REVIEW

Diagnosis of Patients with Syncope in Emergency Medicine

Shingo Hori

Department of Emergency Medicine, Keio University Hospital, Tokyo, Japan

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Abstract. Syncope is a common medical problem, which accounts for 3.5% of emergency room visits. It includes diverse clinical etiologies, from cardiac origin with poor prognosis to reflex-mediated hypotension with benign clinical course. Trauma is not rare in patients with syncope, e.g. bruises or lacerations on the head and face were recognized in 17%. Accordingly, patients presenting with syncope may have a risk of sudden cardiac death, or risk of trauma if the episodes are repetitive. It is a physician’s task to diagnose syncope and identify its cause. The history is an essential part of the initial evaluation. Electrocardiography (ECG) is necessary in every case. However, organic disease as a cause is identified in 20% of syncope in routine work-up, and the remaining cases are reflex induced hypotension (neurocardiogenic syncope), misdiagnosed arrhythmia, coronary spasm or unknown. Recent investigations suggest the usefulness of provocation to diagnose neurocardiogenic syncope. Two important non-invasive provocations to reproduce syncope are carotid sinus compression and tilt table test. In patients with syncope who visited emergency room, tilt test was positive in 25%, whereas the response to carotid sinus compression was positive in 21%. One or both of the tests was positive in 39%, suggesting that neurally-mediated syncope accounts for a significant number of patients. (Keio J Med 43 (4): 185-191, December 1994)

Key words: neurally-mediated syncope, tilt table test, carotid sinus syndrome, sudden death

It is not well known that syncope or faintness is a common medical problem presented in the emergency department. Although most of its clinical course is benign, it may cause serious trauma or could be an ominous prodrome of sudden death. Therefore, it is necessary for emergency room physicians to provide an efficient strategy for the work-up of syncope. The aim of this review is to describe the present status of the art of diagnosing patients with syncope in the emergency department. In addition to the general work-up, recent progress in neurally-mediated syncope, and the possible risk of sudden death related to syncope will be discussed.

Definition of Syncope

Syncope is a transient global cerebral ischemia, associated with a loss of consciousness and postural tone. According to the definition, syncope is caused by a sudden episodic fall of blood pressure. A cessation of cerebral blood flow for less than 10 seconds or profound systolic hypotension of less than 50 mmHg is adequate to cause syncope. A classic study described young volunteers who became unconscious on a tilt table when their mean blood pressure suddenly fell to 25 mmHg. Following syncope and assuming the supine position by falling, the spontaneous recovery of blood pressure and consciousness is the usual course.

Etiology

Causes of syncope are shown in Table 1, which include diverse clinical etiologies, e.g. structural disease of the heart or gastrointestinal tract, functional impairment of blood pressure regulation etc. Some of the causes are lethal, while others are benign. Further, a great number of disorders mimic syncope, e.g. epilepsy, subarachnoid hemorrhage, hypoglycemia, conversion reaction, post-traumatic amnesia, etc, which make the physician’s task of diagnosis more difficult. There is little data available on the incidence of syncope in Japan. According to our experience, during the sixty-five-month period from August 1988 to December 1993, of 10,828 patients who visited the emergency room by ambulance, 379 patients had syncope (3.50%).
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Table 1 Etiologies of Syncope

1. Organic or Degenerative Disease
   a) Cardiac Arrhythmias
      Ischemic heart disease: Acute myocardial infarction, angina pectoris
      Other cardiovascular diseases: Hypertrophic obstructive cardiomyopathy, aortic stenosis,
      pulmonary embolus, pulmonary hypertension, etc.
   b) Other organic diseases: Gastrointestinal bleeding, anaphylaxis, etc.
   c) Orthostatic hypotension due to impaired autonomic function:
      Parkinsonism, chronic idiopathic orthostatic hypotension, etc.

2. Neurally-mediated Syncope
   a) Vasovagal syncope
   b) Carotid sinus syndrome
   c) Situational syncope

3. Syncope Related to Medication
   Antihypertensives, antiarrhythmics, etc.

4. Syncope of Unknown Etiology

Incidence and Prognosis

The Framingham Study revealed that more than 3% of the general population experienced syncopal episodes during thirteen biennial examinations. According to the study, subjects with syncope had a benign prognosis as shown by the low incidence of cardiovascular and cerebrovascular events and sudden death. However, up to 6% of all admissions to hospitals in the United States are related to syncope and an enormous amount of money is consumed for its work-up. Syncope accounts for about 3% of patients who visit the emergency room. Among them, cardiac causes account for 8% to 25% of patients with a one-year mortality of 30% in Kapoor and colleagues' report. Therefore, prompt diagnosis and management of the cardiac causes of syncope are absolutely necessary in the emergency room.

There is little data available on the incidence of syncope in Japan. According to our experience, during the sixty-five-month period from August 1988 to December 1993, of 10,828 patients who visited the emergency room by ambulance, 379 patients had syncope (3.50%). Interestingly, the incidence is similar to the data reported in the United States. In Tokyo, more than 400,000 emergency calls for an ambulance are recorded annually, suggesting that about 14,000 patients with syncope are transported to the hospital. Our preliminary study of the incidence of syncope in the Japanese population has shown that 3.4% of 7,000 people experienced syncope and that the number of people with syncope is several times the number of syncope patients transported to the hospital by ambulance (unpublished data). Thus, it is likely that an annual incidence of syncope in Tokyo ranges from 50,000 to 100,000, and the incidence in the general population is very close to that reported in other advanced countries.

Age and Sex of Patients with Syncope

The distribution of the age and sex of patients with syncope who visited our emergency room is shown in Figure 1. The age range is wide. Generally, the number of males is greater than the number of female patients (213 vs 166). A unique exception to this male dominance...
exists in the younger generation. In the age range of 20–30, the number of female patients is almost twice that of males (51 vs 27). The high incidence of syncope in the young female population is limited to a narrow range from 20 to 25 years old. The most common cause in this age group is vasovagal syncope. The susceptibility of young females is also recognized in the case of faintness following venipuncture during the periodic physical check-up (unpublished data). A proposed hypothesis is that some characteristic in their lifestyle may be related to a susceptibility to syncope in this young female group, such as a lack of physical exercise and their desire for weight reduction.

**Trauma**

Occasionally syncope may be missed in a patient who has suffered a trauma. We treated a middle-aged man with the several surgical sutures on his face, who had experienced multiple episodes of syncope but not diagnosed until his final visit to us. Because syncope itself is symptomless, trauma is the most outstanding clinical feature and attracts the attention of the emergency room staff. In addition, post-traumatic amnesia makes history-taking difficult. Bruises or lacerations on the head and face were recognized in 16.6% of the 379 patients with syncope in the present series. One had a rupture of the eye ball. Seven fell on the railroad track. Linzer reported that in the syncopal patient, lacerations and fractures of the arm, leg and hip are common. From our experience, however, fractures are common in the face, e.g. jaw and zygoma, and rare in the hip and shoulder. Accordingly it is an easily recognizable sign for the emergency room physician to suspect syncope when the patient has trauma to the face or head.

**Diagnostic Procedures**

**History**

The history is an essential part of the initial evaluation. In syncope, the patient does not realize the situation and a description by an observer is very helpful to determine whether the event was truly syncope. The mode of onset and recovery can provide important clues to identify the cause of syncope. Posture just before syncope should be addressed. Standing is common but sitting is not rare. If syncope develops while supine, it is less likely to be true syncope. Spontaneous pain preceding the event is a serious warning sign. Chest oppression suggests myocardial ischemia. Headache associated with vomiting and drowsiness is a sign of subarachnoid hemorrhage. Numbness in the limbs associated with dyspnea and tachypnea before syncope suggests hyperventilation syndrome. On arrival at the emergency room, the patient with syncope looks very quiet and weak, while a patient with epilepsy is restless and looks around frequently. Seizure, if prolonged more than a few minutes, confirms epilepsy. However, a short period of seizure can be observed in syncope. Atypical tonic or clonic motor activity may accompany syncope due to sudden and severe hypotension caused by arrhythmia such as ventricular tachycardia or prolonged asystole, complicating a clinical distinction of syncope from epilepsy. Premonitory symptoms such as nausea, epigastric discomfort, diaphoresis and yawning usually precede syncope, all of which are believed to indicate vasovagal syncope. However, these symptoms are provoked by hypotension, except for a sense of warmth which is produced by muscle vasodilatation. More specific for vasovagal syncope is a triggering event preceding the syncope such as painful stimuli, psychological stress such as bad news, an unpleasant sight such as blood or an invasive medical procedure, etc. An abrupt onset without premonitory symptoms suggests arrhythmia. Effort syncope is associated with myocardial ischemia, arrhythmia, athlete’s blackout, cardiac obstructive mechanism, such as outflow obstruction, and pulmonary hypertension. The relationship with meals, swallowing, cough, miction and defecation suggest situational syncope. Movement of head and neck may precede syncope in carotid sinus syndrome. In syncope, the recovery of consciousness is always prompt, whereas epilepsy is associated with postictal confusion. If the head was hit during syncope, posttraumatic amnesia may complicate the clinical picture.

A detailed medication history is necessary especially for the aged population. Cardiovascular drugs may induce syncope by inappropriate vasodilatation, bradyarrhythmia and tachyarrhythmia and aggravation of carotid sinus hypersensitivity. Common medications inducing syncope in the present study were: β blocking agents, nitrates, ACE inhibitors, digitalis, calcium blocking agents, antiarrhythmics, etc.

**Physical examination**

The physical signs of a patient who has just arrived at the emergency room are full of positive findings to make the diagnosis. This is true of patients with syncope. The skin and mucosal surface of the conjunctiva look pale due to generalized vasoconstriction by an augmented sympathetic activity following syncope. Blood pressure is normal or relatively low, and is rarely high. The values should be carefully assessed by comparing with the patient’s previous pressure level. Orthostatic blood pressure change gives critical information about the cause of syncope, but the examination should be delayed until structural diseases of the heart and great vessels are negated. Trauma on the face or head indicates a sudden collapse causing an abrupt fall. Dangerous arrhythmia is
frequently associated with trauma. Both bites in the tongue and scratches to the skin on the back of the fingers and hands suggest generalized seizure. Asymmetrical weak or absent peripheral pulse suggests acute dissection of the aorta. Enuresis suggests generalized seizure, but occasionally occurs in syncope. Examination of the heart may disclose a heart murmur in an aortic stenosis, aortic regurgitation in an aortic dissection, hypertrophic subaortic stenosis, or high pitched pulmonary second sound in pulmonary hypertension. Mild confusion due to a subarachnoid hemorrhage or cerebral concussion may be difficult to discriminate from a weak and quiet attitude in a patient with syncope.

**Non-invasive testing**

Electrocardiography (ECG) is necessary in every case. The syncope related findings should be sought, which includes arrhythmias, ST elevation or depression in myocardial ischemia, QT prolongation, and a shift of the electrical axis in right ventricular overload. ECG monitoring for one hour in the emergency room is useful for screening arrhythmias. In the peripheral blood count, leukocytosis of up to 12,000/µl occurs even if not associated with a structural disease. Gastrointestinal bleeding and hypovolemia as causes of syncope are usually diagnosed by a history of hematemesis or occult blood, but it is not rare for an elevated blood urea nitrogen level to provide a diagnostic clue. Elevated creatine phosphokinase (CPK) suggests epilepsy, rather than myocardial necrosis. Of interest, the ammonia level is increased just after a generalized seizure which then decreased in 30 minutes post-seizure (unpublished data). If a patient is not in shock, a significantly negative base excess indicates epilepsy. In every case, hypoglycemia should be negated. Hypocapnia in the blood gas analysis confirms hyperventilation. Chest X-ray may not be necessary routine in the presence of ultrasound echocardiography in the emergency room. Both an electroencephalogram and a computed tomography have a low diagnostic yield when used to evaluate patients with syncope who have no focal neurologic abnormality and a negative neurologic history.8,22

**Diagnosis of neurally-mediated syncope**

Two important non-invasive provocative tests to reproduce syncope are carotid sinus compression19,23–25 and the tilt table test.5,9,26–30 The former has been traditionally applied for many years for the diagnosis of carotid sinus hypersensitivity, but it has not been widely used. The latter has been recently proposed for the diagnosis of vasovagal syncope and has been used for a growing number of patients for the past several years. The background for the increasing prevalence of the tilt table test is two-fold, first, the risk of syncope as a sign of sudden cardiac death has been generally accepted,1,2 and secondly, the financial cost for the workup of syncope is great.6,12 In the United States, the estimated number of patients who annually visit the emergency room with syncope is about 300,000 and the financial cost for admission cases amounts to 750 million dollars.8 Thus, a cost-effective approach to identify the causes of syncope is needed. In our hospital, the tilt table test is performed on an outpatient basis and identifies vasovagal syncope if the response is positive. Because vasovagal syncope is most common among the causes of syncope, the number of candidates for the test is estimated to be large. Further, carotid sinus compression could be simultaneously examined in association with the tilt table test.31 Carotid sinus compression on tilting appears more physiological than in the supine posture, and tilting increases the sensitivity of the test.

Using a tilt table with a footboard for weight bearing, an upright tilt of 45 to 80 degrees is used for patients with recurrent syncope of an unknown etiology for 10 to 60 minutes according to various protocols,26–30,32,33 occasionally supplemented by intravenous isoproterenol.34–36 The positive response to tilting involves reproduction of syncope or pre-syncope in association with profound hypotension or bradycardia. The sensitivity and specificity of the test in patients with recurrent syncope is reported to be between 27 and 75%, and between 86 and 100%, respectively. Supplementation of isoproterenol (1–6µg/min DIV) increases sensitivity from 27% to 87%34 but may decrease the specificity of the test.37 The mechanism of hypotension provoked by the tilt test in patients with vasovagal syncope is believed to be an augmentation of the Bezold-Jarisch reflex38 by activating mechanoreceptors located in the inferior wall of the ventricle. The nerve impulse travels via the vagal or glossoopharyngeal nerve to the brain stem, where the impulse inhibits the sympathetic drive and produces prominent vasodilatation.

Carotid sinus compression19,24–25 is a procedure which places gentle pressure on the wall of the carotid sinus, where baroreceptors exist in the adventitia. Physiologically, a deformation of the arterial wall induced by a rapid change in intracavitary pressure, modulates impulses from the baroreceptor, which then travels to the brain stem via the carotid sinus nerve and the glossoopharyngeal nerve. Efferent nerves are the same as in the tilt table test. Vascular tonus is regulated by the feedback loop including the carotid sinus. In carotid hypersensitive patients, who are usually old and male, a mild compression on the sinus wall provokes transient bradycardia (maximum RR interval >3 sec) and/or hypotension (a maximum decrease in systolic pressure >50 mmHg). Diagnosis of carotid sinus syndrome requires a demonstration of a hypersensitive carotid sinus in the presence
of a history of syncope. A real-time monitoring of blood pressure is necessary to record the maximum change in blood pressure, which has necessitated invasive arterial pressure monitoring. Recently, a non-invasive device to measure pressure wave form by a volume compensation method has been developed as shown in Figure 2.

In our emergency department, patients with syncope who do not have any identified cause are considered to be candidates for evaluation by tilt table testing or carotid sinus compression. From our experience, the tilt test was positive in 17 of 68 patients (25.0%), whereas the response to carotid sinus compression was positive in 15 of 72 patients (20.8%). One or both of the tests was positive in 22 of the 57 patients (38.6%) in whom both tests were performed. The results suggest that evidence for neurally-mediated syncope was shown in a significant number of patients. Other than the tilt table and carotid compression tests, eye ball compression is reported to be useful as a provocative procedure. All of these procedures are to provoke hypotension or bradycardia by interrupting the neural regulation of blood pressure control.

Situational syncope is the third category of neurally-mediated syncope. It is also called vago-vagal syncope and is different from the vasovagal mechanism. The reflex loop consists of the vagal nerve as its afferent and also its efferent. The diagnostic dilemma in situational syncope is the absence of any diagnostic criteria other than the history. An example of this problem is shown in the case of an 82-year-old male who fell down due to syncope just after urination. His response to carotid sinus compression was positive with a prolonged asystole for 8 seconds, which is an indication for permanent pacemaker implantation. If the evaluation for carotid sinus had not been performed, he would have been erroneously diagnosed as miction syncope. Accordingly, the diagnosis of situational syncope should be put aside until vasovagal and carotid sinus syndrome are ruled out.

Invasive testing

An indication for invasive testing is recurrent syncope in patients with structural heart disease. Patients with recurrent syncope from a cardiac disease who do not have the specific cause of the syncope identified and treated, have a high one-year mortality rate of up to 30%. The diagnostic yield of electrophysiological study in this population has been reported to range between 18% and 75%. Treatment of abnormalities detected by electrophysiological studies prevents recurrence of syncope in most patients. In contrast, in patients with no underlying heart disease, electrophysiological studies result in clinically significant abnormalities in 12% to 20%. In patients without structural heart disease, the incidence of sudden cardiac death is very low, and the spontaneous remission rate of syncope is high.

Coronary vasospasm is common in Japan, and Niigata University recently reported that a significant percentage of syncope of unknown etiology is related to coronary vasospasm. In the reported cases, the vasospastic episode was documented by electrocardiogram during resuscitation, or by provocative testing with ergonovine during coronary angiography. About 20% of patients with coronary spasm have a history of syncope, whereas coronary spasm accounted for 4 of 11 patients (36%) with syncope of unknown etiology who visited emergency medicine. A standard for the clinical indication for coronary angiography with ergonovine provocation in syncope has not been established and further study is warranted.

In the present study, structural diseases accounted for 20% (47 patients) of all syncope patients, among which the cardiac causes were 61% (29 patients). Coronary artery disease including vasospasm was diagnosed in 14 patients, followed by arrhythmia in 10 patients. In coronary artery disease, diagnosis was based on a history of chest pain preceding the syncope or ECG findings suggestive of ischemia.

Risk of sudden death related with syncope

Patients with syncope may be at risk for sudden death: First, the one-year mortality of cardiac patients with syncope who do not have another identified cause of the syncope is exceedingly high. This is a documented high risk group. Second, there are reported cases who received cardiopulmonary resuscitation among patients with vasovagal syncope without structural heart disease. In tilt table testing, prolonged asystole for more than 10 seconds is revealed, which is called a
malignant vasovagal syndrome. Occasionally cardiopulmonary resuscitation was necessary on the tilt table when asystole was prolonged for more than 30 seconds. There were four cases with prolonged asystole for more than 10 seconds on tilt testing in our series (Fig 2). During the prolonged asystole, pallor, tonic and clonic muscle activities, and ocular deviation were observed. They also shouted simultaneously with seizure activity. The malignant vasovagal syndrome accounts for 2% of all tilt-induced syncope in the present study, which is reported to be as high as 28% of tilt-positive patients if the prolonged RR interval is defined as more than 4 seconds. Grubb and colleagues reported that 3 of their 10 cardioinhibitory patients had received bystander cardiopulmonary resuscitation for several minutes, but were awake and in sinus rhythm when paramedic personnel arrived.

The third category is related to the posture during syncpe. It is not rare for syncpe to occur when a patient is sitting; a spontaneous recovery is less likely to occur because the patient does not fall. The blood pressure level required for syncpe is generally less than 50 mm Hg systolic, which hinders normal respiration; the central respiratory center is depressed and a simultaneous loss of muscle tone deprives effective ventilation. As a result, a loss of ventilation and profound hypotension could induce an irreversible catastrophe in a patient. Two patients were found pulseless, with no ventilation, pallor, and comatose, while they were sitting in a chair outside of a hospital. A bystander began cardiopulmonary resuscitation and spontaneous respiration and circulation recovered in a few minutes, without any medication. No evidence of structural diseases including the heart was found and they were discharged. We are not sure if cardiopulmonary resuscitation, other than lying down, was necessary for their recovery, but it is certain that death was inevitable if they remained seated for a longer period. The personnel of ambulances witness many cases of cardiopulmonary arrest in the sitting position. Even if syncpe is not the malignant vasovagal syndrome, or not due to a cardiac cause, a prolonged and profound hypotension which is not relieved may induce an irreversible arrhythmia, myocardial ischemia, and eventually a cardiopulmonary arrest. Although the risk of sudden death produced by syncpe in the sitting position is not an established concept yet, adequate education should be given to patients with recurrent syncpe and their families.

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