

# Postural Orthostatic Tachycardia Syndrome

Payam Safavi-Naeini, MD  
Mehdi Razavi, MD

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**From:** Department of Cardiology (Drs. Razavi and Safavi-Naeini), Texas Heart Institute; and Department of Cardiology (Dr. Razavi), Baylor College of Medicine; Houston, Texas 77030

## Address for reprints:

Mehdi Razavi, MD,  
Department of Cardiology,  
Texas Heart Institute,  
6624 Fannin St.,  
Houston, TX 77030

**E-mail:** razavi@bcm.edu

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The term postural orthostatic tachycardia syndrome (POTS) was first used by a team of researchers from Mayo Clinic led by neurologist Philip Low, in 1993.<sup>1</sup> However, the disorder was not new; over the last 160 years, it has been known by many different names, such as neurocirculatory asthenia, orthostatic tachycardia, and orthostatic intolerance.<sup>2</sup> Patients with POTS can be misdiagnosed as having severe anxiety, panic disorder, or chronic fatigue syndrome, because of their similar clinical features.<sup>3</sup>

## Definition and Epidemiology

The principal feature of POTS is orthostatic intolerance, and it is defined clinically<sup>4</sup> in the presence of

- Common symptoms that occur with standing, such as lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue;
- An increase in heart rate of 30 beats/min or more when moving from a recumbent to a standing position that lasts more than 30 s (or  $\geq 40$  beats/min in individuals 12–19 yr of age); and
- The absence of orthostatic hypotension ( $>20$ -mmHg drop in systolic blood pressure).

The prevalence of POTS is around 0.2% in the general population, and an estimated 500,000 to 1,000,000 individuals in the United States have the disorder.<sup>4</sup> Postural orthostatic tachycardia syndrome can affect individuals of either sex at any age, but 75% to 80% are female, and most patients are between the ages of 15 and 25 years at diagnosis.<sup>4,5</sup>

## Pathophysiology and Subtypes

Several mechanisms for POTS have been described, including autonomic denervation, deconditioning, hypovolemia, hyperadrenergic stimulation, and hypervigilance.<sup>6</sup> Different mechanisms may coexist in some patients.

**Neuropathic POTS.** Neuropathic POTS is the most common type, and up to 50% of patients have a restricted autonomic dysfunction of small and distal postganglionic sudomotor fibers, commonly of the feet and toes.<sup>7</sup> In addition, peripheral denervation leads to decreased norepinephrine spillover in the lower limbs during activation of the sympathetic nervous system. This effect causes the obstruction of compensatory vasoconstriction during upright posture, allowing excessive pooling of blood in blood vessels of the lower limbs and splanchnic beds. Decreases in venous return lead to sympathetic activation and reflex tachycardia.<sup>7</sup>

**Hypovolemic POTS.** Low blood volume (both red cell and plasma) has been reported in up to 70% of patients with POTS.<sup>8</sup> Compared with healthy people, POTS patients paradoxically have low levels of plasma renin activity and aldosterone despite their hypovolemia. In this low-flow subtype of POTS, angiotensin II levels are 2 to 3 times higher than normal. However, these patients have blunted systemic vascular and hypertensive response to angiotensin II compared with that in healthy subjects.<sup>8</sup>

**Hyperadrenergic POTS.** Hyperadrenergic POTS is characterized by an excessive increase in plasma norepinephrine levels ( $\geq 600$  pg/mL) and a  $\geq 10$ -mmHg rise in systolic blood pressure while standing upright for 10 min.<sup>8</sup> In hyperadrenergic POTS, there are often prominent sympathetic activation symptoms, such as increased blood pressure, palpitations, anxiety, tachycardia, and tremor.<sup>9</sup> Hypersensitivity to isoproterenol

is common in these patients; dosages that do not induce hemodynamic changes in healthy individuals will cause marked tachycardia.<sup>8</sup>

### The Role of Deconditioning

Previously, reduced left ventricular mass, stroke volume, and blood volume in patients with POTS had been attributed to physical deconditioning (that is, being out of shape), and it was thought that deconditioning could trigger symptoms of orthostatic intolerance. However, a more recent study has shown that deconditioning is not

the primary underlying mechanism for POTS. Oldham and colleagues<sup>10</sup> showed that exercise intolerance does not result from a lack of enough exercise, but from low ventricular filling pressures even during maximum effort.

### The Role of Anxiety and Hypervigilance

The prevalence of anxiety, somatic vigilance, and suicidal ideation is significantly higher in patients with POTS.<sup>2,5,11</sup> Some of the physical symptoms of POTS, such as tachycardia and palpitations, are similar to those of anxiety, but POTS is not caused by anxiety.<sup>5</sup>

**TABLE I.** Recommendations for Investigation of Postural Orthostatic Tachycardia Syndrome

	Class	Level
A complete history and physical exam with orthostatic vital signs and 12-lead ECG should be performed on patients being assessed for POTS.	I	E
Complete blood count and thyroid function studies can be useful for selected patients being assessed for POTS.	IIa	E
A 24-hour Holter monitor may be considered for selected patients being assessed for POTS, although its clinical efficacy is uncertain.	IIb	E
Detailed autonomic testing, transthoracic echocardiogram, tilt-table testing, and exercise stress testing may be considered for selected patients being assessed for POTS.	IIb	E

ECG = electrocardiography; POTS = postural orthostatic tachycardia syndrome

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**TABLE II.** Recommendations for Treatment of Postural Orthostatic Tachycardia Syndrome

	Class	Level
A regular, structured, and progressive exercise program for patients with POTS can be effective.	IIa	B-R
It is reasonable to treat patients with POTS who have short-term clinical decompensations with an acute intravenous infusion of up to 2 L of saline.	IIa	C
Patients with POTS might be best managed with a multidisciplinary approach.	IIb	E
The consumption of up to 2–3 L of water and 10–12 g of NaCl daily by patients with POTS may be considered.	IIb	E
It seems reasonable to treat patients with POTS with fludrocortisone or pyridostigmine.	IIb	C
Treatment of patients with POTS with midodrine or low-dose propranolol may be considered.	IIb	B-R
It seems reasonable to treat patients with POTS who have prominent hyperadrenergic features with clonidine or alpha-methyl dopa.	IIb	E
Drugs that block the norepinephrine reuptake transporter can worsen symptoms in patients with POTS and should not be administered.	III	B-R
Regular intravenous infusions of saline in patients with POTS are not recommended in the absence of evidence, and chronic or repeated intravenous cannulation is potentially harmful.	III	E
Radiofrequency sinus node modification, surgical correction of a Chiari malformation type I, and balloon dilation or stenting of the jugular vein are not recommended for routine use in patients with POTS and are potentially harmful.	III	B-NR

POTS = postural orthostatic tachycardia syndrome

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## Diagnosis

A diagnosis of POTS is usually suspected on the basis of characteristic signs and symptoms. To confirm the diagnosis, patients need a complete medical history to evaluate the triggers, time of onset, severity of orthostatic intolerance, possible associated nonorthostatic symptoms, and precipitating or aggravating factors; patients should also undergo comprehensive cardiac and neurologic examinations.<sup>5,9,12</sup> A standard test for diagnosing POTS is the head-up tilt test with noninvasive beat-to-beat hemodynamic monitoring (Table I).<sup>13</sup>

## Treatment

Because POTS has a variety of causes, no single treatment is effective for everyone, and combinations of approaches are often needed. Both nonpharmacologic and pharmacologic interventions are useful in the treatment of POTS (Table II); however, the former should always be tried first.<sup>14</sup> The core of nonpharmacologic therapy includes educating patients to avoid orthostatic intolerance triggers and increasing their understanding of the mechanisms of POTS. Increasing blood volume by adding extra salt to the diet and drinking more fluids, as well as reducing venous pooling by using compression garments, is recommended.<sup>4,5,13</sup>

Medications that are commonly used in the treatment of POTS include  $\beta$ -blockers, midodrine, fludrocortisone, central sympatholytic agents, pyridostigmine, ivabradine, octreotide, and erythropoietin.<sup>8</sup> Medications such as norepinephrine transport inhibitors should be avoided.

The long-term prognosis of POTS is not well studied, but almost 50% of adolescents with POTS who were evaluated by questionnaire in one study had fully recovered from symptoms at an average of 5 years after initial therapy.<sup>15</sup>

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