other forms of cardiac disease, not even associated with left ventricular dysfunction, can predict a malignant course. These include patients with right ventricular dysplasia or a prolonged QT interval (congenital or drug-induced). Both may occur in young patients and may lead to a malignant outcome. A cardiac history, however, does not prove a cardiac cause for syncope. It is still possible that the patient with underlying heart disease has a non-cardiac cause for syncope including a neurocardiogenic or an unknown cause [67].

*Pay attention to associated, temporally related, symptoms.* Angina in association with the episode suggests an ischemic etiology; heart failure may suggest a hemodynamic or arrhythmic cause; a coughing bout suggests a pulmonary cause; jerking of the hand suggests a neurologic etiology; melena suggests a gastrointestinal etiology, etc. The symptoms may not be obvious or directly related. This includes fever causing hypotension by sepsis, constipation causing straining, and a Valsalva maneuver leading to hypotension and bradycardia.

*Consider medications.* Medications and medication combinations, particularly in the elderly, may be contributory, if not causal, for syncope in a substantial number of patients. Assess changes in medications preceding syncope. Check for anti-hypertensives, antiarrhythmic drugs, diuretics, and

psychotropic drugs in particular, and check dosage. Check for electrolyte (e.g., potassium) abnormalities. A patient may develop torsade de pointes if taking a class IA antiarrhythmic drug, especially if hypokalemia is present. Consider the additive effects of drugs. For example, digoxin and amiodarone may cause bradycardia or lead to digoxin toxicity. Several antihypertensive drugs may not control blood pressure adequately but trigger profound hypotension at another time because of marked vasodilation. Some drugs can cause torsade de pointes by lengthening the QT interval. This may be more apparent in the elderly and in women. Recently, we saw a case of gatifloxacin causing torsade de pointes associated with marked QT prolongation in an elderly woman.

*Consider the family history of death or syncope.* Syncope patients with a family history of congenital long QT interval syncope or right ventricular dysplasia have a higher risk of arrhythmic death, especially if other family members died of the problem. Patients with hypertrophic cardiomyopathy or the Wolff–Parkinson–White syndrome who have a family history of sudden death related to the same presumed diagnosis also have a high risk of cardiac arrest. There may be a familial history of neurocardiogenic syncope [247].

*Consider risk factors for sudden death.* Recent data indicate that selected patient can benefit from an ICD implant even if syncope is not present. Regardless of the evaluation performed for syncope, keep in mind the possibility that an ICD may improve the prognosis in patients with left ventricular dysfunction and heart failure symptoms [248–250].

*Talk to previous doctors.* The more information you have to assess the patient's medical problems the better.

#### Case 11

A 65-year-old woman with a 20-year history of neurocardiogenic syncope passes out again. As my patient, I suggested that she was checked out locally. I was expecting a call from the doctor who evaluated her in the emergency room to review her history. Instead, he admitted her and did the following: ruled out a myocardial infarction, per-

formed carotid Doppler testing, performed a computerized tomography (CT) scan of the brain, and an EEG. All this could have been avoided by a call to the treating doctor.

As indicated in Table 1.4, the differential diagnosis for patients with syncope varies with age. While the middle aged (40–65 years), the elderly (65–80 years), and the very elderly (80 years and over) have an incremental risk for mortality (see Chapter 18), the young and pediatric age groups are also at risk for specific serious underlying causes. Based on these and other historical findings, the patient can be targeted for further diagnostic evaluation. Response to treatment of a condition such as neurocardiogenic syncope can also vary with age.

### Physical examination

The physical examination can provide important supporting clues to a diagnosis suspected by the history. Attention should be directed to the vital signs, the cardiovascular examination, and the neurological examination (Table 1.8).

*Patients' orthostatic vital signs should be obtained.* This includes blood pressure taken supine, sitting and standing, initially and after several minutes, with attention to change in the heart rate (if present) and to symptoms. Evidence for an abrupt drop in blood pressure with standing, especially with reproduction of symptoms, suggests volume depletion as a potential cause. The heart rate should rise with standing in a volume-depleted patient with the anatomic nervous system intact. In patients with idiopathic orthostatic hypotension, diabetes, amyloidosis, or autonomic insufficiency, the blood pressure can drop over several minutes in the standing position but the heart rate may not change. If the heart rate increases  $> 30 \text{ b min}^{-1}$  with minor blood pressure drop, consider postural orthostatic tachycardia syndrome (see Chapter 13).

*Respiratory rate and pattern may indicate a pulmonary cause.* Hyperventilation may be the cause of syncope [251,252]. Tachypnea may indicate pneumonia, pulmonary embolus, or congestive heart failure.

*Temperature changes.* These may indicate sepsis, hypothyroidism, or renal insufficiency.

**Table 1.8** Physical findings: key points.

<i>Finding</i>	<i>Implication</i>
Heart rate – slow, fast	Arrhythmic cause for syncope, acute illness, gastrointestinal bleed
Respiration rate – slow, fast	Hyper-/hypoventilation, pneumothorax, heart failure
Carotid massage	Carotid hypersensitivity
Blood pressure	Orthostatic hypotension, drug-induced hypotension, volume depletion
Neck vein distension	Pulmonary embolus, congestive failure, cardiac causes
Skin pallor	Blood loss, neurocardiogenic cause
Carotid bruits	Concomitant heart disease. Unlikely, primary cause for syncope
Heart murmur	Obstructive or other cardiac syncope
Left ventricular lift	Heart failure with cardiac syncope
S3 gallop	Heart failure with cardiac syncope
Rash	Anaphylaxis causing syncope
Abdominal tenderness	Blood loss, or hypotensive cause for syncope
Absent or variable pulses	Dissecting aneurysm, subclavian steal
Neurologic findings	Seizure, stroke, transient ischemic attack
Stool guaiac	Blood loss

*Carotid sinus massage.* This can give insight into carotid sinus hypersensitivity (see Chapter 14). The use of carotid sinus massage in older patients with syncope has recently been emphasized [253–256]. The SAFE PACE trial suggests that a pacemaker implant with a positive carotid sinus massage may be of benefit for elderly patients.

There are no firm standards for performing the carotid sinus massage and, not surprisingly, the results can therefore be highly variable. Even if it is positive (i.e., a long sinus pause or prolonged AV block, blood pressure decreases 50 mmHg, sinus pause > 3 s), as it is frequently in the elderly even without symptoms, other causes for syncope should be explored. A carotid massage is an integral part of the physical examination of the syncope patient but the results cannot be relied upon to diagnose the cause of syncope. It is a diagnosis of exclusion. It should be considered if there is a suggestive history, such as the onset of symptoms with neck compression from position or shaving.

An evaluation of the pulses can provide insight into the presence of a dissecting aneurysm or subclavian steal. The carotid impulse may reveal evidence for aortic stenosis but a carotid bruit does not provide a direct cause for syncope. However, it may indicate the presence of other atherosclerotic lesions such as coronary artery disease (cardiac cause for syncope) or subclavian artery occlusion (subclavian steal related syncope).

*The cardiovascular examination is crucial.* This may reveal murmurs consistent with hypertrophic cardiomyopathy, aortic stenosis, mitral valve prolapse, or pulmonary hypertension. Tricuspid regurgitation may indicate carcinoid syndrome or endocarditis (two rare causes for syncope). If the baseline murmur is provoked by a Valsalva maneuver, this may indicate that hypertrophic cardiomyopathy is present and is the cause of syncope. Evaluate the presence of an LV lift, abnormal impulse, an S4 and an S3 gallop, all potential indicators of cardiac disease that may be responsible for syncope. An S3 gallop could indicate the presence of congestive heart failure. Consider complete evaluation for congestive heart failure. Evidence of Eisenmenger's syndrome, pulmonic stenosis, prosthetic valve dysfunction, presence of a permanent pacemaker or implantable defibrillator, aortic stenosis, or a tumor plop (atrial myxoma) can provide further clues to the diagnosis of syncope and the risk for the patient.

Lung examination may reveal congestive heart failure. If present, suspect a potentially serious cardiac cause for syncope and consider the need for further inpatient evaluation. While a pulmonary embolus may be missed, a pneumothorax could be found. Wheezing may indicate post-tussive syncope or a hypoxic cause for syncope.

An abdominal examination may reveal evidence of a gastrointestinal catastrophe. Specifically, a

vagal response to a ruptured viscus or a gastrointestinal bleed are possibilities. The abdominal examination may reveal tenderness consistent with an acute abdomen or an ulcer. The stool guaiac can reveal the presence of a gastrointestinal bleed.

A neurological evaluation may indicate focal or localizing signs or evidence for a systemic neurologic process such as Parkinson's disease. Assess for evidence of a tremor, unilateral weakness, and visual changes. Changing neurological signs are also important. A new neurological deficit in a patient with syncope should be considered a premonitory sign for a cerebrovascular accident.

*The complexion may indicate anemia or shift in blood flow [257]. Pallor occurring transiently during an episode may indicate neurocardiogenic syncope, but if it persists after awakening consider blood loss as the cause. Marked bradycardia can also cause a dusky or pale appearance. Bright red pallor may indicate carbon monoxide intoxication. Cyanosis can indicate a cardiopulmonary process such as a right-to-left shunt with Eisenmenger's physiology. The extremities may demonstrate clubbing.*

The physical examination and history remain the cornerstones for initial evaluation of the patient with syncope. This approach is cost-effective and may help to prescribe other necessary, and help avoid unnecessary, diagnostic procedures. Unfortunately, for most patients, the physical examination is negative and further evaluation will be needed to help to understand the cause for syncope.

### Diagnostic testing

The proper diagnostic approach requires careful analysis of syncope in light of all available clinical findings. Diagnostic tests need to be used sparingly. Often inappropriate and expensive evaluations are undertaken (Table 1.9). When used properly, they will increase the diagnostic yield compared with the history and physical examination alone. No specific test is always helpful and no specific battery of tests is ever indicated or always useful. All testing must be tailored to the individual patient, based on the findings of the history and physical examinations and with knowledge of the sensitivity and specificity of each test to identify the cause for syncope. An abnormal test result does not necessarily indicate the cause for syncope and does not necessarily sanction a "wild goose chase." An abnormal tilt

**Table 1.9** Initial evaluation after admission.

---

*Should these be routine?*

Computed tomography scan  
Carotid Doppler  
Electroencephalogram  
Cardiac enzymes  
Neurology consult  
Cardiac catheterization  
Exercise test

*NO!*

---

table test result or the presence of inducible monomorphic ventricular tachycardia on electrophysiologic testing must be interpreted carefully in light of the clinical situation.

Extensive and repeated diagnostic evaluations are generally unrewarding, expensive, painful, and possibly risky. Repeat inpatient evaluations are discouraged unless new clues are uncovered. If the patient is evaluated for syncope but no cause can be diagnosed initially, further admissions are highly unlikely to arrive at a diagnosis and benefit the patient.

Even with appropriate diagnostic testing, a likely cause for syncope may not be found in many patients. Fortunately, most patients with an undiagnosed cause for syncope will not have a recurrence but if they do, they tend to have a benign long-term prognosis. As part of a proper evaluation, it is important to know when to stop testing.

Occasionally, laboratory (blood) tests can identify the cause for syncope. However, a routine battery of blood tests is rarely productive. The hemoglobin may provide a diagnosis of acute blood loss as a cause for syncope in approximately 5% of patients [14]. An SMA-6 has an even smaller diagnostic yield. It may help to detect a seizure if metabolic acidosis is present [149,258]. An elevated blood urea nitrogen (BUN), creatinine, or sodium level may indicate fluid depletion. An abnormal potassium value may indicate an arrhythmic cause for syncope. Oxygen desaturation may indicate a pulmonary embolus. As part of a general screening evaluation, it is probably useful and cost-effective to obtain a hemoglobin and perhaps an SMA-6, but it is not clear that even this evaluation is worthwhile. Drug levels (such as digoxin), and

other blood tests should be obtained based on the history.

### Use of diagnostic testing

Several tests should be considered: ECG, tilt table test, echocardiogram, electrophysiologic test, treadmill test, or a monitor. The more tests, the more abnormalities will be found. Some clinicians use a “routine” battery of tests that are useless, expensive, and misleading (Table 1.9). It is not clear how some tests and approaches (such as use of carotid Doppler testing, EEG, MRI scans, CT scans, neurology consultations) emerged.

*All patients should have an ECG.* An ECG is simple, inexpensive, risk free, and may provide helpful information in 5–10% of patients (Table 1.10). Twenty to eighty percent of patients will have an abnormal, but non-diagnostic ECG, which is useful in 7%. The presence of a bundle branch block in a patient with syncope indicates the presence of His–Purkinje disease and may indicate the possibility of complete heart block [259,260]. Bundle branch block can also be an indication of organic heart disease. Up to 30% of patients with syncope and bundle branch block will have the induction of sustained monomorphic ventricular tachycardia on electrophysiologic testing [261–264]. A patient with undiagnosed syncope and a bundle branch

block should therefore be considered for an electrophysiologic test. The ECG can also show ventricular pre-excitation (Wolff–Parkinson–White syndrome), ectopic beats, heart block, ventricular hypertrophy, atrial fibrillation, a myocardial infarction (new or old), a long QT interval (arguably, > 0.500 s), or sustained ventricular tachycardia. An abnormal ECG can point towards a diagnosis and a normal ECG may help exclude the need for an aggressive evaluation approach [265].

The signal-averaged ECG is not particularly useful in patients with syncope but may have a specific role to determine if a patient with intact left ventricular function (LVEF  $\geq$  0.40), but underlying coronary artery disease (with no bundle branch block), has a risk for ventricular tachycardia or arrhythmic death, and would otherwise benefit from electrophysiologic testing [266–268].

An echocardiogram may be appropriate to evaluate ventricular function and valvular heart disease but, if the ECG is normal, there is no cardiac history, and there are no abnormalities found on physical examination, this does not need to be obtained urgently. Younger patients, without a history of heart disease and with a normal physical examination, will be unlikely to benefit from an echocardiogram. Patients with suspected neurocardiogenic syncope do not need an echocardiogram. A chest X-ray may show cardiomegaly or pulmon-

**Table 1.10** The electrocardiogram: to evaluate syncope.

<i>Finding</i>	<i>Significance</i>
Normal or non-specific	Common, does not rule out serious cause
Complete heart block	Pacemaker indicated
Second-degree heart block	Correlate with symptoms. Pacemaker may be indicated
First-degree heart block	No obvious significance in most cases
Delta waves	Wolff–Parkinson–White pattern. Possible supraventricular tachycardia
Sinus bradycardia	Non-specific – may indicate sick sinus syndrome
Myocardial infarction	Acute: arrhythmia, hemodynamic problem Old: risk for death, arrhythmia
Epsilon waves	Right ventricular dysplasia
Bundle branch block	Possible heart block, or ventricular tachycardia
QT prolongation (> 0.500)	Possible torsade de pointes
Ectopic beats	No known significance
Atrial fibrillation	May indicate underlying structural heart disease, arrhythmic cause
Supraventricular tachycardia	Rare. Likely cause for syncope
Ventricular tachycardia	Rare. Likely cause for syncope
Paced rhythm	Pacemaker malfunction

ary edema and should be obtained if there is other evidence on examination but, as a routine screen, it adds little but an increase in cost. No other tests are required as part of the initial evaluation.

The use of monitoring is described in more detail in other chapters but includes the use of external loop recorders and implanted monitors. The use of these devices depends on the clinical scenario, the capability of the patient to push the button on an external recorder for an episode, and the risk the patient has for recurrence. The use of implanted monitors is described in detail in Chapter 19.

## What to do after the initial evaluation

### When to hospitalize the patient

A key aspect in the evaluation and treatment is syncope is to decide whether and when to admit a patient who has had syncope. Based on the information collected as part of the history, physical examination, and initial evaluation, appropriate decisions can be made regarding hospitalization (Table 1.11) [269,270]. This has become increasingly important in a time of managed medical care. With the costs of hospital admissions escalating, prudent admission criteria are required. Many hospitals are developing practice guidelines to care for patients with syncope (Fig. 1.3a,b). The SEEDS study [271] showed that a syncope unit may facilitate proper management, decrease costs, shorten length-of-stay, and improve outcomes compared to patients managed in the hospital in a standard fashion.

There are some potential benefits of hospitalization. It can be useful to diagnose and treat the cause for syncope, to prevent death, injury and symptoms, and to satisfy medicolegal requirements

(the “standard-of-care”). However, in most cases, hospitalization is unnecessary. It can be associated with iatrogenic complications for syncope patients. Despite hospitalization, syncope often remains undiagnosed. The prognosis and recurrence rates may not change. If a patient has previously been hospitalized, repeated hospitalizations for recurrent syncope are rarely productive (and helpful in < 15% of such patients). Clearly, considering the scope of the problem of syncope, the lack of benefit of admission, and the present medical environment, hospital admission for syncope should be considered carefully and used prudently.

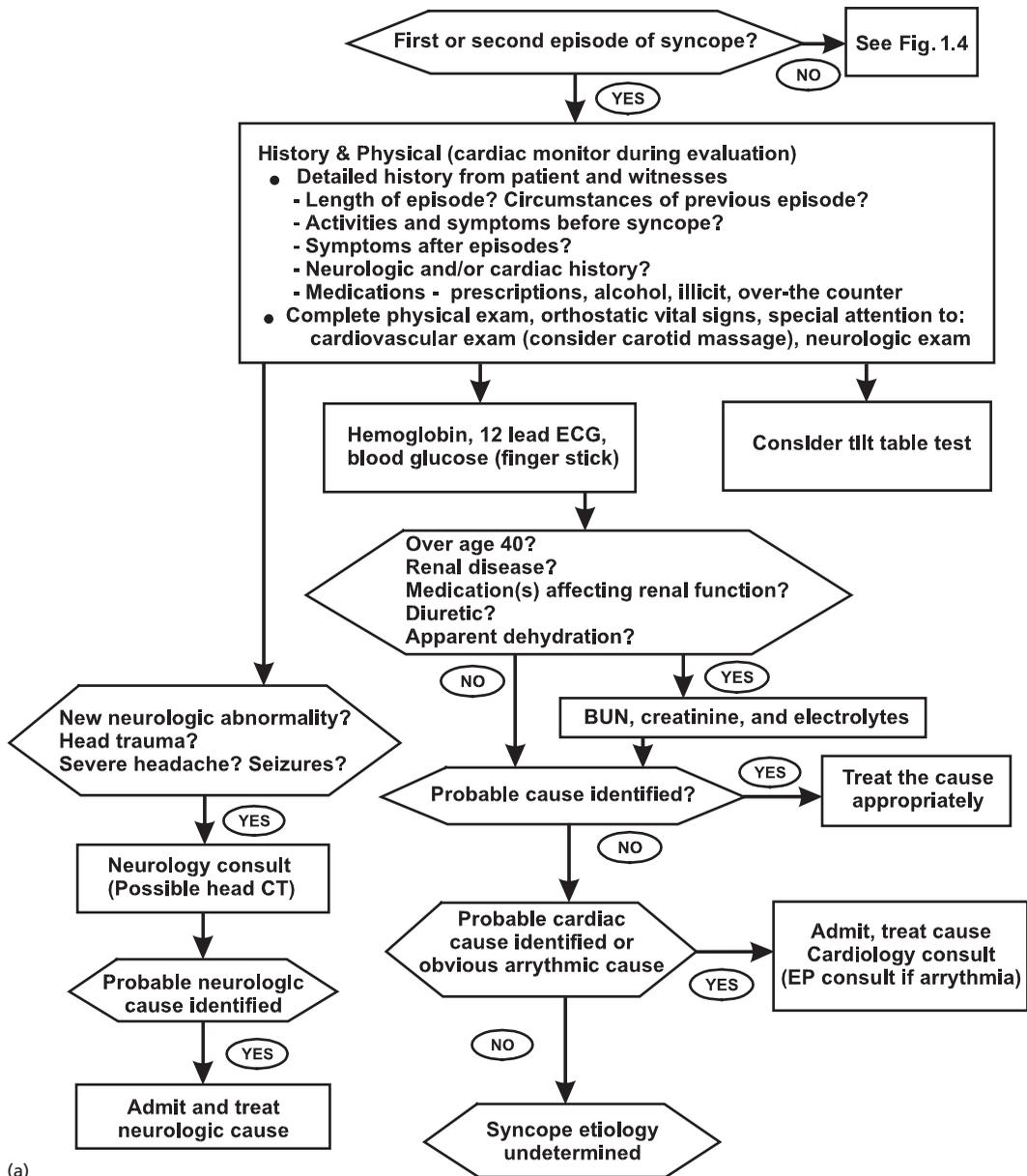
The reasons given to hospitalize are as follow:

- 1 to monitor the patient suspected of having a serious, poorly tolerated arrhythmia;
- 2 to perform tests not readily performed as an outpatient;
- 3 to formulate and undertake specific treatment plans not possible as an outpatient (cardiac catheterization or electrophysiologic testing when a life-threatening arrhythmia is suspected);
- 4 for medicolegal purposes;
- 5 when the patient is having multiple, closely spaced episodes;
- 6 when there is a new neurologic abnormality or a suspected neurologic cause, new seizure disorder, transient ischemic attack, or stroke;
- 7 when the patient is elderly, has been injured, or is at risk for serious injury;
- 8 when there is a severe abnormality on physical examination;
- 9 when any cardiovascular cause is suspected (resulting from an arrhythmia or caused by a hemodynamic problem);
- 10 when there is symptomatic orthostatic hypotension;
- 11 for the patient with suspected “malignant” vasovagal syncope or vasovagal syncope that is difficult to control and causes severe symptoms.

Often, the reason to admit is to make sure the patient does not have frequent and recurrent symptoms, or is on the verge of developing a more serious problem. If the risk of discharge from the emergency room is low, there is little reason to admit a patient (Figs 1.3 & 1.4). Besides protecting a patient from a life-threatening risk, expected results of hospitalization include finding the cause for syncope and initiating a treatment that cannot be performed on an outpatient basis. This could

**Table 1.11** Criteria for hospitalization.

Malignant arrhythmia or cardiovascular cause suspected
New neurologic abnormality present
Severe injury present
Multiple frequent episodes
Severe orthostatic hypotension
Uncontrolled “malignant” vasovagal syncope
Elderly patient
Treatment plans not possible as an outpatient



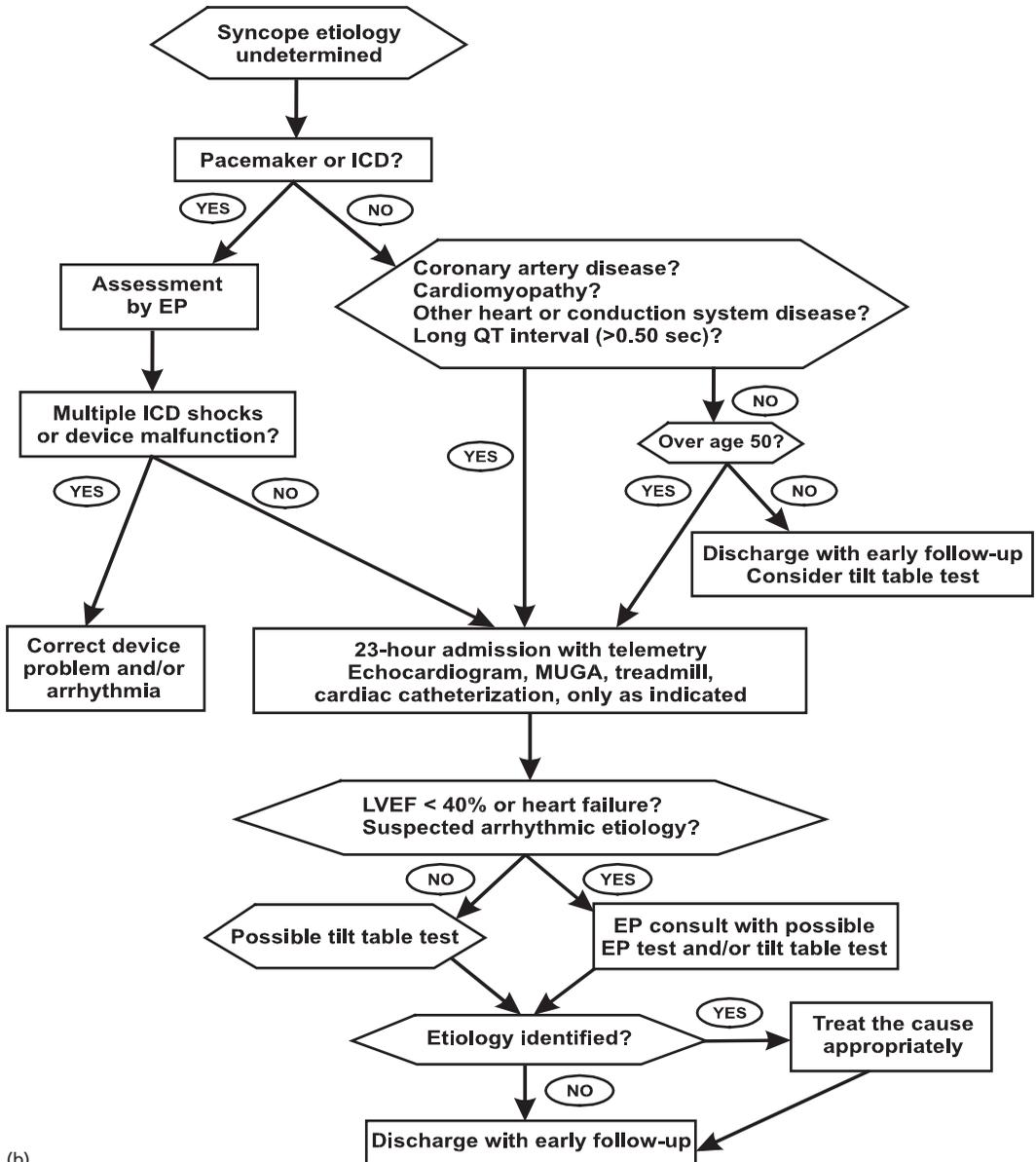
(a)

Fig. 1.3 Evaluation of recent onset syncope (a & b). BUN, blood, urea, nitrogen; CT, computerized tomography; ECG, electrocardiogram; EP, electrophysiology; LVEF, left ventricular ejection fraction; MUGA, multiple gated acquisition.

include treatment of a cardiac arrhythmia with drugs, surgery, or implanted devices. Patients who are suspected to have a new neurologic event may benefit from close inpatient observation for worsening of their condition. Hospital admission is also based on patient concerns.

When considering hospital admission, several additional factors must be appraised: patient age,

cardiac risk factors, circumstances of the episodes, history from the patient and witnesses, underlying medical conditions, and results of the physical examination. Hospitalization should be considered to formulate and undertake specific diagnostic and therapeutic plans that cannot be performed as an outpatient. The goals for hospitalization must be clear before admission because non-directed



(b)  
Fig. 1.3 (cont'd)

admissions for syncope are generally non-productive. The prognosis and recurrence rate of syncope may not change. Patients who do not benefit from hospitalization include those with isolated episodes of syncope and no apparent heart disease, those with recurrent episodes but normal physical examination, echocardiogram, ECG and no cardiac risk factors, and those who have undergone a previous

complete evaluation as repeat hospitalizations to evaluate such patients is generally unrewarding.

Mozes *et al.* [272] found that prolonged in-patient monitoring was rarely productive. In this study, for patients hospitalized with syncope, a diagnostic evaluation, leading to an appropriate therapeutic intervention was present in 24%, consistent with other reports. With admission based on

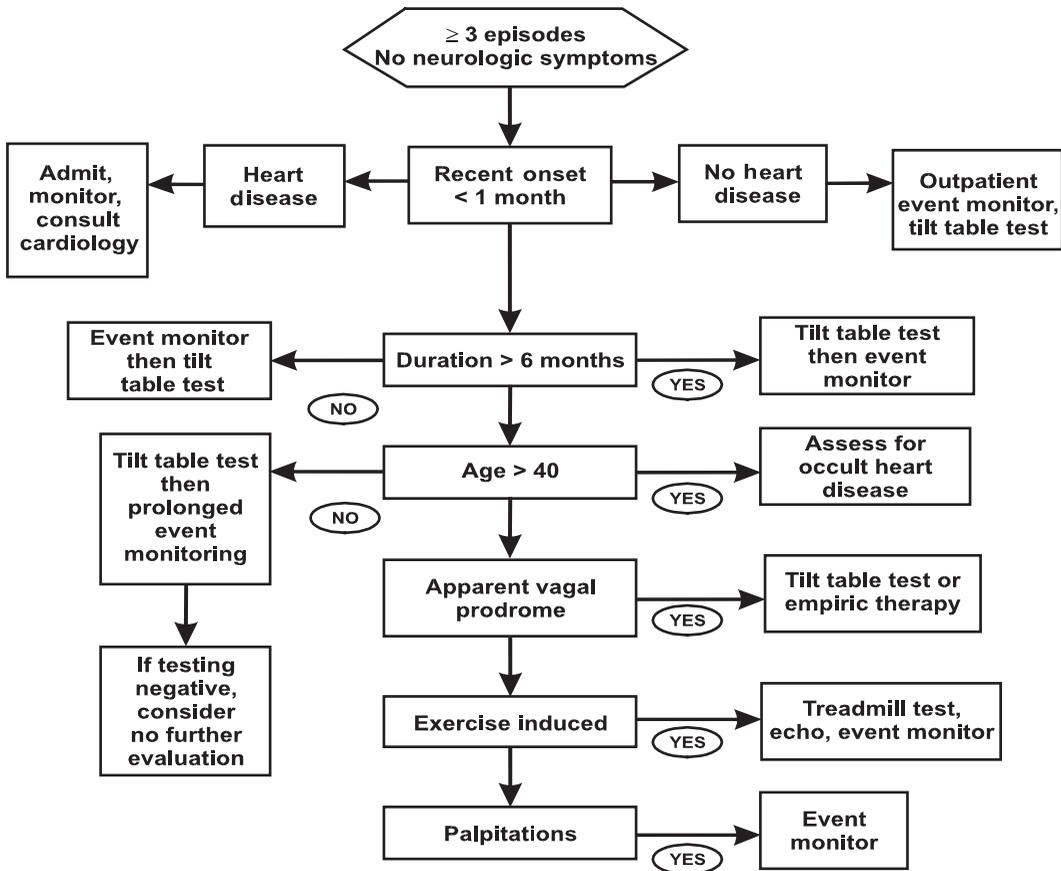


Fig. 1.4 Recurrent undiagnosed syncope.

the history, physical examination, and the ECG, 85% of hospitalizations could be avoided.

In a study of 350 patients, clinical judgment was compared with “objective” diagnosis-related group (DRG) criteria to evaluate the need for and benefit of hospitalization [273]. This study included patients with syncope. In this report, physicians’ clinical judgment outperformed objective DRG data in identifying that patients needed and benefited from acute-care hospitalization.

Medicode ICD-9-CM codes for syncope under 780, “general symptoms”. Medicode ICD-9-CM 780.2: “syncope and collapse” includes blackouts, fainting, vasovagal attacks, “near” or “pre” syncope but excludes carotid sinus syncope, heat syncope, neurocirculatory asthenia, orthostatic hypotension, or shock. ICD-9-CM 780.4 codes: “dizziness and giddiness” includes “lightheadedness and vertigo”. Sometimes, syncope coding includes DRG 427.89,

“cardiac dysrhythmia,” 427.9, “cardiac dysrhythmia, unspecified.”

At my prior institution, over 1 year, 236 syncope patients were admitted with these diagnoses. The average length of stay was 3.7 days. Third party payers applied less pressure for discharge during hospitalization as long as a treatment plan was in place, which is appropriate because for hospitalization to be worthwhile, a plan needs to be in place at the time of admission.

Unless a new diagnostic assessment plan is established, in one report of 161 patients admitted (Ferrick PACE 1997), 75% did not benefit from admission. Repeated admissions are even less useful.

**When to consult a specialist**

Patients often visit primary care physicians, appropriately so, for initial episodes of syncope in an

emergency room or in a clinical setting. While internists, emergency physicians, and family practitioners see the bulk of syncope patients, consultation can become necessary. A consultant should be considered after the complete initial evaluation has been undertaken and an etiology is suspected that requires disease-specific evaluation and treatment. The history and physical examination provide the best clues to the diagnosis and to decide when to call in a consultant.

The first step in evaluating syncope is *not* to call a neurologic or an electrophysiologic consult, although both can be helpful for specific patients. A neurologic consult will rarely provide useful guidance unless there are no specific clues in the history or physical examination. An electrophysiologist will help to:

- 1 assess the risk of an arrhythmic cause for syncope using electrophysiologic testing;
- 2 provide information concerning the prognostic risk of syncope;
- 3 evaluate potential autonomic causes for syncope, including neurocardiogenic causes;
- 4 perform tilt table testing and evaluate the results;
- 5 manage (diagnose and treat) arrhythmic causes of syncope.

Because the electrophysiologist can help to manage the patient with potential arrhythmic causes for syncope, he or she should be called early when there is organic heart disease, bundle branch block, or a history of arrhythmia. A cardiologist should be called to help to evaluate the patient with suspected cardiovascular disease causing syncope including aortic valve disease, hypertrophic cardiomyopathy, other cardiomyopathies, or coronary artery disease.

A psychiatrist may be needed when a psychiatric etiology seems likely. A good consultant will help to direct the evaluation of the patient with syncope promptly, properly, and efficiently, without inappropriate testing. In this way, the consultant should actually improve the quality of care and lower the total costs. Electrophysiologists are likely not called often enough to see patients with syncope. Neurologists are often called too early to help with the management and should be called only if there are neurologic signs. Any neurologic testing should be performed with the aid of a neurologist. Autonomic medicine is rapidly emerging as a separate medical specialty that deals with patients with

difficult to treat neurocardiogenic and dysautonomic syncope.

### When to carry out diagnostic tests

A variety of tests are used to evaluate patients with syncope, as described in the European guidelines [1]. Frequently, the following “complete” work-up is planned (Table 1.9): carotid Doppler examination, cardiac enzymes, prolonged inpatient telemetry monitoring, echocardiogram, treadmill test, head CT scan, and neurology consult. It is not clear where this “shotgun” approach originated but it has no scientific basis and it is not advocated because it will almost never lead to a diagnostic cause for syncope. It is expensive and time consuming but ubiquitous.

CT and MRI brain scans are almost never warranted, especially if there are no neurologic findings. While an abnormality may be found, such as tumor or cerebrovascular accident, this may be concomitant (and, perhaps, asymptomatic) rather than a cause for syncope.

The EEG has been used as a screen in several reports that evaluate syncope. The routine and undirected use of the EEG for undiagnosed syncope has not been helpful and cannot be recommended without other suggestive clinical information. On one occasion I found the test to be useful when a patient had a neurocardiogenic episode on the EEG as a result of the electrodes and appeared to seize.

Several diagnostic tests can help to evaluate syncope but it is important to consider the sensitivity, specificity, and diagnostic accuracy of any test used. An abnormality found does not necessarily indicate that it caused syncope. Induction of ventricular tachycardia on electrophysiologic testing or a hypotensive bradycardic episode on a tilt table test is suggestive, but not indicative, of the cause for syncope. Any finding must be considered in light of all clinical findings and must be interpreted before using the results to initiate therapy. The test must be evaluated on its own merits and chosen based on the finding uncovered from the history and physical examination.

### Tilt table testing

The tilt table test is used to evaluate neurocardiogenic causes for syncope, especially if the cause for syncope is otherwise unclear [81,273–275]. The tilt

table test has been in use since before the 1950s to evaluate syncope [33]. It helps to assess a reflex mechanism that is only now beginning to be understood [276–280]. Over the past decade, the use of, and indications for, tilt table testing have expanded tremendously. It has changed the evaluation and treatment of patients with suspected neurocardiogenic and dysautonomic syncope (see Chapters 2, 3 and 7).

Not all patients with possible neurocardiogenic syncope require a tilt table test. If a patient has a clear history of neurocardiogenic syncope or has episodes related to a specific situation, the test may not be needed. Sensitivity and specificity issues may influence use of the tilt table but there is no other “gold standard” method to evaluate the presence of neurocardiogenic reflexes implicated as cause for syncope (the reflex itself may not be abnormal) [281]. A negative test can occur even in the presence of an obvious cause for neurocardiogenic syncope and a positive test can occur when syncope clearly results from other causes [282]. As with electrophysiology, testing a positive test (especially if “borderline” positive) may potentially be misleading. Always consider that there may be other (or multiple) causes for syncope. This problem was well illustrated in the case of the basketball player, Reggie Lewis, who had syncope and a positive tilt table test but died suddenly of ventricular fibrillation while playing basketball. When syncope clearly appears to be a result of neurocardiogenic causes, treatment plans can potentially begin without a tilt table test (although some authors wish to determine exact response patterns during tilt table testing as a guide to therapy). Guidelines for tilt table testing have been published [281]. The tilt table is best considered when there is suspected neurocardiogenic syncope in patients in whom the cause is not obvious (see Chapters 2 and 7) or in those with syncope of otherwise unknown origin.

### Holter monitoring

Holter monitoring is often ordered for patients with syncope but it rarely diagnoses a serious underlying arrhythmic cause and rarely provides useful information unless the patient has an episode with the monitor attached. In several large studies using Holter monitoring, the correlation

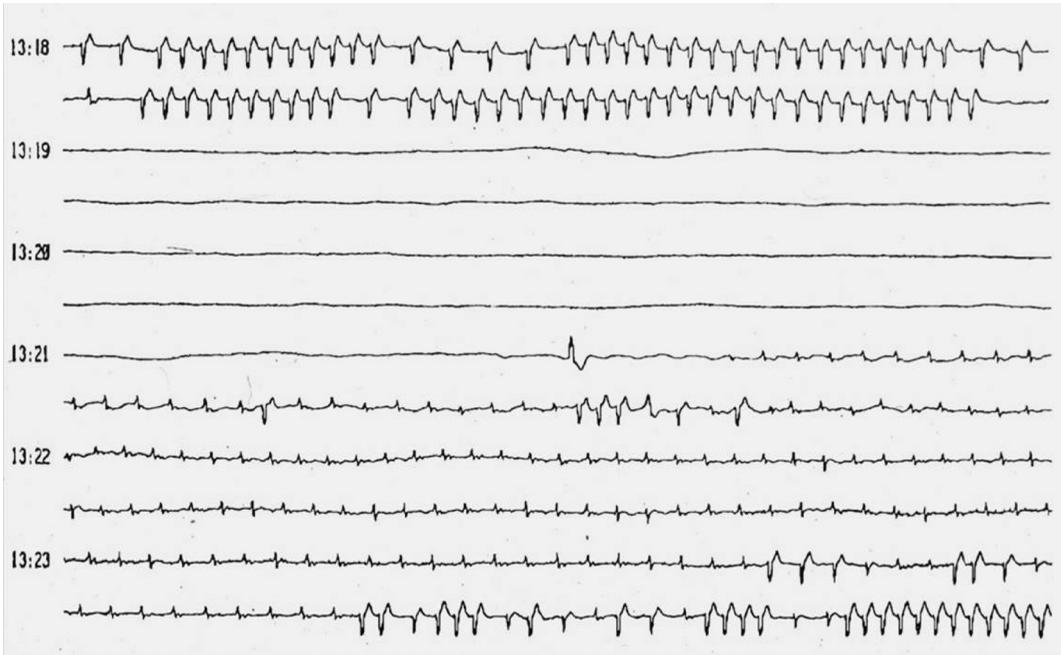
between arrhythmic abnormalities and symptoms, including syncope, was < 5% [283–287]. If an asymptomatic abnormality is detected, it may not be the cause for syncope and may lead to further unnecessary diagnostic and, perhaps, therapeutic interventions [288]. Asymptomatic non-sustained ventricular tachycardia, premature ventricular beats, sinus pauses, or sinus bradycardia may have no specific meaning in this setting and may confuse, rather than reveal the cause for the syncope. The only reason to consider a Holter monitor is when a patient has multiple or frequent episodes of syncope or related symptoms over a short period of time (Fig. 1.5). Prolonged Holter monitoring is an option to evaluate selected patients but there are now better methods to monitor for arrhythmias in the long term.

### Endless-loop recorders – event recorders

External endless-loop recorders have emerged as highly prescribed, quite useful devices to manage syncope and assess its potential arrhythmic causes [289] (Table 1.12). The newer devices are technologically superior, smaller, and with a larger battery capacity. They can be used to capture and save episodes even minutes after they have occurred. These devices can be attached to the patient for weeks or months at a time.

A tape continuously records the ECG so that if a patient passes out, the episode can be saved by pushing a button on the recorder after awakening. Therefore, the episodes could be recorded and played back by the patient over the phone or by other knowledgeable individuals. The time interval recorded before the button is pushed is often programmable but acceptably long compared with the length of routine syncope episodes. Few data are published on this technology, which is now used routinely to evaluate syncopal episodes. This technique is quite useful to diagnose a potentially syncopal arrhythmia cost-effectively. Outpatient use of this device should be reserved for patients who are responsible and intelligent enough to learn how to use the device and who are willing to do so.

Implanted loop recorders can help to diagnose the cause for syncope when it is difficult to capture an episode with an external loop recorder or if the episodes are quite far apart. This small implanted



**Fig. 1.5** A Holter monitor performed on a patient with recurrent, frequent episodes of syncope. The patient was admitted to the hospital and had a Holter monitor placed. The patient had more than 2 min of asystole.

**Table 1.12** Holter monitor versus endless-loop recorder.

To assess	AV block, sinus node dysfunction supraventricular/ventricular tachycardia
<i>Holter</i>	
Advantage	For patients unable to comply with event recorder, or frequent episodes
Disadvantage	Rare correlation of rhythm to symptoms for Holter
<i>Endless-loop recorder</i>	
Advantage	Long-term evaluation to correlate symptoms with rhythm
Disadvantage	Requires knowledge of how and when to use

device can automatically detect rapid and slow rhythms and can be triggered by the patient to save an event. There is evidence that implantable recorders may be useful before other technology in the diagnosis of an arrhythmic cause for syncope [5,290] (Fig. 1.6) (see Chapter 19).

### Electrophysiologic testing

Most arrhythmias that cause syncope are paroxysmal, infrequent, and unpredictable. They can be difficult, if not impossible, to diagnose. Electrophysiologic testing has emerged as a useful method

to assess arrhythmic causes for syncope (Table 1.13) (see Chapter 6) and to assess the risk for arrhythmic death. A consensus document outlines the recommendations on the use of electrophysiologic testing for syncope [291]. Various arrhythmias and clinical conditions can be evaluated by electrophysiologic testing but the test has differing capabilities to assess each rhythm disturbance (Table 1.14). A compilation of electrophysiologic test results are shown in Fig. 1.7 and Table 1.15. Abnormal test results are seen in 7–50% of patients selected for study [17,41,43–45,206–208,212–214,262–264,292–298].

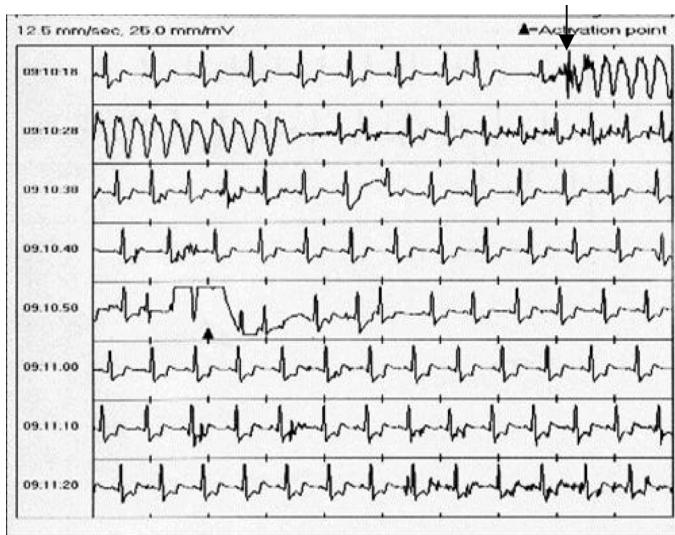


Fig. 1.6 Implantable loop recorder showing non-sustained ventricular tachycardia in a syncope patient.

Table 1.13 When to perform electrophysiologic testing.

Coronary artery disease with left ventricular dysfunction\*  
 Dilated cardiomyopathy  
 Valvular cardiomyopathy\*  
 Bundle branch block\*  
 Congestive heart failure, any cause\*  
 Supraventricular tachycardia but not temporally associated syncope  
 Wolff–Parkinson–White syndrome  
 Possible, for undiagnosed syncope multiple recurrence

\* Cardiac catheterization, may need to be performed first, on a case-by-case basis.

Table 1.14 Electrophysiologic testing: to evaluate syncope.

Sustained ventricular tachycardia (also to assess risk for death)  
 Supraventricular tachycardia (rare finding at electrophysiologic testing)  
 Bradycardia – fair → poor to evaluate the sinus node  
 Heart block – fair → poor to evaluate the AV node

**Caveats**

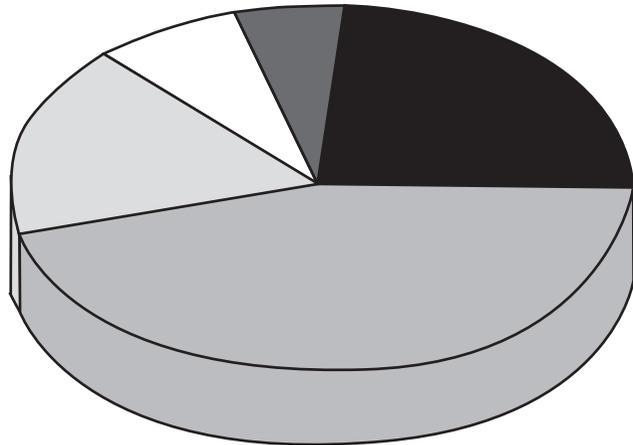
May not find the cause for syncope  
 Not predictive for all populations  
 Multiple abnormalities common  
 Not clearly indicative for cause for syncope  
 Patients may need an ICD or pacemaker for another indication

This wide range of results reflects patient selection. The electrophysiologic test is an invasive method to try to initiate an arrhythmia by stimulation of the atria and ventricles (see Chapter 6). The goal is to try to uncover a clinically important arrhythmia that caused syncope.

The main use for electrophysiologic testing in patients with syncope is to evaluate the presence of monomorphic ventricular tachycardia. It can provide the cause for syncope and will help to determine the long-term prognosis. (The two might not be related.) Induction of sustained monomorphic ventricular tachycardia is the most common abnormality seen in patients selected for electrophysiologic testing, higher than would be expected in a matched non-syncopal population with similar

structural heart disease. Induction of sustained ventricular tachycardia likely indicates that it was the cause for syncope but a negative test does not rule out ventricular tachycardia.

Results are disease-specific. The electrophysiologic test has the highest sensitivity and specificity to detect sustained monomorphic ventricular tachycardia and the cause for syncope in patients with coronary artery disease who are not acutely ischemic. Another group with a high incidence of inducible ventricular tachycardia are patients with an underlying bundle branch block. Up to 30% of these patients will have ventricular tachycardia induced.



**Fig. 1.7** Electrophysiologic testing. Patients with syncope of undetermined origin (12% of patients had multiple abnormalities). AVN/HP, AV node/His–Purkinje; SND, sinus node disease; SVT, supraventricular tachycardia; VT, ventricular tachycardia.



**Table 1.15** Electrophysiologic testing for syncope-selected studies.

Study	All patients	Positive test	VT	SVT	SND	AVB	Other
Bass [207]	70	37	31	3	0	3	0
Denes [293]	89	53	13	13	15	58	0
DiMarco [214]	25	17	9	0	1	3	4
Doherty [294]	119	78	31	6	4	5	32
Gulamhusein [297]	34	6	0	3	3	0	2
Hess [41]	32	18	11	0	5	1	1
Kall [45]	175	52	29	4	9	11	0
Krol [210]	104	31	22	2	2	6	0
Morady [215]	53	30	24	0	2	0	4
Olshansky [44]	105	41	28	13	1	3	5
Reiffel [299]	59	29	8	3	15	13	0
Teichman [213]	105	112	36	16	19	69	20

AVB, atrioventricular block; SND, sinus node dysfunction; SVT, supraventricular tachycardia; VT, ventricular tachycardia.

Several conditions can place patients at risk for malignant arrhythmia but cannot be effectively evaluated by electrophysiologic testing. The ejection fraction can further select which patients will have an abnormal electrophysiologic test result. In one report [210], 31 of 104 syncope patients had ventricular tachycardia induced on electrophysiologic testing. If the left ventricular ejection fraction was < 0.40, ventricular tachycardia was induced

in 35% of the patients, whereas for those with an ejection fraction > 0.40, only 3% had ventricular tachycardia induced. Patients with normal or near normal left ventricular ejection, even in the presence of structural heart disease, will likely have a normal electrophysiologic test unless other evidence is present (e.g., idiopathic ventricular tachycardia). The test is now not generally recommended as a first-line test for patients with a left ventricular

**Table 1.16** Electrophysiologic testing. Does therapy prevent recurrent syncope and sudden death?

Study	Patients	Follow-up	Syncope Effective Rx	Sudden death Effective Rx	Syncope Ineffective Rx	Sudden death Ineffective Rx
Bass [207]	70	30	20	31	50	47
Kall [45]	175	24	0	3	27	25
Olshansky [44]	87	26	12% (14%)	0% (8%)	30% (54%)	16%

Figures in brackets indicate lack of compliance with therapy.

ejection fraction > 0.40; however, it may be useful if other testing is negative, if syncope recurs, if there is a late potential on signal-averaged ECG, or if there are prolonged episodes of non-sustained ventricular tachycardia on monitoring. The Holter monitor, however, does not appear to be a good method to assess which patients will benefit from electrophysiologic testing [44,299,300].

The test can miss a tachycardia that is responsible for syncope. Non-sustained ventricular tachycardia can cause syncope but the sensitivity of the electrophysiologic test to evaluate this rhythm is low. Electrophysiologic testing can miss ventricular tachycardia such as in patients with dilated or valvular cardiomyopathy. The electrophysiologic test cannot assess the “clinical” arrhythmia accurately for patients with polymorphic ventricular tachycardia, hypertrophic cardiomyopathy, or the long QT interval syndrome.

Occasionally, the electrophysiologic test should be considered for a patient with frequent episodes of syncope when no other cause can be found even if the ejection fraction is intact. In such a patient with recurrent episodes, the tilt table test should be performed first. If negative, an electrophysiologic test may be diagnostic but a negative result would be expected in over 70% of such patients. One possible abnormality that may be found is an idiopathic monomorphic ventricular tachycardia which can be cured by radiofrequency ablation during testing. Another is a poorly tolerated supraventricular tachycardia, even possible in patients without apparent structural heart disease. In one study of syncope patients, 13 of 105 had a supraventricular tachycardia induced (four of these patients had ventricular tachycardia induced also) [44]. The incidence of supraventricular tachycardia induction varies between studies but is relatively

rare. Induction of supraventricular tachycardia is rare in previously asymptomatic patients. Therefore, if induced and associated with hypotension or hemodynamic collapse, it should be considered a cause for syncope and treated, perhaps with radiofrequency ablation. The electrophysiologic test is not adequate to assess atrial flutter or fibrillation, or to assess the ability of the AV node to conduct very rapidly or very slowly under all conditions.

The use of electrophysiologic testing to evaluate tachycardia in syncope patients appears warranted. Patients who have therapy guided by electrophysiologic testing appear to have less syncope recurrence and reduced mortality (Table 1.16), although no prospective, randomized trials have been performed. Olshansky *et al.* [44] have shown that if tachycardia is induced and is suppressible by medication, 14% had recurrent syncope or cardiac arrest if they took medications that appear to be effective versus 54% who were non-compliant with medications in a 25.8-month follow-up. However, there are studies suggesting that electrophysiologic testing is useful in syncope patients.

Electrophysiologic testing is fair, at best, to evaluate sinus bradycardia and AV block in patients with syncope [296,299,301]. An abnormal sinus node recovery time is relatively specific to detect sinus node disease but its presence does not indicate that sinus node dysfunction caused the syncope; also sensitivity is low. If the sinus node recovery time is more than 3 s and there is no other apparent cause for syncope, sinus node dysfunction is the likely cause for syncope and a pacemaker should be implanted. His–Purkinje conduction can be evaluated by the electrophysiologic test but rarely is an abnormal finding noted and significant infra-Hisian block can be missed. An HV interval > 100 ms is a probable cause for syncope if no other cause

can be found. If there is a bundle branch block, pacing-induced infra-Hisian block can be seen. Procainamide or other class IA antiarrhythmic drugs can be used to “stress” the His–Purkinje system and determine the presence of pacing-induced infra-Hisian block [302,303]. Fujimura *et al.* [296] found that only two of 13 patients had the correct diagnosis of infra-Hisian block determined by electrophysiologic testing. If present, it is the likely cause for syncope and a pacemaker should be implanted. Atrioventricular block in the AV node as cause for syncope cannot be evaluated accurately.

The electrophysiologic results derived must be interpreted in light of the clinical situation and are not always helpful [304]. An induced arrhythmia may not be the cause of syncope, but simply a laboratory artefact [305]. Induction of ventricular fibrillation only has little, if any, clinical significance in syncope patients. Patients generally do not pass out from ventricular fibrillation; they die [306]. Induction of non-sustained, monomorphic, ventricular tachycardia is similarly difficult to interpret.

We found several years ago that 21% of our primary electrophysiologic tests had been to evaluate and diagnose a potential cause for syncope. The test was performed on outpatients with a history of syncope and during an acute hospitalization for a recent episode of syncope. We still advocate the use of electrophysiologic testing in patients with heart disease and syncope, although the test is being used less and less in lieu of empiric ICD implantation.

While electrophysiologic testing is useful for a subset of syncope patients, there are several concerns:

- 1 not all arrhythmias are diagnosed accurately;
- 2 multiple “soft” abnormalities may be found, none of which may be responsible for syncope;
- 3 autonomic effects influencing a tachycardia are not adequately evaluated;
- 4 sinus node and AV node dysfunction cannot be evaluated fully.

### Other testing

**Cardiac echo.** The echocardiogram is useful but cannot be recommended as an initial screening tool unless the history or physical examination warrants its use [307]. Pericardial tamponade, valvular abnormalities, aortic valve disease, and hypertrophic cardiomyopathy can all cause syn-

cope and these abnormalities can be quantitated by the echocardiogram. The main reason to perform an echocardiogram, even without obvious physical findings, is to assess the presence of left ventricular dysfunction or right ventricular enlargement (resulting from right ventricular dysplasia) that may suggest the presence of a ventricular arrhythmia. The test should be considered to evaluate left ventricular function in patients over 50 years old even if there is no history consistent with heart disease and even if the ECG is normal. It adds expense but is safe and unlikely to lead to therapeutic mishap.

**Signal-averaged ECG.** The signal-averaged ECG is useful to detect risk for cardiac arrest and monomorphic ventricular tachycardia in syncope patients with apparent heart disease and is therefore useful in some patients with syncope [308–310]. An abnormal result consists of the presence of a “late potential” or a prolonged QRS complex. The chance of finding the presence of ventricular tachycardia is related to the extent of the abnormalities observed (i.e., if three out of the three observed criteria: QRS duration, amplitude of the last 40 ms of the QRS complex, and length of the low amplitude signal at the end of the QRS complex).

This non-invasive test has its highest predictive accuracy when coronary artery disease is present. The main use of the signal-averaged ECG is for patients who have coronary artery disease and syncope but have preserved ventricular function (ejection fraction > 0.40). If the ejection fraction is < 0.40, proceeding directly to electrophysiologic testing is recommended.

The signal-averaged ECG, however, may provide some adjunctive information in patients with coronary artery disease and ejection fraction < 0.40 should the electrophysiologic test be negative. The test may be falsely negative (and may miss the risk of ventricular tachycardia) if there has been an inferior myocardial infarction. Also, the test lacks predictive accuracy in patients who do not have coronary artery disease. It may be falsely positive when a bundle branch block is present.

The use of other non-invasive tests as general screen for syncope, including T-wave alternans and heart rate variability, are of uncertain utility to predict the need for ICDs.

### Cardiac catheterization

Cardiac catheterization is advocated for patients with suspected heart disease and syncope. Cardiac catheterization may find an underlying structural heart problem but the test is not justified unless there is a history suggestive of a significant valvular problem or adequate suspicion for an ischemically mediated arrhythmia. The blanket use of cardiac catheterization in syncope patients, even when heart disease is diagnosed, is certainly not warranted, is probably overused, and can only be recommended on a case-by-case basis.

### Treatment

Once a cause for syncope has been identified, treatment should be *considered*. Treatment for all the conditions mentioned is beyond the scope of this chapter and is discussed elsewhere. Not all patients who pass out require treatment even if the cause is identified. For example, a patient who has an isolated vasovagal episode resulting from a specific situation unlikely to be reproduced does not require therapy.

#### Case 12

A 52-year-old woman had a viral syndrome associated with diarrhea, nausea, and vomiting. Fluid intake was inadequate. After abruptly standing up from bed, she developed nausea and lightheadedness. Several minutes later she became diaphoretic and collapsed, waking up on the floor. After hydration and recovery from her viral infection, no further therapy was indicated.

### Management of recurrent syncope, no cause identified

Proper evaluation of the syncope patient, before evaluation becomes futile and excessive, depends on patient age, underlying medical conditions, and ensuing physical limitations imposed upon the patient. For patients with an unidentified cause for syncope, no specific therapy can be prescribed and no studies clearly document a valid, rational treatment plan. In many such patients, syncope will not recur or episodes will be rare and nothing more needs to be done, but, depending on the patient, an aggressive approach may be needed. The prognosis

for patients with syncope of undetermined etiology using appropriate methods to evaluate the cause is relatively good in the short term. The recurrence rate of syncope can be up to 30% [15,38].

For patients with recurrent syncope, reassessment may be necessary. Even *after* further extensive or repeated evaluation, however, no cause for syncope is ever found in up to 85% of these patients. Hospitalizations for repeat monitoring, tilt table testing, and electrophysiologic testing are therefore rarely indicated. Perhaps certain aspects of the history were not completely considered and should be revisited. It is likely that the majority of patients with SUO have an autonomically mediated cause and are likely to have neurocardiogenic syncope. Always consider psychological causes as well (see Chapter 12). While such patients with undiagnosed syncope generally have a good prognosis [15,282], specific patient subgroups fare poorly (e.g., patients with dilated cardiomyopathy) and syncope recurrence is always possible. For some patients with recurrent, debilitating episodes, a trial of empiric therapy may be warranted.

In the elderly, the empiric placement of a pacemaker has been considered an option but this remains highly controversial [311–315]. It has been shown with extensive monitoring that transient bradyarrhythmias can be diagnosed as the cause for syncope when no other cause can be found [223].

While some patients with undiagnosed syncope appear to benefit from pacing, it is always best to have good justification for a pacemaker. With newer techniques for monitoring, this is now possible.

Empiric therapy for SUO is usually no better and can even be worse than no therapy at all [211,316,317]. Moazez *et al.* [211] found that the recurrence rate of syncope was even worse if empiric therapy was given. Therapy guided by electrophysiologic testing may have helped prevent syncope recurrence [211,316].

Recent data suggest that an adenosine triphosphate (ATP) infusion may provide information regarding the need for a pacemaker in patients aged over 60 years [318]. If the infusion of ATP causes a > 10-s pause, this suggests highly active muscarinic vagal receptors and indicates that a pacemaker may eliminate syncopal episodes if no other cause is diagnosed.

*Case 13*

An 85-year-old man with recurrent syncope collapses with increasing frequency. The initial evaluation was negative. An electrophysiologic consult was called to rule out an arrhythmic cause for syncope. Further history was obtained. The patient collapsed in the morning at breakfast. Apparently the patient was being treated with increasing dosage of acetaminophen with codeine for arthritis and haloperidol at night for sleep. The patient was seen to be confused in the morning and did not really have syncope. After the drugs were stopped the “syncope” stopped.

*Case 14*

A 51-year-old New York Heart Association functional class I woman with dilated cardiomyopathy, ejection fraction of 0.25, and left bundle branch block, plowed her car into a truck, destroying it, after she passed out. When she awoke, she did not remember anything. History and physical examination were otherwise negative. On the monitor, she had a three-beat run of ventricular tachycardia. An electrophysiologic test was negative. She had passed out a year before but did not see a doctor.

*Therapy.* An empiric implantable defibrillator was placed.

*Case 15*

A 17-year-old woman with more than 10 episodes of syncope, once when driving a car, has no history of medical problems, a normal physical examination (except sinus bradycardia and occasional junctional rhythm), a normal ECG, and a normal tilt table test. She has seasonal asthma. An event monitor was not helpful.

*Therapy.* Theophylline was started for presumed neurocardiogenic syncope and she remains asymptomatic for 3 years.

*Case 16*

An 80-year-old male patient who lives in a nursing home falls frequently. He takes amlodipine and hydrochlorothiazide for hypertension. He collapsed at the nursing home and broke his right hip. Initially, upon attaching a monitor, he was found to be in atrial fibrillation with a rate of 50 and an associated blood pressure when awake of 165/70 mmHg

without orthostatic signs. An echocardiogram showed left ventricular hypertrophy and intact left ventricular function.

*Therapy.* An empiric pacemaker was placed and he remains symptom-free.

*Case 17*

A 39-year-old woman with history of mitral valve prolapse passed out suddenly without warning on two occasions. She takes no medication.

*Physical.* No orthostatic signs, a midsystolic click was present. ECG was normal. Echocardiogram showed mitral valve prolapse. A tilt table test was negative. An event monitor was given for 1 month but she had no symptoms.

*Therapy.* No further evaluation was performed and no therapy was given.

*Case 18*

A 52-year-old hypertensive woman without known history collapsed at home and came to the emergency room with a rapid rate in atrial fibrillation, evidence for Wolff–Parkinson–White syndrome, and a blood pressure of 90/60 mmHg. She remained slightly lethargic even after DC cardioversion. Her sister stated that she had the worst headache of her life before collapsing at home. A CT scan revealed a subarachnoid bleed.

*Therapy.* After resection of her berry aneurysm, and with no further therapy for Wolff–Parkinson–White syndrome, she recovered without incident.

### **A protocol to evaluate syncope in the emergency room** (see also Figs. 1.3a,b & 1.4, pp. 24–26)

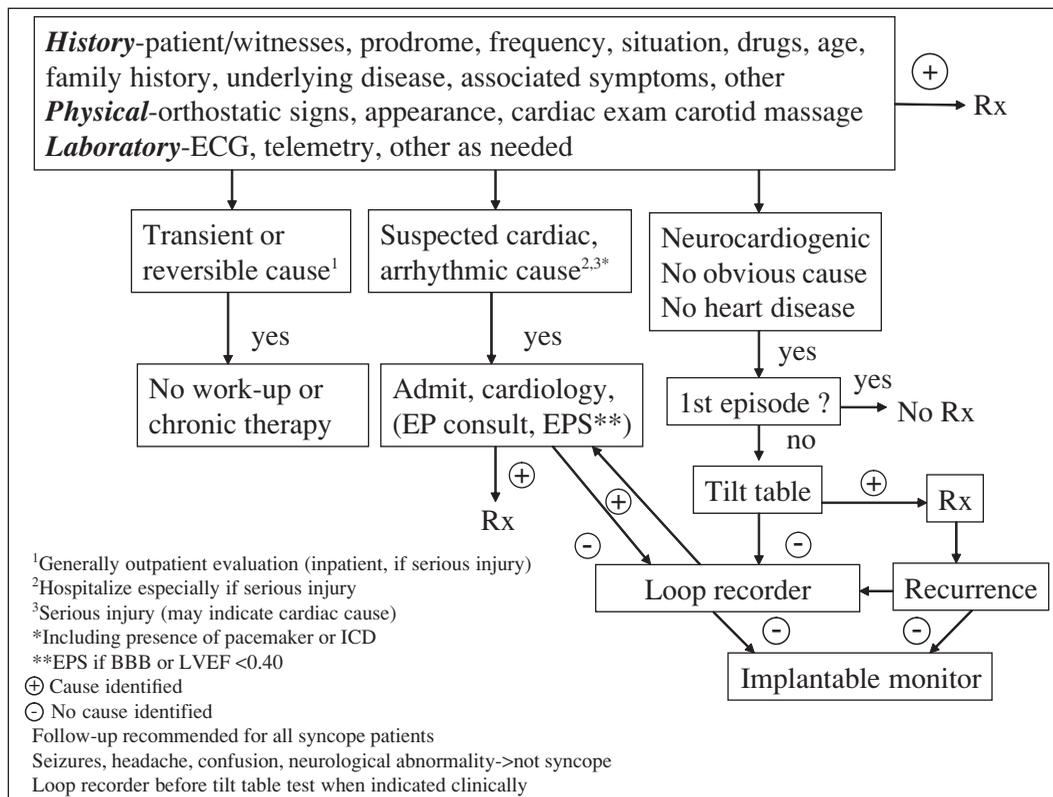
After an initial history (including evaluation of prodrome, palpitations, cardiovascular disease, seizures, and medications) and physical examination (including orthostatic vital signs, a complete cardiac and neurologic examination, carotid massage as needed) in the emergency room or other outpatient setting, an ECG, a hemoglobin test, a blood glucose test, and cardiac monitoring are obtained (during evaluation in the emergency

room). If the patient is older than 40 years, is taking a diuretic or a vasodilator, has evidence for dehydration or renal disease, a BUN, creatinine and electrolytes are ordered. If there is history of a new neurologic abnormality, head trauma, or a severe headache, a head CT scan is considered in conjunction with a neurology consult; otherwise, a CT scan is not ordered. If no specific etiology of syncope is identified, attention is directed to categorization by age and underlying medical conditions. Is there pacemaker or implanted defibrillator present, is there potential for malfunction? Did the implanted defibrillator discharge? Is there a long QT or corrected QT interval, either continuously or intermittently (> 0.500 s)? Is there a bundle branch block? Is there a known or suspected heart condition? If the answer to any of these questions is “yes,” the patient is admitted. If there is an implanted defibrillator or a pacemaker, it is interrogated immediately, even before admission. If the patient is older than

50 years, but the answer to the above questions is “no,” the patient is either discharged with early follow-up by the following physical or an internist or is admitted for a 23-h (“outpatient”) admission with a bedside cardiac monitor. In the hospital, an electrophysiologic consult is obtained if there is a history of heart disease, impaired left ventricular function, bundle branch block, pacemaker, or ICD. Testing directed at the specific cause of syncope is planned and performed in the hospital or as an outpatient. If no cause is identified, the patient is discharged, often with an event monitor. A tilt table test is considered.

### An algorithm to manage syncope

A valid universal algorithmic approach to syncope is shown in Fig. 1.8. Such an approach can be applied to the great majority of patients who have syncope. Specific intricacies of each patient’s problems must



**Fig. 1.8** A universal algorithmic approach to syncope. BBB, bundle branch block; ECG, electrocardiogram; EP, electrophysiology; EPS, electrophysiology studies; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction.

be considered. These intricacies may further direct proper diagnostic approaches and therapeutic strategies.

## Summary

This chapter reviews an initial approach to patients who present with syncope. It is not meant to be inclusive. Throughout the chapter, the reader is referred to other chapters for more in-depth coverage of the many topics presented.

## Conclusions

Syncope is a common manifestation of many disease processes. The problem is recurrent and handicapping in a minority of cases. Patients with syncope and heart disease, particularly when there is impaired left ventricular function, bundle branch block, evidence for congestive heart failure, or a positive family history, appear to be at particularly high risk of death and require an aggressive initial approach. Patients who benefit most from hospitalization include those with suspected cardiac disease, the elderly, those with serious injuries, and those with new neurologic findings.

Diagnostic tests should be used sparingly, directed by a carefully performed history and physical examination. No series of tests is universally applicable. Extensive, undirected testing and repeat hospital admissions are usually unrewarding and expensive.

Over the past few decades, there have been advances in the ability to evaluate the syncope patient properly. The initial management is best directed by the savvy clinician who can discern clues from the history and physical examination to direct further diagnostic evaluation when needed. Up to half of patients with syncope remain undiagnosed, indicating that while we have come a long way we still have a long way to go.

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