

Syncope in athletes: A guide to getting them back on their feet

Fainting during exercise may be a life-threatening sign; cardiologic and neurologic testing help guide treatment

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Practice recommendations

- Following inconclusive cardiovascular and neurological testing, an echocardiogram, stress test with Holter monitor, and possibly tilt table testing are appropriate ways to determine whether a vasovagal response is to blame for a young athlete's exercise-induced fainting episodes (C).
- Advise patients with exercise-induced syncope to increase fluid and salt intake while exercising (B). Strength training can also be helpful (B). Most drug therapies, such as beta-blockers, vasoconstrictors, and anti-arrhythmics, have inconsistent results (A). Use of permanent pacemakers are not effective (B).

Strength of recommendation (SOR)

- A Good-quality patient-oriented evidence
 B Inconsistent or limited-quality patient-oriented evidence
 C Consensus, usual practice, opinion, disease-oriented evidence, case series

An 18-year-old woman was referred to us for evaluation after fainting on several occasions during a track workout. She'd been a competitive athlete for several years, and the episodes began 3 months earlier. She reported that they happen shortly after she started to run. She

also told us that just before a spell, she had a sense of fatigue and severe leg pain.

Bystanders who witnessed one of the episodes reported that her eyes rolled upwards right before she fell; they saw no tonic-clonic activity that would indicate a seizure. We learned that the spells were short-lived and followed by immediate recovery with no mental deficits, such as confusion. On several occasions, she suffered superficial skin abrasions, but fortunately no serious injuries had occurred.

■ We suspected exercise-induced syncope

Prompt diagnosis of syncope in athletes is essential as it may be a marker for sudden cardiac death. The differential diagnosis, however, is broad (TABLE). Syncope in adolescents is often associated with fasting and eating disorders, excessive heat, alcohol, abdominal straining, exercise, hypoglycemia, growth spurts, lack of sleep, and low blood pressure.

Few clues from her history and exam

The clinical evaluation requires a careful and detailed history, including taking a family history to exclude familial causes of sudden

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TABLE

**Differential diagnosis
 for exercise-induced syncope**

Anaphylaxis	Hypertrophic cardiomyopathy
Aortic stenosis	Hypoglycemia
Atrial fibrillation	Hypoxia
Brugada syndrome	Left ventricular hypertrophy
Cardiac dilatation	Pulmonary hypertension
Cardiac ischemia	Sick sinus syndrome
Catecholamine-dependant polymorphic ventricular tachycardia	Vasodepressor reflex
	Ventricular fibrillation
Commotio cordis	Ventricular tachycardia
Dehydration	Wolff-Parkinson-White abnormality
Eating disorders	

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**All patients
 should have an
 ECG to exclude
 arrhythmias and
 cardiomyopathy**

death, such as long QT syndrome. In our patient's case, there was no family history of sudden death or arrhythmias. She was a nonsmoker, nondrinker, and denied using any illicit drugs. She had been taking phenytoin for suspected seizure activity, but the spells continued.

On further investigation, we discovered that our patient would faint predictably 14 minutes into a competitive 5K run. She had recently adopted a more aggressive "early breakaway" strategy: she would run the initial part of the race at a pace of about 6 minutes per mile and slow down gradually towards the end.

We also learned that she had never fainted during weight training or when running at a less aggressive pace. Other than fatigue and extreme leg pain, she could not recall any other symptoms before falling, such as nausea, dizziness, weakness, or palpitations.

Her resting seated left arm blood pressure was 110/60 mm Hg and her heart rate was regular at 53 bpm. On cardiac auscultation, we heard no murmurs or abnormal cardiac sounds in the supine or standing positions. Cardiac palpation did not reveal a distal point of maximal impulse, which can suggest cardiac dilatation or cardiomyopathy.

On examination, she had normal results for muscle strength and reflexes. A sensory exam also had normal results. We ordered blood work; her CBC, electrolytes, thyroid-stimulating hormone level, creatinine phosphokinase, and liver function tests all had normal results.

**The next step:
 Cardio, neuro tests**

If the patient's history and physical examination yield normal results, he or she will require further tests, including the ones listed below.

**Exclude arrhythmias and myopathy
 Electrocardiogram (ECG).**

All patients should have an ECG. Most young patients and athletes have a variation in the sinus rate due to sinus arrhythmia. This is a normal finding and does not suggest a cause of syncope.

Prolongation of the PR interval or QRS duration may suggest the presence of atrioventricular nodal or conduction disease, respectively. A prolonged PR interval or left bundle branch block is very unusual in young patients; in the presence of syncope, these require further evaluation. The presence of isolated right bundle branch block is a less significant finding.¹

The presence of a short PR interval and slurring of the QRS upstroke suggests Wolff-Parkinson-White syndrome. Abnormalities in the QRS morphology may suggest left ventricular hypertrophy or hypertrophic cardiomyopathy. You should also exclude abnormalities in repolarization such as prolonged QT interval, Brugada syndrome, and catecholamine-dependent polymorphic ventricular tachycardia.

A careful measurement of the corrected QT interval (QTc) is essential. The normal value of the QTc interval is <0.43 seconds. Prolonged QT interval may be due to presence of genetic or acquired (ie, drug-related) long QT syndrome. Acquired long QT syndrome can

occur when a patient is taking an antiarrhythmics such as amiodarone, or, more rarely, an antipsychotic such as haloperidol and ziprasidone.

Echocardiogram. All patients should have an echocardiogram before exercise stress testing to look for abnormalities such as aortic stenosis, left ventricular hypertrophy, and hypertrophic cardiomyopathy. When assessing for left ventricular enlargement, keep in mind that the left ventricular mass may be larger than what is seen in nonathletes. This condition, known as “athlete’s heart,” is mainly due to an increase in the cardiac cavity size and some increases in the left ventricular thickness. These patients show a preserved left ventricular ejection fraction.²

Pulmonary hypertension can also be evaluated using echocardiography; however, this is a rare cause of exercise-induced syncope.

Stress testing. Stress testing can reveal several different abnormalities found among patients with exercise-induced syncope. It may reveal ischemic changes on the electrocardiogram that suggest atherosclerotic coronary artery disease or anomalous take-off of the coronary arteries. Stress testing may also provoke neurocardiogenic syncope.

EEG and CT. Electroencephalography can show changes that suggest epilepsy as a cause of syncope. Exercise-induced temporal lobe seizures are extremely rare, but are another possible cause of loss of consciousness.

Computerized tomography of the chest combined with coronary CT angiography can be very useful in evaluating patients for structural abnormalities such as aortic dissection, pulmonary embolism, and especially coronary anomalies.

The search for other mechanisms

After patients have undergone the standard round of testing as described above, any further investigation will need to be customized to the patient. If structural cardiac abnormalities and arrhythmias

are excluded (as was the case with our patient), the potential diagnoses are narrowed to neurocardiogenic syncope and orthostatic hypotension—2 common causes of sudden-onset syncope with sudden recovery.

Neurocardiogenic syncope. A common final mechanism of any syncope is a drop in blood pressure and low cerebral perfusion. This may be triggered by stimulation of the carotid baroreceptor reflex via cardiac hypercontractility, inadequate cardiac filling, or volume depletion. Volume depletion is more likely in endurance athletes who are exposed to prolonged exertion, such as marathon runners. Some patients with vasovagal mechanism may experience an aura of nausea prior to the loss of consciousness.

Another important mechanism of exercise-induced syncope is sudden vasodilatation or lack of vasoconstriction.³ Syncope can occur at peak exercise or immediately after stopping exercise. Syncope occurring after stopping exercise may be due to overwhelming vagal input during sympathetic withdrawal.

Several of these physiologic changes are accentuated during exercise and contribute to syncope. A strong cardiac contraction associated with exercise can trigger an abnormal baroreceptor reflex by stimulating cardiac mechanoreceptors.

Orthostatic intolerance. Syncope in distance athletes is sometimes due to orthostatic intolerance. Orthostatic hypotension may occur due to volume depletion and the increased contractility of the athlete’s heart—this may subsequently induce a neurocardiogenic mechanism of syncope. This is evaluated by measuring upright blood pressure after prolonged exertion.

Echocardiograms performed in athletes during upright tilt testing have proven that strong cardiac contractions occur during orthostatic stress.⁴ It has also been shown that syncopal athletes have a stronger cardiac contraction than nonsyncopal athletes.⁵ Athletes have increased cardiac distensibility—ie,

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Stress testing may reveal cardiac abnormalities; it may also provoke a fainting spell

increased variations of internal cardiac diameter over a range of equivalent filling pressures. This causes the cardiac contraction to be on the steep part of the Starling pressure–volume curve, so that a sudden drop in filling pressure results in a sudden fall in cardiac output and low blood pressure.⁶ Other researchers have found evidence against this, however.⁷

Loss of blood pressure can be caused by either sudden sympathetic withdrawal or parasympathetic overload. In some patients, syncope cannot be blocked by the use of atropine.⁸ A short diastolic filling time resulting from a rapid rate during exercise may decrease the ventricular filling in athletes and also result in low cardiac output due to the mechanism described above.

Orthostatic intolerance has been reported in ultra-marathon runners due to volume depletion;⁹ however, in light of the relatively short time to onset in our patient, and the lack of orthostasis after recovery, we did not suspect that this mechanism was at work.

Tilt table testing can be helpful

Reports on exercise-induced syncope in athletes show that a significant percentage of patients have a positive tilt table test, suggesting either an associated or independent abnormality of autonomic regulation.¹⁰

Positive tilt tests vary between 26% and 76% in these patients. In a series of 24 athletes with recurrent exercise-induced syncope, 19/24 were initially positive on tilt testing; after therapy only 2/24 remained positive.¹¹ However, some may have been patients with underlying vasodepressor syncope exacerbated by exercise and may not have truly had “exercise-induced” syncope. It is not possible to define the exact sensitivity and specificity of tilt tests for these patients because of small sample sizes. We feel that a tilt test should be ordered, as it may suggest a diagnosis in some cases.

Invasive tests are not usually needed

Invasive electrophysiology testing has little role in athletes with syncope. Most well-conditioned athletes have a relative bradycardia due to high vagal tone, but it is extremely rare that they require a permanent pacemaker.¹² Although some of these patients may have abnormal sinus node function when assessed by electrophysiology testing, to adequately test sinus node function in these patients you should perform autonomic blockade using atropine and propranolol; then an intrinsic heart rate (without the effects of autonomic tone) can be measured.

In most cases, you need to see the rhythm during an episode for accurate diagnosis. This requires a 12-lead ECG, and possibly a Holter monitor or event recorder. Remember that abnormal findings during a tilt table or electrophysiology test may be unrelated to the cause of syncope.

Anomalous take-off of coronary arteries should be excluded. In the past this required cardiac catheterization, but can now be assessed noninvasively with magnetic resonance angiography or CT.

What testing revealed about our patient

Our patient’s ECG showed nonspecific ST-T wave abnormality with no evidence of Wolff-Parkinson-White abnormality or conduction system disease. An echocardiogram showed a left ventricular end diastolic dimension of 50 mm (normal range, 40–62 mm) and a left ventricular ejection fraction of 55% (normal is 55%–60%). We saw no valvular abnormality and no evidence of left ventricular hypertrophy to suggest hypertrophic cardiomyopathy.

A stress test was performed using the Bruce protocol, during which the patient exercised for 13 minutes and achieved a heart rate of 184 bpm. She did not have any symptoms of loss of consciousness, and we saw no abnormal ST-T segment changes.

A tilt test was performed with and without isoproterenol, during which time her

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Echocardiograms during an upright tilt test have shown strong contractions occur during orthostatic stress

heart rate reached 125 bpm. There was no syncope or loss of consciousness.

A cardiac CT test was performed, which excluded coronary anomalies. The exercise test was repeated using a modified protocol with a pace set to simulate her level of exercise. The treadmill was set at a speed of 9.6 mph (a 6.25-minute mile) with no incline. Sixteen minutes into the test she had a sudden loss of consciousness and fell. She was diaphoretic with a weak, thready, rapid pulse and cool extremities.

Shortly after her fall, we recorded her blood pressure using a cuff sphygmomanometer—it was 169/95 mm Hg with a heart rate of 140 bpm. However, the patient had recovered consciousness by the time the blood pressure was recorded. The duration of loss of consciousness was less than 15 seconds. No hypotension or arrhythmias were recorded.

The exercise test with new protocol was repeated, but with placement of an intra-arterial blood pressure monitor and continuous electroencephalographic monitoring. Sixteen minutes into the test the patient requested that we stop, due to fatigue and leg pain. Just prior to this, at peak exercise, her blood pressure was 220/30 mm Hg and heart rate was 185 bpm. Immediately after stopping the treadmill, we measured a precipitous drop in intra-arterial blood pressure—down 45/4 mm Hg—and her heart rate slowed to 178 bpm. This was associated with reproduction of clinical symptoms. She lay down, and her blood pressure recovered to >120 mm systolic within seconds.

Electroencephalographic monitoring did not show any epileptiform activity. Serum blood glucose recorded during the spell was 86 mg/dL. Our interpretation was that she had a brief precipitous vasodepressor syncope triggered by exercise.

■ Management: Changing habits, medication

You can advise patients with exercise-induced syncope to avoid strenuous exercise, but this is not acceptable for

many athletes. If the patient is on certain drugs, such as vasodilators for the treatment of hypertension, these must be discontinued and another category of drug substituted, such as angiotensin-converting enzyme inhibitors.

The athlete should also increase his or her fluid and salt intake. This can be achieved with increased use of sports drinks or salt tablets (strength of recommendation [SOR]: **B**). Of course this must be done in moderation and titrated to each individual athlete's needs.

Many Rx options; we started with fludrocortisone

Pharmacotherapy for treatment of vasovagal syncope has been extensively tested, but no medication is reliably effective. Beta-blockers are sometimes prescribed, but randomized clinical trials have failed to show a predictable benefit (SOR: **A**).¹³ Pindolol may induce less bradycardia due to intrinsic sympathomimetic activity.¹⁴

Other possible medications include midodrine, fludrocortisone, theophylline, clonidine, and serotonin reuptake inhibitors. Vasoconstrictors (such as midodrine) and fludrocortisone are more likely to be effective for patients with orthostatic hypotension than vasovagal syncope (SOR: **B**).¹⁵ Fludrocortisone may cause weight gain and fatigue and affect performance in athletes.

Disopyramide is a class I antiarrhythmic agent that has additional effects of negative inotropy and a vagolytic effect. This decreases the stimulation of the carotid baroreceptors and interrupts the vagal efferent pathway. We have found this to be very useful and well-tolerated. Theoretically, though, because of its negative inotropic effect, it may decrease cardiac output enough to affect athletic performance. Initiate the drug with telemetry monitoring to detect any pro-arrhythmic electrocardiographic changes, such as torsades de pointes or QT prolongation. Prevention of the hyperdynamic cardiac contraction can

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If medication is needed, we generally try fludrocortisone first, then beta-blockers, and then disopyramide

trigger an abnormal baroreceptor reflex and block the efferent limb of the vagal response to counter the bradycardia and vasodepressor response.¹⁶

If pharmacotherapy is required, we generally prescribe drugs in the following sequence—first fludrocortisone, then beta-blockers, and, if these do not help, disopyramide. These should be first given in the hospital with telemetry monitoring to check for QT prolongation. If these are ineffective, try paroxetine or midodrine. In refractory cases, we may use various combinations of these drugs.

Disopyramide and a changed running strategy

Several mechanisms related to vigorous exercise played a role in our patient's case. During exercise, she developed a very high systolic pressure with a low diastolic pressure, resulting in a high pulse pressure that possibly led to stimulation of carotid baroreceptors. Cardiac hypercontractility related to exercise was probably a contributing factor as well. Severe leg pain prior to syncope suggested involvement of a pain-mediated mechanism.

We prescribed disopyramide 150 mg twice daily for our patient. We also recommended that she do specific exercises—to strengthen her leg muscles—and modify her running strategy.

After 2 months of therapy, she resumed competitive running successfully without any further episodes of syncope. She was able to achieve a new personal record for a cross country run by running a slower pace of 6 minutes 20 seconds per mile initially and running faster only at the end of the race. She had no recurrences of syncope during 6 months of follow-up. ■

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Disclosure

No potential conflict of interest relevant to this article was reported.

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We recommended our patient do leg-strengthening exercises and modify her running strategy to slower starts and quicker finishes