JAMA | Review

# Postural Orthostatic Tachycardia Syndrome (POTS)
## A Review

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**IMPORTANCE** Postural orthostatic tachycardia syndrome (POTS) is a chronic autonomic disorder characterized by excessive orthostatic tachycardia and multisystem symptoms that affects an estimated 0.1% to 1% of the US population. POTS can substantially impair daily functioning and quality of life.

**OBSERVATIONS** Consensus criteria define POTS by chronic symptoms of orthostatic intolerance accompanied by a sustained heart rate increase of at least 30 beats/min (≥40 beats/min in adolescents aged 12-19 years) within 10 minutes of standing or head-up tilt, in the absence of orthostatic hypotension, defined as a decrease in either systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg with positional change. POTS symptoms may include palpitations, lightheadedness, nausea, vomiting, gastroparesis, anorexia, generalized weakness, and muscle pain, despite absence of structural pathology within cardiovascular, gastrointestinal, and neurological organs. POTS predominantly affects females (approximately 90% of cases), with peak incidence from ages 13 to 29 years. However, the true prevalence remains uncertain partly due to underrecognition and lack of a specific diagnostic code for POTS until 2022. Common symptoms include lightheadedness, palpitations, fatigue, cognitive dysfunction ("brain fog"), exercise intolerance, nausea, bloating, constipation, diarrhea, and sleep disturbance. In a survey of 4835 patients, approximately 70% reported substantial functional impairment and loss of school or work participation, and median diagnostic delay was 24 months. In 30% to 40% of cases, symptoms began within 3 months after infections, such as SARS-CoV-2, Epstein-Barr virus, and influenza. Initial evaluation should exclude other conditions that cause sinus tachycardia, including thyroid disease, adrenal insufficiency, pheochromocytoma, cardiomyopathy, valvular heart disease, congenital heart disease, chronic lung disease, medication effects (eg, stimulants, norepinephrine reuptake inhibitors, and diuretics), anemia, and dehydration. First-line treatment includes nonpharmacological strategies to improve cardiac preload, including increased fluid and sodium intake, lower-body compression garments; avoidance of heat exposure, dehydration, and prolonged standing; and structured supervised aerobic training. Pharmacological therapies should be individualized and may include β-blockers, ivabradine, midodrine, fludrocortisone, and pyridostigmine, although evidence supporting many therapeutic interventions is limited by small studies and lack of large, randomized trials.

**CONCLUSIONS AND RELEVANCE** POTS is a chronic autonomic disorder associated with functional impairment and reduced quality of life that is diagnosed based on characteristic orthostatic symptoms in the absence of orthostatic hypotension after excluding alternative causes of sinus tachycardia. Treatment involves nonpharmacological measures (such as increased fluid and sodium intake), lower-body compression garments, structured exercise training, and individualized pharmacological therapy.

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Postural orthostatic tachycardia syndrome (POTS) is a chronic autonomic disorder defined by a sustained heart rate increase of more than 30 beats/min (>40 beats/min in individuals aged 12-19 years) within 10 minutes of standing or head-up tilt, in the absence of orthostatic hypotension. Additionally, resting heart rate in the recumbent position should be less than 100 beats/min, and characteristic symptoms of autonomic dysfunction such as lightheadedness, palpitations, fatigue, cognitive impairment, or exercise intolerance, must be present for at least 3 months. Proposed pathophysiological mechanisms include peripheral sympathetic dysfunction, altered blood volume regulation, exaggerated sympathetic activation, physical deconditioning, immune-mediated mechanisms, and cerebrovascular dysregulation.

Although the term *POTS* was introduced in the early 1990s,[1,2] related syndromes, such as Da Costa syndrome (Soldier's Heart and Effort Syndrome) and neurocirculatory asthenia, have been described for more than a century. The diagnosis of POTS has increased during and after the COVID-19 pandemic, but it frequently remains underrecognized and misdiagnosed, so the true prevalence is uncertain.[3] Recent estimates suggest that 0.1% to 1% of the US population—predominantly women of childbearing age—are affected, with approximately 70% experiencing substantial functional impairment, such as loss of school or work participation, and reduced quality of life.[4-6] Patients frequently experience diagnostic delays with a median of 24 months from symptom onset to diagnosis of POTS.[3]

This review summarizes current evidence on the pathophysiology, diagnosis, and management of POTS.

## Methods

We reviewed the medical literature on POTS using PubMed and Embase from January 1, 1990, through May 26, 2026. Search terms included *postural orthostatic tachycardia syndrome*, *POTS*, *orthostatic tachycardia*, and *postural orthostatic syndrome*. Randomized clinical trials, cohort studies, and consensus statements from major autonomic societies were prioritized. We also reviewed reference lists of key articles identifying additional relevant publications. A total of 1841 articles were retrieved from the search. Of these, 103 articles were included in this review, consisting of 74 observational studies, 14 randomized clinical trials, 2 systematic reviews or meta-analyses, 3 narrative reviews, and 3 guidelines or position statements. An additional 7 references that provide historical, epidemiological, pathophysiological, or methodological context were not part of the formal review.

## Discussion

### Pathophysiology

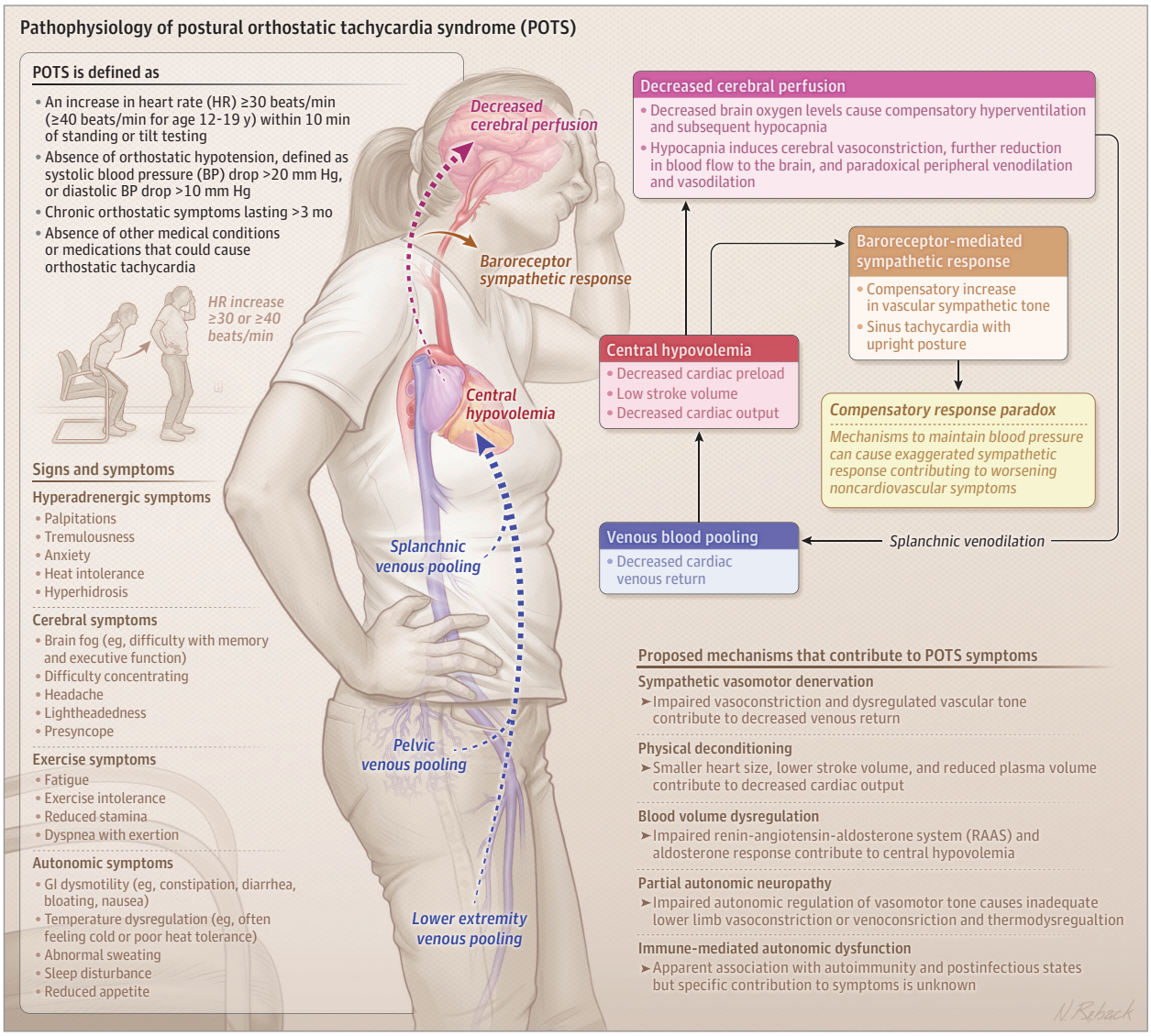
The dysregulation of the autonomic nervous system in POTS may involve multiple etiologies, including sympathetic vasomotor denervation, immune-mediated autonomic dysfunction, physical deconditioning, and altered blood volume regulation. All these etiologies cause central hypovolemia due to excessive blood pooling contributing to the orthostatic tachycardia of POTS (**Figure 1**), which is exacerbated during standing and exercise. Although central hypovolemia is not directly measured in routine clinical practice, it is supported by physiological studies (such as invasive cardiopulmonary exercise tests, cardiac magnetic resonance imaging [MRI], radionuclide blood volume assessments, and segmental bioelectrical impedance studies) that demonstrate reduced stroke volume, impaired venous return, and plasma volume deficits in patients with POTS.[7-9] Reduced cardiac preload in both the systemic and pulmonary circulations may contribute to persistent fatigue, cognitive impairment ("brain fog"), and dyspnea despite normal oxygen saturation and absence of structural cardiopulmonary disease, independent of posture or activity level.[8,10-12] In response to reduced cardiac preload, a compensatory baroreflex-mediated increase in sympathetic tone is triggered, particularly during standing, resulting in sinus tachycardia. The sinus tachycardia response is generally considered a homeostatic mechanism to maintain systemic blood pressure and cerebral perfusion and to prevent syncope. In some patients, this response is associated with elevated plasma norepinephrine, reflecting exaggerated sympathetic activation. Occasionally, excessive tachycardia may precipitate vasovagal syncope via a cardiovascular reflex triggered by ventricular underfilling.[13] Beyond the compensatory tachycardia, the hyperadrenergic response contributes to a range of noncardiovascular symptoms associated with the fight-or-flight state, such as feeling anxious, hyperhidrosis, reduced appetite, gastrointestinal dysmotility (eg, nausea, bloating), and insomnia. These compensatory responses can be exaggerated, persistent, and functionally maladaptive in POTS. Patients with POTS can experience paradoxical coexistence of impaired sympathetic function (affecting peripheral vasculature) and sympathetic hyperfunction (affecting the heart with resultant tachycardia; Figure 1).

Patchy denervation of peripheral sympathetic vasomotor nerves is one of the primary causes of excessive blood pooling in the lower body,[14,15] which was supported by norepinephrine spillover studies demonstrating reduced release of the sympathetic nervous system neurotransmitter norepinephrine from the lower extremity vasculature,[16] and corroborated by blunted muscle sympathetic nerve activity in the lower legs of a subset of patients with POTS.[17] This regional sympathetic failure leads to impaired vasomotor tone, excessive blood pooling, and impaired cardiac venous return. Partial peripheral autonomic denervation can be evaluated in clinical practice using quantitative sudomotor axon reflex testing, which measures sweat production in response to localized stimulation with the neurotransmitter acetylcholine, and has demonstrated a patchy, nonlength-dependent loss of sweat production in POTS.[15-17] Skin biopsy shows a reduced intraepidermal nerve fiber density affecting 45% to 53% of patients.[18,19]

In approximately 30% to 40% of cases, symptoms start 2 to 4 weeks after an infectious illness, such as SARS-CoV-2, Epstein-Barr virus, and influenza.[3,20,21] In this context, autoimmunity has been proposed as a contributor to autonomic neuropathy. Small studies have identified autoantibodies against G protein–coupled receptors, including α-adrenergic and β-adrenergic receptors, in many patients with POTS.[22-24]

Patients with POTS have been found to have a 16% reduction in left ventricular mass (cardiac MRI scans) and 13% lower blood volume (radionuclide assessments) compared with healthy controls.[7,25] These changes resemble adaptations observed in prolonged bed rest or spaceflight,[26-28] and some of these changes can be partially

Figure 1. Overview of Proposed Pathophysiology in Postural Orthostatic Tachycardia Syndrome




GI indicates gastrointestinal.

reversed with structured exercise interventions. Although most patients with POTS have not had prolonged bed rest prior to the onset of symptoms, physical deconditioning and subsequent cardiac atrophy represent potentially reversible and modifiable contributors to the pathophysiology of POTS.[25]

Many studies have shown that patients with POTS have a low blood volume when formally assessed using radionuclide studies. Several studies have shown inappropriately blunted plasma renin activity and suppressed aldosterone levels in some patients despite the evidence of hypovolemia, a finding often referred to as the *renin-angiotensin-aldosterone paradox*.[29-32] In the largest prospective study, 15 patients with POTS had a plasma volume deficit of 334 mL compared with 10 mL in controls and had lower aldosterone levels despite similar plasma renin activity.[29] This blunted renin-angiotensin-aldosterone system response may limit the expected compensatory sodium and water retention, thereby contributing to chronic hypovolemia and orthostatic intolerance.[29]

Reduced cerebral blood flow velocity may contribute to the neurocognitive symptoms of POTS (brain fog).[10,33] Transcranial Doppler studies have demonstrated a significant reduction in cerebral blood flow velocity and altered cerebral hemodynamics during standing,[11] potentially due to reduced stroke volume and orthostatic hyperventilation leading to hypocapnia.[34] Hypocapnia induces cerebral vasoconstriction and peripheral vasodilation, which reduces blood flow to the brain. Decreasing brain oxygen levels induce hyperventilation that increases hypocapnia, establishing a feed-forward mechanism that further worsens oxygen delivery to the brain independent of systemic blood pressure (Figure 1).[34,35]

## Epidemiology and Risk Factors

POTS is estimated to affect up to 1% of the US population, although this estimate is based primarily on expert consensus because population-based epidemiological studies are lacking.[36]

**Box. Frequently Asked Questions About Postural Orthostatic Tachycardia Syndrome**

**What are the diagnostic criteria for postural orthostatic tachycardia syndrome (POTS)?**

The diagnostic criteria for POTS includes a sustained heart rate increase of more than 30 beats/min (>40 beats/min in individuals aged 12-19 years) within 10 minutes of standing or head-up tilt without orthostatic hypotension (defined as a decrease in either systolic blood pressure of ≥20 mm Hg or diastolic blood pressure of ≥10 mm Hg within 3 minutes of positional change) and presence of characteristic symptoms of autonomic dysfunction (eg, lightheadedness, palpitations, fatigue, cognitive impairment, or exercise intolerance) for at least 3 months in patients without other medical conditions, disorders, or medications that could cause these symptoms.

**What are nonpharmacological treatments for patients with POTS?**

First-line treatment approaches for POTS are nonpharmacological, including discontinuation of medications that increase heart rate such as amphetamines, atomoxetine, or spironolactone, increasing dietary salt to 10 g daily and water to 3 L daily to expand blood volume, use of lower-body and abdominal compression garments, and supervised exercise training with an aerobic focus. Patients with POTS should avoid dehydration, alcohol consumption, and prolonged standing or sitting and should be encouraged to periodically use physical countermeasures, such as leg crossing, squatting, or isometric muscle tensing, to augment venous return.

**What are pharmacological treatments for patients with POTS and when should they be started?**

Pharmacological treatments should be considered for patients with persistent POTS symptoms despite implementation of nonpharmacological treatments or for those with substantial symptoms at the initial visit, and should be added to nonpharmacological treatments. Commonly used medications include heart rate–lowering medications, vasoconstrictors, blood volume expanders, and sympatholytic medications. Selection of medication should be guided by the predominant physiological disturbance and POTS symptom profile.

A retrospective, electronic health record (EHR)–based study in 2025 of 200 million US patients estimated the age-standardized diagnostic incidence of POTS at 24.5 per 100 000 and its diagnostic prevalence at 100 per 100 000.[6] However, these EHR-based estimates are likely underestimates because the specific *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* diagnostic code for POTS only became available on October 1, 2022.[37,38] Females account for approximately 90% of POTS cases[3,4,6] with the highest incidence in the 13- to 29-year age range, reaching approximately 90 to 100 per 100 000 in females.[6] Multiple studies show an increased risk of POTS following SARS-CoV-2 infection, with approximately 2-fold higher relative risk and pooled absolute rates of approximately 1% (≈108 per 10 000 individuals) among infected populations.[6,39,40] These numbers partially reflect increased clinical recognition during the post–COVID-19 period.[41] An EHR-based study from Cedars-Sinai Medical Center including 284 592 vaccinated individuals and 12 460 patients with SARS-CoV-2 infection reported modestly increased odds of POTS-associated diagnoses 90 days after either a SARS-CoV-2 infection or a COVID-19 vaccination. However, the absolute rates of developing POTS were substantially higher after SARS-CoV-2 infection (2087 per 100 000) than after COVID-19 vaccination (268 per 100 000), corresponding to about a 5.3-fold greater risk following infection.[40]

## Clinical Presentation

In about 30% to 40% of cases, the symptom onset of POTS is acute after a viral or bacterial infection, typically within days to weeks.[3,20] Based on an online, community-based, cross-sectional survey of 4835 individuals with POTS, other reported antecedent events preceding the onset of POTS symptoms included major surgery (12%), pregnancy (9%), vaccination of any type (6%), and physical trauma, such as concussion or traumatic brain injury (4%).[3]

Patients with POTS typically have chronic symptoms of orthostatic intolerance—defined as symptoms that occur during upright posture and improve with recumbency, including lightheadedness, palpitations, fatigue, and presyncope and excessive orthostatic tachycardia upon standing. In addition to orthostatic tachycardia, patients with POTS have symptoms caused by reduced cardiac preload and maladaptive hyperadrenergic response. In the aforementioned online survey of 4835 individuals with POTS, cognitive impairment (or brain fog), was frequently reported as difficulties with concentration (94%) and memory problems (87%).[3] Neuropsychological studies of patients with POTS suggest more selective deficits in domains such as attention and processing speed than among healthy controls; however, overall cognitive performance often overlaps with wide normal range from normative data, despite subjective cognitive concerns.[12,42,43] Although individual symptoms may fluctuate in severity over time, a cross-sectional survey of 227 patients with pediatric POTS reported chronic fatigue (97%) and exercise intolerance (83%), defined as the reduced ability to perform activities due to various symptoms.[44] In addition, patients frequently exhibit hyperadrenergic symptoms such as sinus tachycardia (88%), insomnia (73%), and excessive sweating (43%).[37] Gastrointestinal symptoms including nausea, epigastric pain, bloating, and alternating constipation and diarrhea were reported in up to 90% of patients in the aforementioned survey of 4835 individuals with POTS,[3] and about 30% also had a diagnosis of irritable bowel syndrome.[3]

## Assessment and Diagnosis

The diagnosis of POTS requires symptoms of orthostatic intolerance for at least 3 months and, per the consensus criteria from the Canadian Cardiovascular Society, a sustained heart rate increase of at least 30 beats/min (≥40 beats/min in individuals aged 12-19 years) within 10 minutes of assuming an upright posture (**Box**).[38,41,45,46] The diagnosis of POTS also requires that tachycardia occurs without significant orthostatic hypotension, defined by a sustained blood pressure decrease of more than 20/10 mm Hg. Resting supine heart rate is typically normal or only mildly elevated (and within the broad normal range); high resting heart rate (>100 beats/min) should prompt evaluation with a Holter monitor for alternative diagnoses such as inappropriate sinus tachycardia or other cardiac arrhythmias (such as atrial tachycardia). The differential diagnosis includes other medical conditions (eg, cardiomyopathy, hyperthyroidism, alcohol withdrawal, and Addison disease) and medications that increase heart rate (eg, such as stimulants, norepinephrine reuptake inhibitors, diuretics, and vasodilators),[47] and transient

states such as acute infection, acute dehydration, or short-term reductions in physical activity (eg, following an acute illness or hospitalization).

A detailed history should focus on the onset and evolution of symptoms, recent infections, potential triggers such as acute dehydration, allergies, neuropathic or autoimmune conditions, family history of connective tissue or genetic disorders, and the effect of symptoms on daily function. A thorough review of medications is important, particularly for those that increase heart rate or impair autonomic function such as stimulants, or norepinephrine reuptake inhibitors,[48] diuretics (eg, spironolactone or furosemide), venodilators (eg, nitrates), or anticholinergics. Physical examination should include chest auscultation to evaluate for abnormal cardiac or pulmonary findings, abdominal examination (eg, abdominal tenderness or bloating), inspection of the skin and mucosal surfaces for dryness or rashes, assessment of motor strength, sensory function, deep tendon reflexes to identify neurological abnormalities, and evaluation for joint hypermobility.

Patients being evaluated for POTS typically undergo electrocardiography, complete blood count, metabolic panel, serum cortisol level to exclude adrenal insufficiency, and thyroid function testing to evaluate for hyperthyroidism. Additional testing, including echocardiography, Holter monitoring, or testing for pheochromocytoma, may be performed in certain patients based on suggestive clinical findings.

After these conditions are excluded, patients being evaluated for POTS should undergo testing to assess changes in heart rate that occur with a change in position from lying down to standing up. This positional testing can be performed with a tilt-table test, the criterion standard test that is performed in a medical setting, or an active stand test, which can be done in the primary care setting. A tilt-table test may be helpful when patients are unable to stand unsupported, if symptoms are difficult to reproduce, or when confirmation of the diagnosis is needed. The active stand test, which replicates real-life movement, is sufficient for diagnosis of POTS in many cases. During this test, after establishing the baseline heart rate in a supine position for 5 to 10 minutes, patients stand up quickly and remain standing for 10 minutes. Heart rate, blood pressure, and symptoms are recorded every minute, and the diagnosis of POTS is confirmed if the heart rate increase of at least 30 beats/min (≥40 beats/min in adolescents) is sustained for 2 or more consecutive measurements throughout the 10-minute period without orthostatic hypotension, defined by a systolic blood pressure (BP) decrease of at least 20 mm Hg and/or diastolic BP decrease of at least 10 mm Hg.[41] Patients whose heart rate increases more than 30 beats/min (≥40 beats/min in adolescents) early after standing, but then normalizes, do not meet the orthostatic tachycardia criteria for POTS (**Figure 2**).

For patients with an uncertain diagnosis or inadequate initial response to therapy for POTS, specialized autonomic testing may be considered. Additional testing may include autonomic function tests to assess cardiovagal and sympathetic baroreflex function, quantitative sudomotor axon reflex testing, which measures sweat response to acetylcholine via the autonomic nervous system, and cutaneous nerve biopsy to evaluate for small fiber and autonomic neuropathy. Although these specialized tests are not required for the diagnosis of POTS, they can identify associated neurological disorders and prompt a targeted evaluation for potentially treatable underlying causes such as diabetes or autoimmune diseases.

## Overlapping Syndromes

Patients with POTS often have at least 1 medical condition that may contribute to their symptoms. In a large international online patient survey involving 4835 patients mainly from North America, 83% of patients had 1 or more comorbidity.[3] Conditions that are commonly associated with or overlapping with POTS are summarized in **Table 1**.[49-74]

## Treatment

The primary treatment goal is to improve daily functional capacity and quality of life rather than to normalize heart rate or eliminate all POTS symptoms. Functional goals can be assessed with outcomes such as the ability to perform activities of daily living, increases in daily step counts, or decreased absences from work or school. It is useful to prioritize treatment of the most debilitating symptoms during each clinic visit.

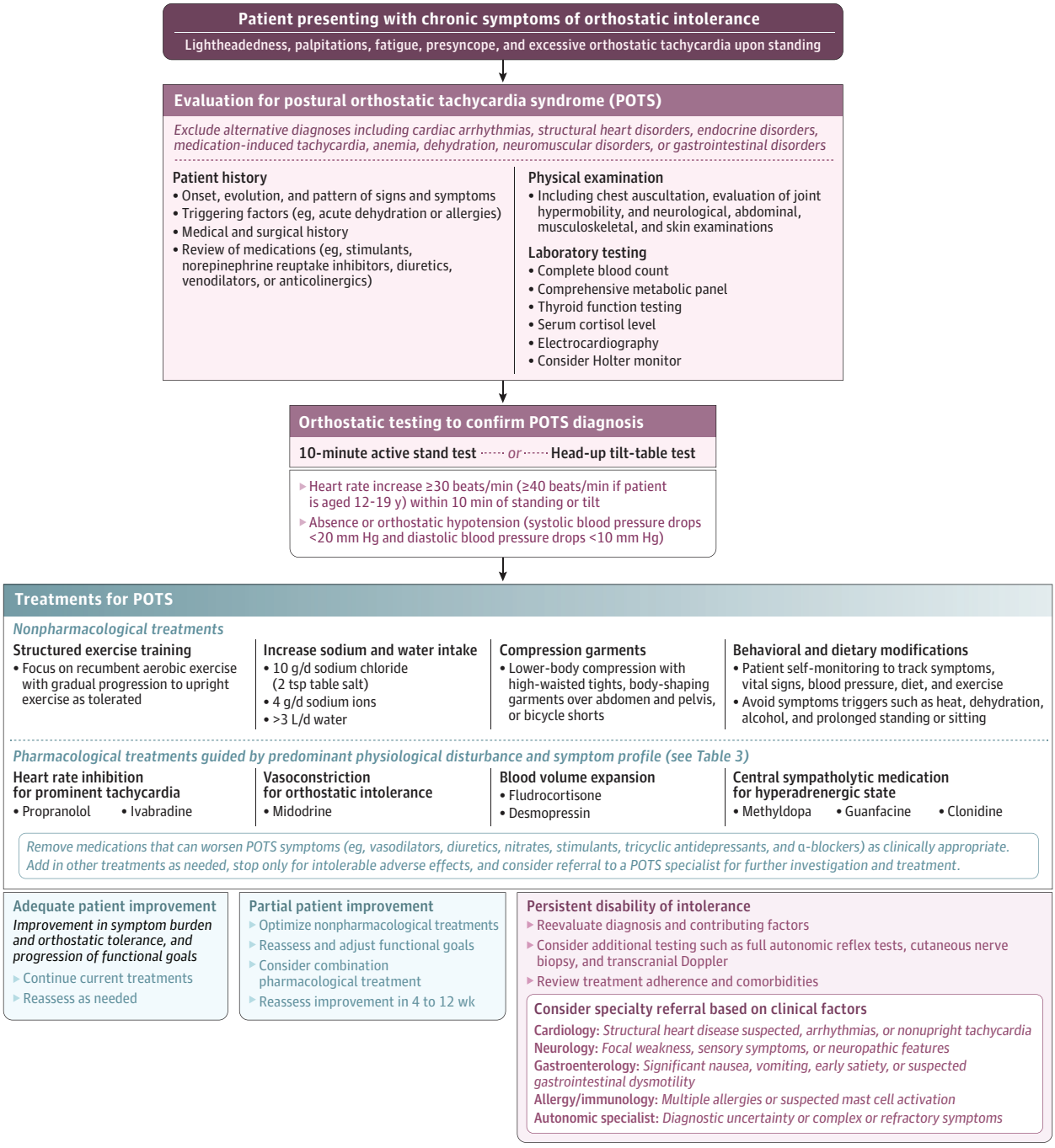
### Nonpharmacological Treatments

***Structured Exercise*** | Structured exercise training under some supervision is a first-line therapy for POTS (Box).[41,45] Exercise increases venous return, cardiac preload, and stroke volume, which has been associated with improvements in orthostatic tachycardia, standing intolerance, and quality of life. However, overexertion can exacerbate symptoms of POTS; a supervised exercise program by physical therapists or exercise physiologists is strongly recommended.[41,45] Exercise should be initially performed in a recumbent or horizontal position (eg, recumbent bike, swimming, rowing) to minimize orthostatic symptoms. Intensity of cardiovascular training and degree of upright position should be gradually increased based on individual tolerance. Many experts recommend resistance training in lower extremities and core muscles in the early phase of exercise training, which can enhance venous return via skeletal muscle pump mechanisms, but high-quality evidence supporting specific resistance training protocols is limited (**Table 2**).[75-81]

Although guidelines from 2015 Heart Rhythm Society and 2020 Canadian Cardiovascular Society statements advocate exercise training for POTS, the seminal work was from a nonrandomized before-after study, in which 19 patients with POTS completed a 3-month structured, supervised aerobic exercise program.[75] Exercise training increased stroke volume, expanded blood volume by 7%, increased left ventricular mass by 12%, reduced orthostatic heart rate, and improved patient-reported quality of life.[75] This study focused on aerobic reconditioning with nonupright exercise, using a rowing machine, a recumbent bike, or swimming, with a small amount of resistance training focused on weightlifting up to twice weekly.

There is only 1 published randomized clinical trial and several prospective cohort studies published about exercise in POTS.[38,41,45,75,76] In a randomized clinical trial[76] of 49 patients, a 12-week semisupervised exercise program (8 supervised sessions combined with home-based training) demonstrated clinically meaningful improvements in peak oxygen (uptake increase of 3.4 mL/kg/min) compared with standard care (3.4 mL/kg/min vs −0.2 mL/kg/min; $P < .001$), peak workload (19 W vs 0 W), improved orthostatic intolerance subscores (−1.98 vs −0.81; $P = .02$), but did not change the total Composite Autonomic Symptom Score-31 (−11.4 vs −6.5; $P = .09$).

Figure 2. Algorithm for the Investigation and Management of POTS




The role physical score from the 36-Item Short Form Health Survey (SF-36) improved significantly (26 vs 5; $P$ = .03).

*Blood Volume Expansion* | To increase cardiac preload, expansion of intravascular plasma volume with a liberal intake of water and dietary salt is the guideline-recommended treatment for patients with POTS. The 2015 Heart Rhythm Society consensus statement[45] recommends intake of 2 to 3 L of water daily and 10 to 12 g salt daily (class IIb, weak recommendation) for patients with POTS who have normal kidney function. In a randomized crossover trial of 14 patients with POTS, a high dietary sodium intake (300 mEq/d) increased plasma volume by approximately 6% and improved orthostatic tachycardia by approximately 10 beats/min, which are clinically meaningful changes.[77] Other studies have replicated these results,[82-84] but there is limited evidence on the optimal dosage, formulation, and duration of sodium and water intake. Experts often recommend adding extra salt (10 g [2 tsp daily]) to food, which is usually well tolerated by patients with POTS. Some experts favor use of an oral rehydration solution due to a theoretical risk of gastrointestinal intolerance and osmotic diarrhea with salt tablets,

Table 1. Conditions That Are Commonly Associated With or Overlapping With Postural Orthostatic Tachycardia Syndrome

| Condition[a] | Frequency in POTS, %[b] | Key clinical features | Clinical relevance |
|---|---|---|---|
| Chronic migraine[49,50] | 40 | Recurrent headaches, photophobia, nausea, dizziness, and sensory hypersensitivity | Migraine is 1 of the most common comorbidities in POTS that may share overlapping pathophysiological mechanisms with POTS and contribute substantially to symptom burden and reduced quality of life |
| Irritable bowel syndrome[51] | 30 | Abdominal pain, bloating, constipation, diarrhea, altered bowel habits | Common gastrointestinal comorbidity that may contribute to symptom burden and impaired quality of life |
| Hypermobile Ehlers-Danlos syndrome[52-56] | 25 | Joint hypermobility, connective tissue laxity | May contribute to venous pooling and orthostatic intolerance |
| Myalgic encephalomyelitis/chronic fatigue syndrome[57-59] | 21 | Severe fatigue, postexertional malaise, cognitive dysfunction, unrefreshing sleep, orthostatic intolerance | Substantial symptom overlap with POTS<br>Postexertional malaise can limit physical therapy |
| Fibromyalgia | 20 | Chronic widespread musculoskeletal pain, fatigue, nonrestorative sleep, and sensory hypersensitivity | Symptoms can be debilitating and may limit physical therapy<br>Recognition of the syndrome may guide rehabilitation strategies |
| Mast cell activation syndrome[55,56,60,61] | 9 | Flushing, urticaria, pruritus, gastrointestinal symptoms | Mast cell mediators may exacerbate autonomic symptoms |
| Hashimoto thyroiditis[18,62] | 6 | Fatigue, weight changes, temperature dysregulation, can overlap with POTS symptoms | Coexistence may suggest immune-mediated mechanisms<br>Because thyroid dysfunction can worsen symptoms resembling POTS, thyroid function should be monitored |
| Sjögren syndrome[63,64] | 3 | Dry eyes, dry mouth, chronic fatigue, neuropathic symptoms | Coexistence may suggest immune-mediated mechanisms should be considered in patients with sicca symptoms, neuropathic symptoms, or other autoimmune features |
| Long COVID[65-74] | Not well established | Persistent fatigue, cognitive dysfunction, orthostatic intolerance, exercise intolerance, and multisystem symptoms after SARS-CoV-2 infection | Common trigger for POTS onset—POTS has been reported in approximately 30%-80% of patients with long COVID<br>Autonomic dysfunction is increasingly recognized as a component of long COVID |

Abbreviations: Long COVID, post–COVID-19 condition; POTS, postural orthostatic tachycardia syndrome.

[a] The conditions listed are not intended to represent a comprehensive differential diagnosis of orthostatic tachycardia. Rather, they are conditions that may overlap with, coexist with, or contribute to symptom burden in patients with POTS. Reported frequencies are approximate and vary across studies because of differences in patient populations, referral patterns, and diagnostic criteria.

[b] Reported frequencies are approximate and vary across studies depending on patient population, diagnostic criteria, and referral patterns. Percentages are based on Shaw et al.[3]

Table 2. Nonpharmacological Treatment of Postural Orthostatic Tachycardia Syndrome[a]

| Intervention | Rationale | Typical recommendations | Study data and outcomes | Practical considerations |
|---|---|---|---|---|
| Structured, supervised cardiovascular training | Increased venous return, cardiac preload, stroke volume, and reconditioning | Begin with horizontal exercise (eg, rowing, recumbent cycling, swimming) and gradually progress intensity and upright activities as tolerated | In a prospective intervention study of 19 patients, 3 mo of supervised exercise training increased stroke volume and cardiac mass, reduced orthostatic tachycardia, and improved quality of life[75]<br>In a randomized trial of 49 patients, a 12-wk semisupervised exercise program improved peak oxygen uptake (3.4 vs −0.2 mL/kg/min), peak workload (19 W vs 0 W), and symptom burden compared with standard care[76] | Exercise should be introduced gradually<br>Overexertion may worsen symptoms<br>Supervision by physical therapists or exercise physiologists is often beneficial |
| Volume expansion | Expands intravascular volume and increases cardiac preload | Approximately 2-3 L of water and 10-12 g of salt daily in patients with normal kidney function | In a randomized crossover study of 14 patients, high sodium intake increased plasma volume by approximately 6% and reduced orthostatic tachycardia by approximately 10 beats/min compared with low sodium intake[77] | Some experts favor oral rehydration solution over salt tablets because of a theoretical risk of osmotic diarrhea<br>Evidence regarding optimal formulation remains limited |
| Compression garments | Reduce venous pooling in the abdomen and lower extremities and increase cardiac preload | High-waisted compression tights, abdominal binders, or combined abdominal and leg compression worn during daytime activities | In a proof-of-concept study, 30 patients with POTS underwent a randomized-order, crossover tilt-test trial of acute lower-body compression with a compression suit (abdomen and legs) vs no compression; lower-body compression reduced the upright HR (mean [SD], 109 [19] beats/min vs 92 [14] beats/min; $P < .001$) and the orthostatic increase in HR (39 [18] beats/min vs 23 [11] beats/min; $P < .001$)[78]<br>Orthostatic symptoms burden decreased from a mean (SD) of 26 (17) au to 12 (10) au ($P < .001$)[78]<br>A study of commercially available compression garments was conducted in a real-world, home setting with patients with POTS (n = 26) to assess orthostatic HR before and 30 min after wearing high-waisted compression tights for 4-6 h, and then repeated orthostatic HR assessments before and 30 min after removing the compression tights; in the morning, the high-waisted compression tights reduced the orthostatic tachycardia from a median of 44 beats/min to 24 beats/min ($P < .001$), the afternoon removal of the compression garments increased the orthostatic tachycardia from a median 28 beats/min to 33 beats/min ($P < .004$)[79]<br>Orthostatic symptoms were significantly better with the compression garments both in the morning ($P < .001$) and afternoon ($P = .005$)[79]<br>Abdomen-only compression has also been shown to be effective in 18 female patients with POTS, with a reduction in morning orthostatic tachycardia from a median of 41 beats/min to 27 beats/min ($P < .001$)[80,81] | High-waisted garments are often easier to use and better tolerated than medical compression stockings<br>Adherence may be limited in hot weather |
| Behavioral modifications | Minimize triggers that worsen orthostatic intolerance | Avoid dehydration, excessive heat exposure, prolonged standing, prolonged sitting, and excessive alcohol intake | Supported primarily by physiological studies and clinical experience | Often effective when combined with volume expansion and exercise training |
| Dietary modifications | Reduce postprandial splanchnic blood pooling and symptom exacerbation | Avoid large meals and minimize high-carbohydrate meals | High-carbohydrate meals have been associated with worsening orthostatic symptoms and increased postprandial tachycardia | Smaller, more frequent meals may be better tolerated |
| Sleep and activity pacing | Reduce symptom flares and cognitive dysfunction | Optimize sleep hygiene, pace activities, and schedule cognitively demanding tasks during periods of lower symptom burden | Evidence is limited and based primarily on expert opinion and clinical experience | Particularly useful in patients with significant fatigue or cognitive dysfunction |

Abbreviations: au, arbitrary units; HR, heart rate; POTS, postural orthostatic tachycardia syndrome.

[a] Nonpharmacological interventions are considered first-line therapy for POTS and are often used in combination. Recommendations are derived from consensus statements, randomized trials, observational studies, physiological investigations, and expert clinical experience.

although comparative evidence remains limited.[85] Buffered, or slow-release, sodium tablets are usually well tolerated, but they are more expensive than regular table salt. In an observational study of 57 patients with refractory POTS, defined as persistent symptoms despite at least 1 pharmacological intervention, acute volume loading with intermittent intravenous (IV) saline bolus infusion, was associated with significant improvements in Orthostatic Hypotension Questionnaire scores (mean change, 3.1 points) and SF-36 quality-of-life scores (mean change, 19.1 [SD, 2.7] points, exceeding the generally accepted minimally clinically important difference of >1 point; higher scores indicate worse symptoms).[84] Similar findings have been reported in smaller observational studies.[84,86-88] However, due to potential risks of infection and thrombosis related to chronic central venous access, the 2015 Heart Rhythm Society consensus statement recommends IV saline infusion up to 2 L at a time only for infrequent, short-term worsening of symptoms (class IIa, moderate recommendation) and advised against long-term IV infusion of saline (class III, not recommended).[45]

*Compression Garments* | Compression garments, including compression tights and abdominal binders, provide external counterpressure and decrease venous pooling in the splanchnic and lower extremity circulation and increase cardiac preload. In a randomized crossover tilt-test study of 30 patients with POTS, lower-body compression (abdomen and legs) reduced the mean (SD) upright heart rate from 109 (19) beats/min to 92 (14) beats/min ($P < .001$) and the orthostatic increase in heart rate from 23 (11) beats/min to 39 (18) beats/min ($P < .001$), yielding a clinically meaningful improvement in orthostatic symptoms (composite symptom score, 26 [17] vs 12 [10]; $P < .001$; with a higher score representing more symptoms).[78] In a home-based study of 26 patients using commercially available compression tights, participants completed 4, 10-minute active stand tests in the morning and afternoon with and without compression tights. Use of high-waisted compression tights while not taking POTS medications reduced orthostatic tachycardia from a clinically significant median of 44 beats/min to 24 beats/min ($P < .001$), and garment removal increased tachycardia from 28 beats/min to 33 beats/min ($P < .004$). Orthostatic symptoms were significantly improved both in the morning ($P < .001$) and afternoon ($P = .005$) with use of compression garments.[79] Even when taking medications for POTS, orthostatic tachycardia (89 beats/min-84 beats/min; $P < .001$) and symptoms ($P = .03$) improved with lower-body compression.[79]

Abdomen-only compression was also shown to be effective in 18 female patients with POTS, with a clinically meaningful reduction in morning orthostatic tachycardia from a median of 41 beats/min to 27 beats/min ($P < .001$).[80] Similar findings were reported in a crossover study of 23 adolescents with POTS (13 males and 10 females; mean [SD] age, 13.4 [0.8] years), in which abdominal compression reduced orthostatic tachycardia (median heart rate changes, 30 beats/min to 41 beats/min; $P < .01$), improved stroke volume ratio (0.76 vs 0.64; $P < .01$), and improved orthostatic symptoms (all $P < .05$).[89] Compression garments may be used continuously or as needed, particularly when daily use is poorly tolerated in hot or humid environments. Experts often recommend high-waist compression athletic wear (eg, triathlon tights, with 15-18 mm Hg of compression) during daytime activities. However, body-shaping garments covering the upper thigh to the bottom of the ribs or compression bicycle shorts may be better tolerated in warmer environments.[80]

*Behavioral and Dietary Modifications* | The goal of behavioral modifications for POTS is to reduce symptom triggers and improve venous return. Patients should avoid heat exposure, particularly in humid environments because heat can cause peripheral vasodilation and reduce central blood volume.[90] In addition, patients with POTS should avoid dehydration, alcohol consumption, and prolonged standing or sitting, which can induce orthostatic intolerance symptoms; patients should be encouraged to periodically use physical countermeasures, such as leg crossing, squatting, or isometric muscle tensing, to augment venous return. Patients with cognitive symptoms should be encouraged to pace activities, optimize sleep hygiene, and perform cognitively demanding tasks when experiencing fewer POTS symptoms.

Large and high-carbohydrate meals should be avoided because they can cause postprandial lightheadedness, likely due to increased splanchnic blood pooling and reduced central blood volume.[91]

### Pharmacological Treatments

Pharmacological therapy may be prescribed along with nonpharmacological measures, particularly in patients with persistent or function-limiting POTS symptoms (Box). Although there are currently no medications for the treatment of POTS that have been approved by the US Food and Drug Administration, several classes of medications are commonly used off-label, including heart rate–lowering medications, vasoconstrictors, blood volume expanders, and sympatholytic medications (**Table 3**).[41,45,81,92-102] Medication selection is often guided by the predominant physiological disturbance and symptom profile (Figure 2). For example, medications that reduce heart rate may be used in patients with POTS who have prominent tachycardia, whereas vasoconstrictors may be considered for those with marked orthostatic intolerance and relatively low systolic blood pressure (eg, <105 mm Hg). Patients with prominent tachycardia may be treated with medications that reduce heart rate such as ivabradine (5 mg twice daily) or low-dose propranolol (10 mg 4 times daily). For patients with marked orthostatic intolerance and relatively low blood pressure, vasoconstrictors such as midodrine (5 mg ≤3 times daily) may be considered as an initial medication to support blood pressure.

For patients with POTS whose symptoms do not improve or worsen with monotherapy, medications from other classes (heart rate lowering or vasoconstriction) or a blood volume expander (eg, fludrocortisone or desmopressin) should be added to the initial medications, unless the initial medication was not tolerated. In patients with symptoms suggestive of a hyperadrenergic state (eg, nocturnal tachycardia, palpitations, sweating, shaking, or acute feelings of panic), a central sympatholytic medication may be added (eg, methyldopa, guanfacine, or clonidine). Pharmacological treatment options for POTS are summarized in Table 3.

## Prognosis

Long-term follow-up data have historically been lacking, but recently published studies provide data about prognosis in pediatric and adult patients with POTS. In a Children's Hospital of Philadelphia POTS Program survey study of 227 patients (mean age, 21.8 years;

Table 3. Medications to Consider for Treating Postural Orthostatic Tachycardia Syndrome[a]

| Medication | Mechanism of action | Typical dose range | Study data and outcomes | Adverse effects | Clinical considerations |
|---|---|---|---|---|---|
| **Vasoconstrictor or vasoconstrictor** | | | | | |
| Midodrine | Selective $\alpha_1$-adrenergic agonist that increases arterial and venous tone, thereby increasing venous return, cardiac preload, and blood pressure | 2.5-15 mg every 4 h (often 3/d, while awake depending on daily activity) | In a randomized crossover study (n = 20), midodrine reduced upright HR by approximately 14-15 beats/min and improved orthostatic symptoms compared with placebo[92]<br>Additional studies have demonstrated improvements in hemodynamics and symptoms of POTS | Piloerection, goose bumps, supine hypertension (8%), feeling of urinary urgency (4%), and scalp pruritus (13.5%)[93]<br>Urinary retention and worsening nonmigraine headache are rare but can be associated with midodrine | Particularly useful in patients with low or low-normal blood pressure and predominant lightheadedness<br>Avoid administration within 4 h of bedtime to reduce supine hypertension |
| **Heart rate inhibition** | | | | | |
| Propranolol | Nonselective β-adrenergic receptor antagonist that reduces sinus rate and sympathetic cardiac stimulation; can cross the brain barrier | 10-20 mg every 4 h up to 4/d | In a randomized crossover trial, low-dose propranolol (20 mg) lowered standing HR by 15 beats/min at 2 h and improved symptom burden compared with placebo, whereas higher-dose propranolol (80 mg) produced greater HR reduction without additional symptom benefit[94]<br>In a separate randomized study, a single 20-mg dose also improved maximal exercise[95] | Excessive bradycardia, fatigue, hypotension (especially if more volume depleted), bronchospasm (occasional)<br>Can exacerbate asthma and COPD<br>Weight gain (rare) | Use caution in patients with asthma or COPD<br>Short-acting medication often allows for better titration to symptoms than longer-acting preparations<br>Propranolol doses >20 mg 4/d are often poorly tolerated and may worsen the orthostatic symptoms<br>The 2020 Canadian Cardiovascular Society position statement on POTS lists low-dose propranolol as a strong recommendation as a first-line drug, whereas the 2015 HRS statement classifies propranolol as a class IIb recommendation that may be considered[41,45] |
| Ivabradine | Selective funny channel ($I_f$) inhibitor that reduces the firing rate of the sinus node without other β-blocker effects | 2.5-15 mg 2/d<br>The typical starting dose is 5 mg 2/d orally, but it can be titrated up or down to optimize symptomatic effects | In a crossover study of 22 patients with POTS with hyperadrenergic features, 1 mo of ivabradine lowered HR and symptoms more than placebo[96]<br>In a comparative effectiveness, blinded, crossover study of ivabradine vs propranolol vs placebo, both propranolol and ivabradine reduced HR more than placebo[97]<br>Patients with POTS preferred ivabradine and propranolol over placebo, but there was not a significant difference in preference between ivabradine and propranolol | Generally well tolerated<br>Prolonged QT interval, bradycardia, fatigue, visual disturbances, especially with night vision (reversible) | More expensive than β-blockers |
| Pyridostigmine | Peripheral acetylcholinesterase inhibitor that increases synaptic acetylcholine at the autonomic ganglia, improving baroreflex-mediated sympathetic vasoconstriction | 30-60 mg 3/d | In a randomized crossover trial (n = 17), pyridostigmine (30 mg) reduced standing HR at 2 h after pyridostigmine vs placebo (mean [SD], 100 [16] vs 111 [14] beats/min, $P$ = .001) and improved orthostatic symptoms, including lightheadedness[81]<br>A retrospective study (n = 208) also demonstrated improvements in orthostatic tachycardia and symptom burden with pyridostigmine therapy[81,98] | Abdominal cramping, diarrhea, increased sweating | Not very potent effect on HR, but works well when combined with other medications, particularly useful in patients prone to constipation |

(continued)

Table 3. Medications to Consider for Treating Postural Orthostatic Tachycardia Syndrome[a] (continued)

| Medication | Mechanism of action | Typical dose range | Study data and outcomes | Adverse effects | Clinical considerations |
|---|---|---|---|---|---|
| **Volume expansion** | | | | | |
| Fludrocortisone | Synthetic mineralocorticoid that promotes renal sodium and water retention and may expand intravascular volume | 0.1-0.3 mg/d | While fludrocortisone frequently used in patients with POTS, randomized clinical trials have not evaluated fludrocortisone for POTS | Worsen headache (migraine); edema; hypokalemia | Monitor serum potassium approximately 1 wk after dose changes and periodically during maintenance therapy<br>At higher doses, hypothalamic-pituitary-axis suppression can occur |
| Desmopressin | Synthetic vasopressin that promotes free-water retention | 0.2 mg/d or 0.1 mg 2/d | In a randomized crossover study (n = 30), desmopressin significantly reduced standing HR (mean [SD], 101.9 [14.5] beats/min) vs placebo (109.2 [7.4] beats/min; $P < .001$) and improved Vanderbilt Orthostatic Symptom scores vs placebo (5 vs −1; $P = .01$) without a significant change in blood pressure [99] | Edema and hyponatremia | Sodium levels should be monitored periodically<br>Can be used as a special-event drug on an as-needed basis or taken daily |
| **Sympatholysis** | | | | | |
| Methyldopa | A false neurotransmitter, which stimulates central $\alpha_2$-adrenergic receptors and decreases central sympathetic nervous system output | 125-250 mg 2/d | Evidence of methyldopa use in POTS is limited to anecdotal reports and expert opinions<br>The 2015 HRS consensus statement classifies clonidine as class IIb recommendation[45] | Hypotension; fatigue (if too much) | Start with 125 mg at bedtime; can help with waking in middle of night with rapid palpitation<br>Particularly helpful in patients who feel adrenaline surges |
| Clonidine | $\alpha_2$-Adrenergic receptor agonist that can decrease central sympathetic tone | 0.1-0.2 mg, 2-3 mg/d, or 0.1 to 0.3 mg/d, transdermal patch changed weekly | In a prospective observational study (n = 33), clonidine was associated with improvements in orthostatic hemodynamics and symptom burden[100]<br>Among 10 patients who continued clonidine for at least 6 mo, 80% reported fewer symptoms than at baseline[100] | Hypotension; fatigue | Rapid onset and rapid offset<br>Abrupt discontinuation may result in rebound symptoms or hypertension |
| Guanfacine | $\alpha_2$-Adrenergic receptor agonist that can decrease central sympathetic tone | 1-3 mg at bedtime | Evidence is limited; randomized studies in POTS are lacking | Hypotension; fatigue (if too much) | Approved for ADHD<br>Will not worsen sinus tachycardia when used for ADHD<br>Longer half-life than clonidine |
| **Miscellaneous** | | | | | |
| Modafinil | Enhance alertness and executive function by increasing dopamine levels in the brain[101] | 100-200 mg 2/d | In a randomized clinical trial (n = 54), modafinil did not significantly increase HR vs placebo but did raise the systolic blood pressure by 5 mm Hg[102] | Increased HR in some, difficulty sleeping | May improve fatigue and cognitive dysfunction in selected patients |

Abbreviations: ADHD. attention-deficit/hyperactivity disorder; COPD, chronic obstructive pulmonary disease; HR, heart rate; HRS, Heart Rhythm Society; POTS, postural orthostatic tachycardia syndrome.

[a] Medication doses represent typical starting or commonly used dose ranges in clinical practice and should be individualized based on patient characteristics, symptoms, and tolerability. Study outcomes are summarized from representative clinical trials and observational studies and do not constitute a comprehensive systematic review of all available evidence.

**Table 4. Medications That May Worsen the Symptoms of Postural Orthostatic Tachycardia Syndrome[a]**

| Medications or class | Potential effects on POTS | Mechanism | Clinical considerations |
|---|---|---|---|
| Atomoxetine | Increased palpitation; worsened orthostatic tachycardia and can worsen orthostatic tachycardia and increase palpitation | Norepinephrine transporter inhibition increases synaptic norepinephrine and sympathetic activation | Commonly prescribed for ADHD<br>In a randomized crossover study (n = 27), atomoxetine worsened standing HR compared with placebo (mean, 121 [SD, 17] beats/min vs 105 [SD, 15] beats/min) and symptom burden in patients with POTS |
| Duloxetine and other serotonin-norepinephrine reuptake inhibitors (eg, venlafaxine, desvenlafaxine) | Can worsen orthostatic tachycardia and increase palpitation | Norepinephrine transporter inhibition increases sympathetic tone | Consider alternative agents when symptoms worsen after initiation or dose escalation |
| Amphetamines and methylphenidate | Can worsen orthostatic tachycardia, increase palpitation, and cause insomnia | Sympathomimetic effects increase catecholaminergic activity | Often used in patients with concomitant ADHD; will often worsen tachycardia, but can improve cognitive function; HR effects may be less with methylphenidate than amphetamines; treatment should be individualized |
| Spironolactone and diuretics (eg, thiazides, furosemide) | Hypovolemia can worsen orthostatic tachycardia and increase palpitation | Reduced intravascular volume and cardiac preload | Sometimes used for bad acne of polycystic ovary syndrome; alternative therapies may be considered in symptomatic patients |
| $\alpha_1$-Adrenergic antagonists (eg, tamsulosin, prazosin, doxazosin, terazosin) | May worsen orthostatic intolerance and tachycardia | Peripheral vasodilation can reduce venous return and blood pressure | May be prescribed for benign prostatic hyperplasia and hypertension, although infrequently used in the typical young patient with POTS |
| Drospirenone-containing oral contraceptives | May worsen orthostatic symptoms in susceptible patients | Drospirenone is a spironolactone analogue with mild antimineralocorticoid activity | Common brand names include Yaz, Yasmin, Ocella; consider alternative contraceptive formulations in patients with worsening orthostatic symptoms |
| Vasodilators (eg, amlodipine, hydralazine) | May worsen orthostatic symptoms and reflex tachycardia | Arterial vasodilation reduces vascular resistance and may trigger compensatory sympathetic activation | Monitor carefully in patients with prominent hypovolemia or worsening orthostatic symptoms after treatment initiation |
| Nitrates (eg, nitroglycerin, isosorbide mononitrate) | May worsen orthostatic intolerance and presyncope | Venodilation increases venous pooling and reduces cardiac preload | May be prescribed for angina and heart failure although infrequently used in the typical young patient with POTS |

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; HR, heart rate; POTS, postural orthostatic tachycardia syndrome.

[a] The medications listed are not contraindicated in patients with POTS and may be clinically indicated for other conditions. However, these agents may exacerbate orthostatic tachycardia, orthostatic intolerance, hypovolemia, or related symptoms in susceptible individuals. Medication review is an important component of the initial evaluation of patients with suspected or established POTS.

median age at POTS symptoms onset, 13 years [IQR, 11-14 years]) who were diagnosed with POTS at age 18 years or younger, the mean symptom duration was 9.6 years.[37] Commonly reported symptoms were fatigue, dizziness, tachycardia, lightheadedness, brain fog, headache, and exercise intolerance. Among these survey respondents, at least 10 symptoms were reported by 85%, with higher rates among females than males (88.1% vs 63.6%, $P < .001$), and nearly 90% continued nonpharmacological therapy (eg, increased fluid or salt intake and exercise) to treat POTS symptoms.[37]

In a survey of 44 adult patients (98% female, mean age, 46 years), from the Vanderbilt University Autonomic Dysfunction Center at a median of 23 years from POTS symptom onset (and a median of 17 years after POTS diagnosis), only 2% reported resolution of symptoms. POTS symptoms improved in 46%, worsened in 25%, were unchanged in 11%, and had a variable course in 16%.[103]

Although there are limited studies reporting survival data, POTS does not appear to be associated with increased mortality. However, POTS is associated with substantial functional impairment, reduced quality of life, and socioeconomic consequences. In a survey of 5556 participants with POTS (90% US respondents), RAND-36 Measure of Health-Related Quality of Life scores demonstrated impairment across multiple domains, and more than 70% reported loss of income due to their POTS symptoms.[4] In a 2021 cohort study that included 526 patients with post–COVID-19 condition (long COVID) associated with autonomic dysfunction and POTS, the median duration of symptoms was 36 months, and 37.5% of patients were unable to maintain employment or academic enrollment.[5]

## Practical Considerations

Patients with POTS should receive treatment for coexisting diseases, including gastrointestinal dysmotility, sleep disturbance, and cognitive dysfunction, and may require referral to specialists for these conditions.

Medications that may exacerbate orthostatic intolerance or tachycardia such as amphetamines, atomoxetine, or spironolactone should be discontinued or adjusted on an individual basis if possible (**Table 4**). For patients with attention-deficit/hyperactivity disorder (ADHD) and POTS, guanfacine may be considered because it does not increase heart rate.

Careful titration of medications to treat symptoms of POTS can help to reduce adverse effects. Short-acting agents such as midodrine or propranolol, which have a duration of action of about 4 hours, can be taken at only certain times of day when symptoms are worse, or before periods of anticipated activity (eg, exercise) rather than on a fixed schedule. This flexible dosing strategy can decrease adverse effects and maximize functional benefits.

Although there are no guideline recommendations about routinely obtaining orthostatic vital signs in the follow-up visits of patients with POTS, some physicians reassess orthostatic vital signs at follow-up clinic visits to combine objective data with patient symptoms. Wearable monitors can provide additional real-world information about heart rate control that can guide changes in pharmacotherapy.

Primary care clinicians may diagnose POTS and initiate therapies. However, referral to a specialist (often neuromuscular specialists or cardiologists with expertise in treating POTS) should be considered for patients with diagnostic uncertainty, atypical features, or persistent POTS symptoms despite initial therapy (Figure 2).

## Limitations

This review has several limitations. First, the quality of evidence was not formally assessed. Second, some relevant articles may have been missed. Third, evidence about treatment of POTS is primarily derived from small, single-center cohort studies and case series. Fourth, use of data from tertiary autonomic centers introduces potential referral bias because these patients often have refractory POTS, and may not be generalizable to patients presenting to primary care clinicians.

# Conclusions

POTS is a chronic autonomic disorder associated with functional impairment and reduced quality of life that is diagnosed based on characteristic orthostatic symptoms in the absence of orthostatic hypotension after excluding alternative causes of sinus tachycardia. Treatment involves nonpharmacological measures (such as increased fluid and sodium intake), lower-body compression garments, structured exercise training, and individualized pharmacological therapy.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