

Syncope in Young Patients II: Presentation and Management of Specific Causes of Syncope

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This article, which is the second part of a 2-part series on syncope in young patients, will review the classifications, etiology, evaluation, and treatment of various types of syncope. The first part of the series, published in the April issue of *Hospital Physician*,¹ presented an approach to the evaluation of a patient with syncope. Case presentations will occasionally be used in this part of the series to illustrate certain clinical points. Particular attention will be paid to the varied manifestations and causes of cardiac syncope (Table 1), which generally denotes a poor prognosis and thus necessitates early recognition and aggressive treatment.

NEUROCARDIOGENIC SYNCOPE

Case 1 Presentation

A 19-year-old woman has a witnessed syncopal episode after standing for 2 hours at a crowded outdoor musical concert on a hot, humid August day. She regains consciousness shortly after falling to the ground and is taken by paramedics to a nearby hospital. On questioning, the patient reports having had 2 similar episodes since June; she says she typically feels nauseous and diaphoretic just prior to fainting. She has no history of previous cardiac problems.

Etiology of Neurocardiogenic Syncope

Neurocardiogenic syncope, also known as vasovagal syncope, is the most common cause of syncope in young persons and results from a maladaptive neurocardiovascular reaction to the assumption of an upright posture for prolonged periods. Paradoxical vasodilation (a vasodepressor response), combined with a bradycardic (ie, cardioinhibitory) response, leads to hypotension, cerebral hypoperfusion, and eventual syncope.²

Clinical Manifestations

Characterized by a prodrome of diaphoresis, nausea, vomiting, and dyspnea, neurocardiogenic syncope usually occurs when persons are in an upright position and resolves spontaneously once they are in a supine position. Aggravating factors that commonly trigger neurocardiogenic syncope include a postprandial state, exertion in a warm environment, a prolonged upright posture, use of diuretics, dehydration, and emotional or stressful situations. In contrast, syncope that occurs while a person is in a supine position or that is associated with a prolonged period of confusion after the syncopal event is less likely to be neurocardiogenic in origin.

Diagnosis and Treatment

In cases of neurocardiogenic syncope, a diagnosis is usually made based on the clinical picture. If necessary, a head-up tilt-table test can be used to confirm the diagnosis. Low-dose isoproterenol infusion has been shown to increase the sensitivity of this test but to result in a lower, although still acceptable, specificity (93%).³

Treatment typically includes avoidance of triggering factors, sufficient intake of fluids and salt, and (occasionally) the use of fludrocortisone. β -Blockers, anticholinergic agents, and selective serotonin reuptake inhibitors have also been administered to patients with neurocardiogenic syncope to counteract the maladaptive neurovascular response, but success of such treatments has varied. Cardiac pacing should be reserved for patients with documented prolonged symptomatic bradycardia.

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Table 1. Cardiac Causes of Syncope

Rhythm disturbances

Tachyarrhythmia

- Wolff-Parkinson-White syndrome
- Long QT syndrome
- Right ventricular outflow tract tachycardia
- Idiopathic (primary) ventricular tachycardia/fibrillation
- Right ventricular dysplasia
- Brugada's syndrome

Bradyarrhythmias

- Infectious causes of rhythm disturbances
- Rhythm disturbances caused by sarcoidosis

Coronary artery defects

Vascular flow defects

- Pulmonary hypertension
- Atrial septal defect
- Tetralogy of Fallot

Outflow obstruction

- Hypertrophic obstructive cardiomyopathy
- Mitral valve prolapse
- Left atrial myxoma
- Pulmonary stenosis
- Pulmonary embolism

Follow-up Discussion of Patient 1

Based on her history, patient 1's syncopal episode is diagnosed as neurocardiogenic syncope. She is encouraged to increase her fluid and salt intake.

CARDIAC SYNCOPE

Rhythm Disturbances

Case 2 Presentation. A healthy 20-year-old man has an episode of sudden cardiac death (SCD) while at work. He is resuscitated by paramedics and transferred to a nearby hospital. On admission, results of electrocardiography (ECG) show pre-excitation and a delta wave in the QRS complex.

Tachyarrhythmias. Tachyarrhythmias are characteristic of several clinical syndromes.

Wolff-Parkinson-White syndrome. Not typically associated with structural heart disease, Wolff-Parkinson-White (WPW) syndrome commonly causes supraventricular tachycardia. With subsequent rapid conduction via the accessory pathway, ventricular fibrillation can occur and result in syncope and SCD. WPW syndrome is also associated with atrial fibrillation accompanied by very

rapid ventricular arrhythmias that are triggered by preferential conduction of fibrillatory waves via the fast conducting accessory tract.

Emergency treatment of stable patients with WPW syndrome is intravenous administration of procainamide; unstable patients typically receive direct-current cardioversion. In cases of WPW syndrome, avoidance of nodal blocking agents (eg, calcium channel blockers, digitalis) when treating atrial fibrillation is key. Definitive treatment is radiofrequency ablation of the accessory pathway.⁴ Treatment of asymptomatic patients with WPW syndrome remains controversial.

Based on his clinical presentation and ECG results, patient 2's condition is diagnosed as WPW syndrome. Unfortunately, he is declared brain dead soon after his arrival at the hospital, and his organs are donated by his family.

Long QT syndrome. Long QT syndrome is caused by defects in the body's potassium and sodium channels that result in prolongation of action potentials and trigger ventricular arrhythmias.⁴ It can be either acquired or congenital. Romano-Ward syndrome, a congenital form, is an autosomal dominant disease, whereas Jervell and Lange-Nielsen syndrome, a more severe form, is an autosomal recessive disease associated with deafness. Long QT syndrome is sometimes a familial disorder and is also associated with a family history of SCD.

Typically, long QT syndrome is diagnosed on the basis of ECG evidence of a corrected QT interval of more than 0.44 seconds; a corrected QT interval of more than 0.50 seconds is associated with an increased risk for SCD. Long QT syndrome is sometimes associated with the presence of decreased heart rates and the absence of QT shortening with exercise.

Standard treatment of long QT syndrome often includes administration of β -blockers and phenytoin. Other treatment modalities include pacemaker placement, left stellate ganglionectomy (to prevent the catecholamine surge that occurs during the induction of ventricular arrhythmias), and placement of an implantable cardioverter defibrillator.⁵

Right ventricular outflow tract tachycardia. Right ventricular outflow tract (RVOT) tachycardia is the most common cause of idiopathic ventricular tachycardia and is associated with either nonsustained monomorphic ventricular tachycardia or exercise-induced sustained ventricular tachycardia. Although some patients may not be aware of their arrhythmia, others may experience palpitations, dizziness, and syncope. The prognosis of patients with RVOT tachycardia is usually benign, and SCD is rare.

with hypoxia. Optimal treatment necessitates early recognition of the tetralogy and surgical correction, prior to development of pulmonary hypertension. Patients with established Eisenmenger syndrome and hypoxia should not be allowed to participate in sports.⁴

Outflow Obstruction

Case 4 presentation. A 22-year-old man has a witnessed syncopal episode while playing in a college basketball game. He has a known family history of SCD. After immediate transfer to the nearest hospital, he undergoes 2-dimensional echocardiography in the emergency department. Results show a left ventricular outlet obstruction that was worsened by prior administration of amyl nitrate.

Case 5 presentation. A healthy 20-year-old woman is found to have an apical diastolic murmur with a click during a routine physical examination. The patient then undergoes 2-dimensional echocardiography.

Hypertrophic obstructive cardiomyopathy. With a prevalence of 1 in 500 in the US population, hypertrophic obstructive cardiomyopathy (HOCM) is now considered more common than was previously recognized,⁴ especially in men and in African Americans. In another study, it was identified as the most common cause (36%) of SCD in athletes.¹⁴ HOCM causes syncope and SCD primarily by way of ventricular tachyarrhythmias and myocardial ischemia; bradyarrhythmias are less commonly involved. Persons at highest risk for the disorder include survivors of cardiac arrest, those with high-risk genotypes, those with a significant family history of SCD, those with massive hypertrophy (wall thickness > 35 mm), and those with sustained or nonsustained ventricular tachycardia.¹⁵ Interestingly, the presence of repolarization (ie, T-wave) alternans is predictive of increased risk for ventricular arrhythmia and decreased survival; conversely, results of electrophysiologic study are not good predictors of mortality in cases of HOCM.

Standard treatment of the disorder involves administration of β -blockers or calcium-channel blockers, although this therapy may not prevent sudden death. High-risk patients should undergo placement of an implantable cardioverter defibrillator, with optional administration of amiodarone. Surveillance of other family members of patients with HOCM is warranted.

Patient 4 receives a diagnosis of HOCM based on the results of his 2-dimensional echocardiography. Because of his personal and family history, he undergoes placement of an implantable cardioverter defibrillator.

Mitral valve prolapse. Mitral valve prolapse is a relatively common entity in the general population, with a

worldwide prevalence of 4% to 5%.⁶ Prolongation of the QT interval can result from delayed repolarization caused by abnormal papillary muscle stretching. Most patients with mitral valve prolapse have a benign course. However, patients with this disorder and significant mitral regurgitation are at increased risk for ventricular tachyarrhythmias that can lead to syncope and SCD; a proposed theory suggests that these ventricular arrhythmias result from endocardial friction lesions in 86% of cases.⁶ Although the prevalence of ventricular arrhythmias is increased in patients with mitral valve prolapse who have significant mitral regurgitation, this fact does not translate into an increased risk for SCD.⁶

Factors that are predictive of SCD in patients with mitral valve prolapse include a personal history of syncope (reported in 50% of patients with mitral valve prolapse who experience SCD⁶), a family history of SCD at young age, and abnormalities on ECG at rest, including a prolonged QT interval.

Asymptomatic patients with mitral valve prolapse require no treatment. Those with palpitation caused only by ventricular ectopy can be treated with administration of β -blockers. Those with tachyarrhythmia can be treated with administration of various antiarrhythmic drugs; however, there is no evidence that suppression of the arrhythmias prevents SCD. Also, studies of mitral valve repair or replacement have yielded mixed results. In high-risk patients, the presence of ventricular tachyarrhythmias should be documented, and placement of an implantable cardioverter defibrillator should be considered.⁶

Results of 2-dimensional echocardiography in patient 5 confirm a diagnosis of mitral valve prolapse; however, there is no evidence mitral regurgitation or left ventricular hypertrophy. On further questioning, she recalls no palpitations or syncopal events. Because she is asymptomatic, her physician decides not to treat her at this time.

Left atrial myxoma. Syncope in patients with left atrial myxoma is caused by obstruction of blood flow to the left ventricle and is usually related to postural changes.

Treatment is surgical removal of the myxoma.

Pulmonary stenosis. Many patients who have pulmonary stenosis survive to adulthood without experiencing any symptoms. However, as the pulmonary valve becomes more fibrotic with age, patients begin to experience symptoms of right ventricle failure, exertion-related dyspnea, and syncope. Diagnosis is easily made based on results of 2-dimensional echocardiography, with determination of the pressure gradient. Symptomatic patients with mild stenosis (ie, a pressure gradient < 25 mm Hg)

can undergo percutaneous valvuloplasty. Patients with moderate and severe stenosis require either valvotomy or valvuloplasty.

Pulmonary embolism. A diagnosis of pulmonary embolism should be considered in any young patient with paraplegia or a clotting disorder who experiences syncope. Usually, if the pulmonary embolism is large enough to cause syncope, the patient will most likely need thrombolytic therapy.

ORTHOSTATIC HYPOTENSION

Typical Presentation and Outcome

Orthostatic hypotension occurs when a susceptible person assumes an upright posture. Persons who experience orthostatic hypotension tend to have decreased arterial pressure, a feeling of light-headedness, and blurred vision. Total recovery from these signs and symptoms follows the assumption of a recumbent position. Orthostatic hypotension is usually aggravated by venous blood pooling and/or volume depletion. The disorder can be an adverse effect of various medications, most notably diuretics, antihypertensive agents, nitrates, tranquilizers, and antidepressants. Avoiding inciting factors and following simple protective measures when assuming an upright posture are usually recommended as standard therapy.

Postural Orthostatic Tachycardia Syndrome

Postural orthostatic tachycardia syndrome is a variant form of orthostatic hypotension that affects young persons. A pathologic disorder, it occurs when insufficient sympathetic activation during standing causes recurrent symptoms of light-headedness, fainting, and syncope. Recently, postural orthostatic tachycardia syndrome has been closely linked to chronic fatigue syndrome in young adults.¹⁶ Diagnosis of postural orthostatic tachycardia syndrome requires first documenting the presence of orthostatic hypotension, tachycardia, and other relevant symptoms on head-up tilt-table testing.

NEUROLOGIC CAUSES OF SYNCOPE

Seizures

An early, essential part of the diagnostic evaluation of patients with syncope of presumed neurologic cause is distinguishing between syncope and a seizure. Common features of seizures include sudden onset, lack of a prodrome, absence of pallor, injury from falling, convulsions, incontinence, prolonged unconsciousness, and postictal confusion. Temporal lobe seizures (ie, absence seizures) are the most difficult to differentiate from syncope. Interestingly, a seizure may

be the initial manifestation of an arrhythmia, especially long QT syndrome,¹⁷ or may occur secondary to prolonged cerebral hypoperfusion in cases of syncope.

Migraines

Syncope is often caused by the vasospasm that is part of the pathophysiology of migraines, especially when they affect the basal arterial system. More specifically, there is the premonitory aura of the migraine itself, followed by loss of consciousness for several minutes. The patient usually awakens with a severe occipital or lateralizing headache.

Transient Ischemic Attacks/Stroke

In young patients, transient ischemic attacks or strokes are generally unlikely to cause syncope. However, when syncope does occur as a result of these neurologic insults, it is more likely to be associated with vertebrobasilar insufficiency and a defect in the medullary arousal center. Although microemboli are most commonly involved in such syncopal episodes, vasculitis and systemic hypotension can also play a role.

Treatment of syncope caused by transient ischemic attacks or strokes should be directed at the cause of the cerebrovascular disease. For example, patients with thrombophilia and clotting disorders may need lifelong anticoagulation, whereas patients with vasculitis will often require immunosuppression with corticosteroids.

MISCELLANEOUS CAUSES OF SYNCOPE

Alcohol

Increased alcohol consumption has been suggested as a cause of syncopal episodes, most likely by aggravating orthostatic hypotension. Even short-term alcohol ingestion elicits hypotension during orthostatic stress because of impairment of vasoconstriction.¹⁸

The increased prevalence of alcohol abuse by young persons necessitates the exclusion of alcohol abuse in any young patient presenting with syncope.

Drugs

Cocaine abuse is known to cause cardiomyopathy, hypertension, aortic dissection, accelerated coronary artery disease, and SCD. Moreover, it has recently been reported that cocaine abuse can cause bradyarrhythmias that first present as syncope.¹⁹ Cocaine abuse has also been reported to cause ventricular arrhythmias and bundle branch blocks. Similarly, heroin and tricyclic antidepressants have been associated with heart block and SCD.²⁰

Hysterical Syncope

Hysterical syncope is seldom associated with injury and most often occurs in young adults in the presence of an audience. Although such syncopal episodes can be prolonged, persons experiencing them generally maintain a normal heart rate and blood pressure. Unlike syncope caused by cardiac and other causes, hysterical syncope is not relieved by assuming a supine position.

Psychogenic Factors

When psychogenic factors are responsible for syncope, the episode is typically characterized by rapid deep breathing, a feeling of chest tightness, palpitations, circumoral and hand numbness, and tingling. Symptoms are reproducible by inducing hyperventilation. Standard treatment is encouraging breathing through a bag or cupped hands and providing reassurance.

Eating Disorders

Both anorexia nervosa and bulimia have been associated with syncope and SCD. Patients with these disorders typically have electrolyte imbalances, bradycardia, and a prolonged QT interval on ECG.²⁰

CONCLUSION

This 2-part series has attempted to provide useful clinical information about the issue of syncope in young patients, first detailing an approach to patients with syncope and then outlining the most common causes of syncope in this population. Despite diagnostic challenges, key elements from the history, physical examination, and laboratory and other evaluations of patients with syncope can often differentiate cardiac and noncardiac causes. Therapy should be directed toward the specific causes of syncope. In the absence of available specific therapy, avoidance of situations in which injury can occur to the patient with syncope is advisable. **HP**

REFERENCES

1. Tadros GM, Oren JW, Costello JM. Syncope in young patients I: an approach to the patient with syncope. *Hosp Physician* 2002;38(4):47-54.
2. Sra JS, Murthy V, Natale A, et al. Circulatory and catecholamine changes during head-up tilt testing in neurocardiogenic (vasovagal) syncope. *Am J Cardiol* 1994;73:33-7.
3. Natale A, Akhtar M, Jazayeri M, et al. Provocation of hypotension during head-up tilt testing in subjects with no history of syncope or presyncope. *Circulation* 1995;92:54-8.
4. Berger G, Dhala A, Friedberg DZ. Sudden cardiac death in infants, children, and adolescents. *Ped Clin N Amer* 1999;46:221-34.
5. Viskin S, Belhassen B. Polymorphic ventricular tachyarrhythmias in the absence of organic heart disease: classification, differential diagnosis, and implications of therapy. *Prog Cardiovasc Dis* 1998;41:17-34.
6. Altemose GT, Buxton AE. Idiopathic ventricular tachycardia. *Annu Rev Med* 1999;50:159-77.
7. Thiene G, Nava A, Corrado D, et al. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med* 1988;318:129-33.
8. McAlister HF, Klementowicz PT, Andrews C, et al. Lyme carditis: an important cause of reversible heart block. *Ann Intern Med* 1989;110:339-45.
9. Hagar JM, Rahimtoola SH. Chagas' heart disease in the United States. *N Engl J Med* 1991;325:763-8.
10. Rizzato G. Extrapulmonary presentation of sarcoidosis. *Curr Opin Pulm Med* 2001;7:295-7.
11. Taylor AJ, Byers JP, Cheitlin MD, Virmani R. Anomalous right or left coronary artery from the contralateral coronary sinus: "high risk" abnormalities in the initial coronary artery course and heterogeneous clinical outcomes. *Am Heart J* 1997;133:428-35.
12. Rich S, Lam W. Atrial septostomy as palliative therapy for refractory primary pulmonary hypertension. *Am J Cardiol* 1983;51:1560-1.
13. Graham TP Jr, Bricker JT, James FW, Strong WB. 26th Bethesda conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities: Task Force 1: congenital heart disease. *J Am Coll Cardiol* 1994;24:867-73.
14. Maron BJ, Shirani J, Poliac LC, et al. Sudden death in young competitive athletes. Clinical, demographic and pathological profiles. *JAMA* 1996;276:199-204.
15. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. *N Engl J Med* 1997;336:775-85.
16. Karas B, Grubb BP, Boehm K, Kip K. The postural orthostatic tachycardia syndrome: a potentially treatable cause of chronic fatigue, exercise intolerance, and cognitive impairment in adolescents. *Pacing Clinical Electrophysiol* 2000;23:344-51.
17. Friedberg CK. Syncope: pathological physiology: differential diagnosis and treatment. II. *Mod Concepts Cardiovasc Dis* 1971;40:61-3.
18. Narkiewicz K, Cooley RL, Somers VK. Alcohol potentiates orthostatic hypotension: implications for alcohol-related syncope. *Circulation* 2000;101:398-402.
19. Castro VJ, Nacht R. Cocaine-induced bradyarrhythmia: an unsuspected cause of syncope. *Chest* 2000;117:275-7.
20. Liberthson RR. Sudden death from cardiac causes in children and young adults. *N Engl J Med* 1996;334:1039-44.