POTS and NOTS



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Disclosures

None

Objectives

- Discuss the underlying pathophysiological mechanisms related to the autonomic nervous system in POTS
- Describe appropriate diagnostic and treatment strategies for postural orthostatic tachycardia syndrome (POTS)
- Identify and distinguish differences between POTS and mimics such as orthostatic intolerance without tachycardia and long-COVID syndrome



POTS

- Most common disorder of the autonomic nervous system (estimated prevalence 170/100,000).
- Female:male ratio 4.5:1, age 15-25 years
- Presentation:
  - Orthostatic intolerance and tachycardia
  - Often after an immune stimulus or a period of bedrest
- More pervasive symptoms: fatigue, unrefreshing sleep, and memory complaints
- Comorbid chronic pain disorders, headaches, and GI disorders

POTS symptom burden

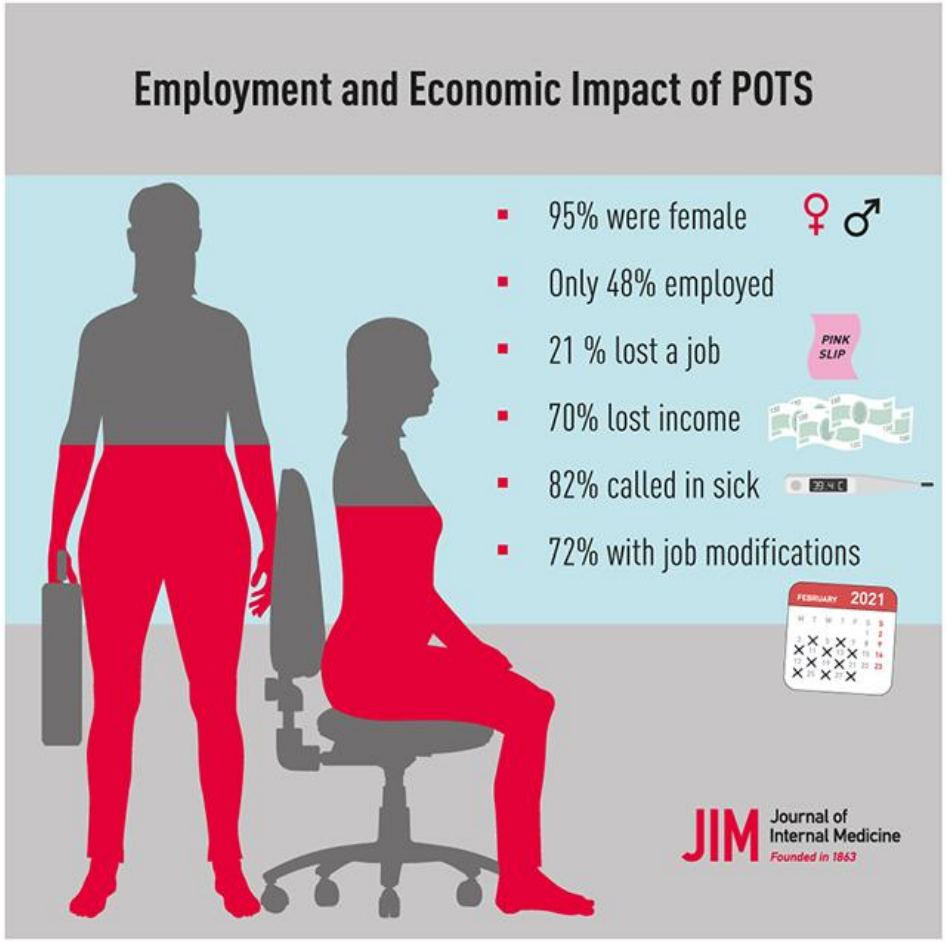
- Health related QOL similar to other chronic disabling conditions (Benrud-Larson et al, 2002)
- Significant economic burden (Bourne et al, 2021)
- Increased risk of suicide (Pederson et al, 2017)

JIM Original Article

doi: 10.1111/joim.12895

The face of postural tachycardia syndrome – insights from a large cross-sectional online community-based survey

B. H. Shaw[1], L. E. Stiles[2,3], K. Bourne[1], E. A. Green[4], C. A. Shibao[4], L. E. Okamoto[4], E. M. Garland[4], A. Gamboa[4], A. Diedrich[4], V. Raj[1,5], R. S. Sheldon[1], I. Biaggioni[4], D. Robertson[4] & S. R. Raj[1,4]



What is POTS?

- **P**ostural **O**rthostatic **T**achycardia **S**yndrome
- Syndrome of chronic orthostatic intolerance
- Postural tachycardia (>= 30 bpm, or >= 40 bpm age 12-19)
- *Without* orthostatic hypotension (drop in SBP >20 mmHg)



Sheldon et al., HRS Expert Consensus Document on POT/IST/VVS, 2015.

What is POTS?

- Cardiac differences in POTS (vs healthy sedentary controls)
  - Higher upright heart rate and total peripheral resistance
  - Lower upright stroke volume and cardiac output
  - Lower LV mass (more than 2 SD→"Grinch syndrome")
  - Lower blood volume



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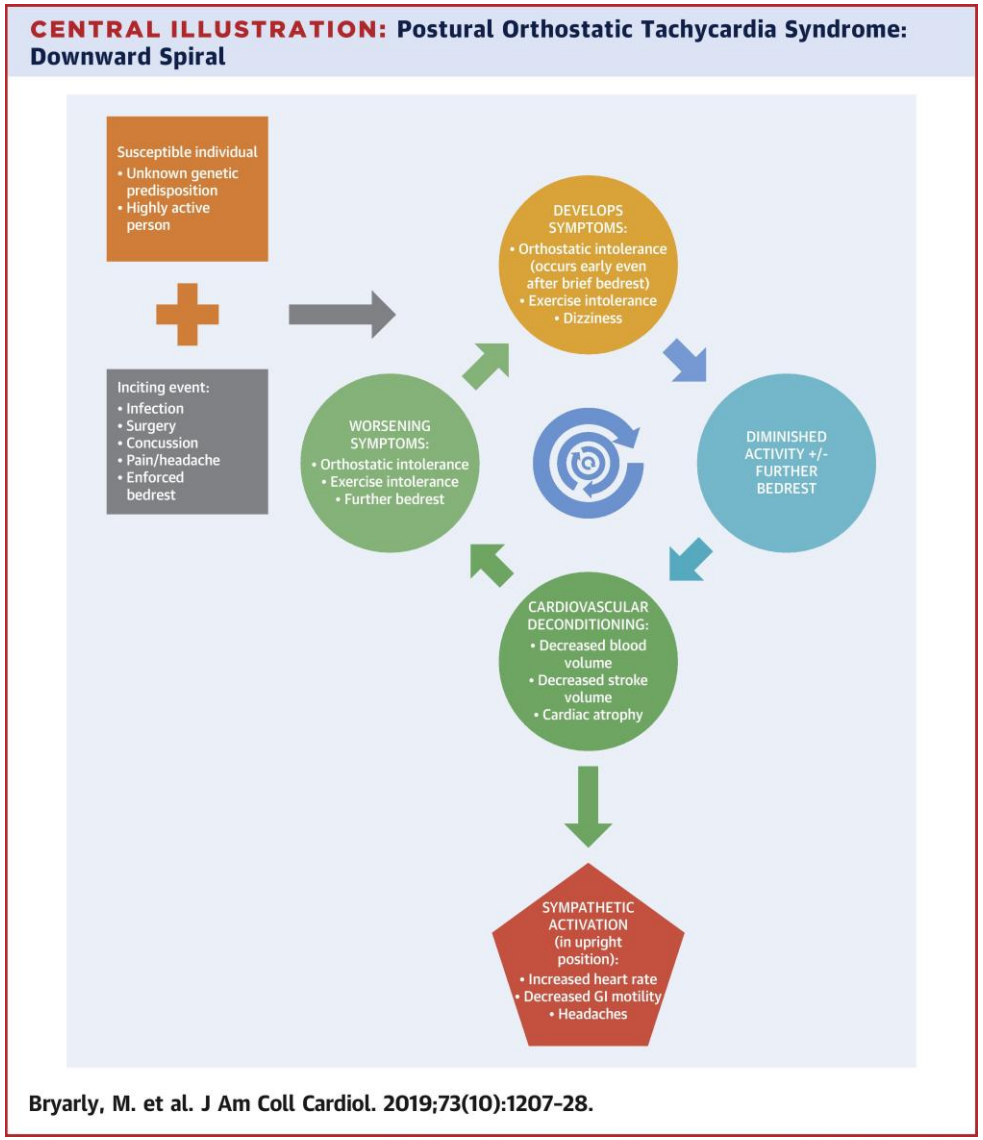
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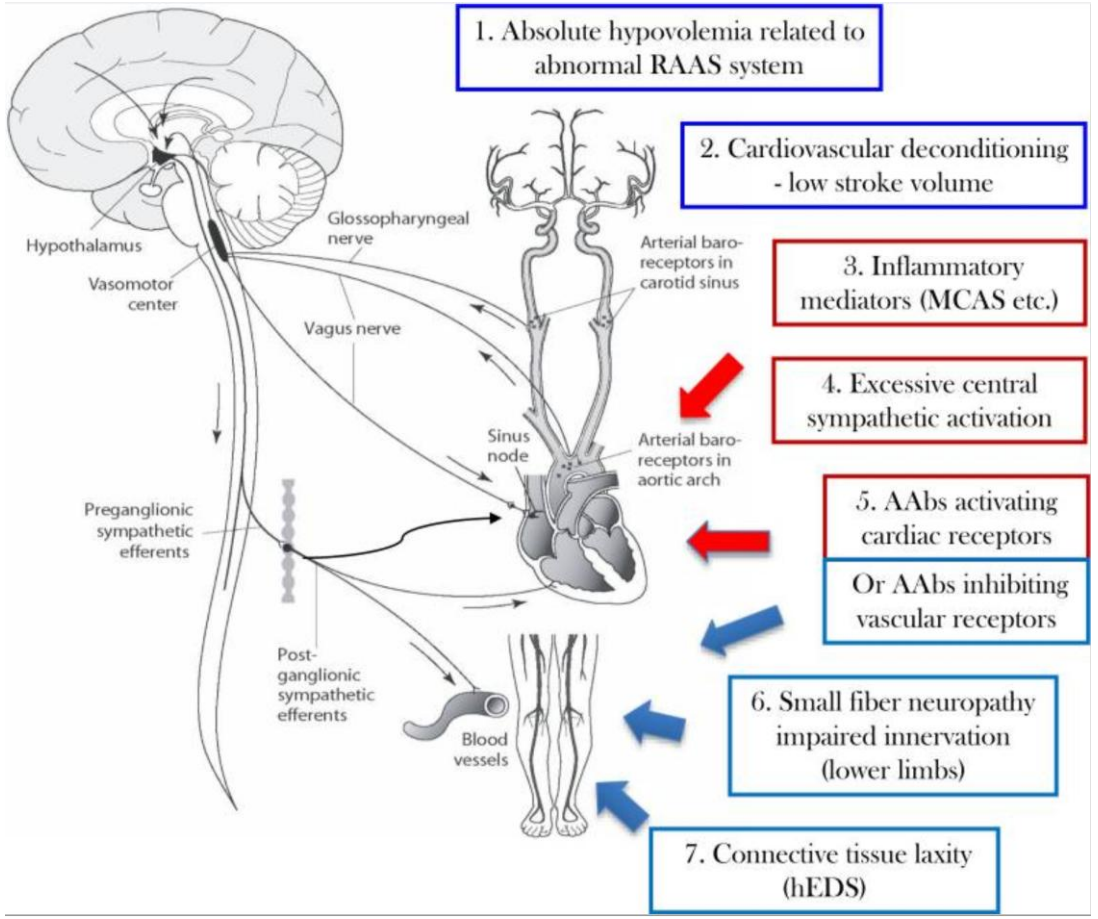
Cardiac Origins of the Postural Orthostatic Tachycardia Syndrome

Qi Fu, MD, PHD,*† Tiffany B. VanGundy, MS,* M. Melyn Galbreath, PHD,*†
Shigeki Shibata, MD, PHD,*† Manish Jain, MD,*† Jeffrey L. Hastings, MD,*†
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Dallas, Texas

Pathophysiology





Vernino et al, Auton Neurosci, 2021.

What is “orthostatic intolerance”?

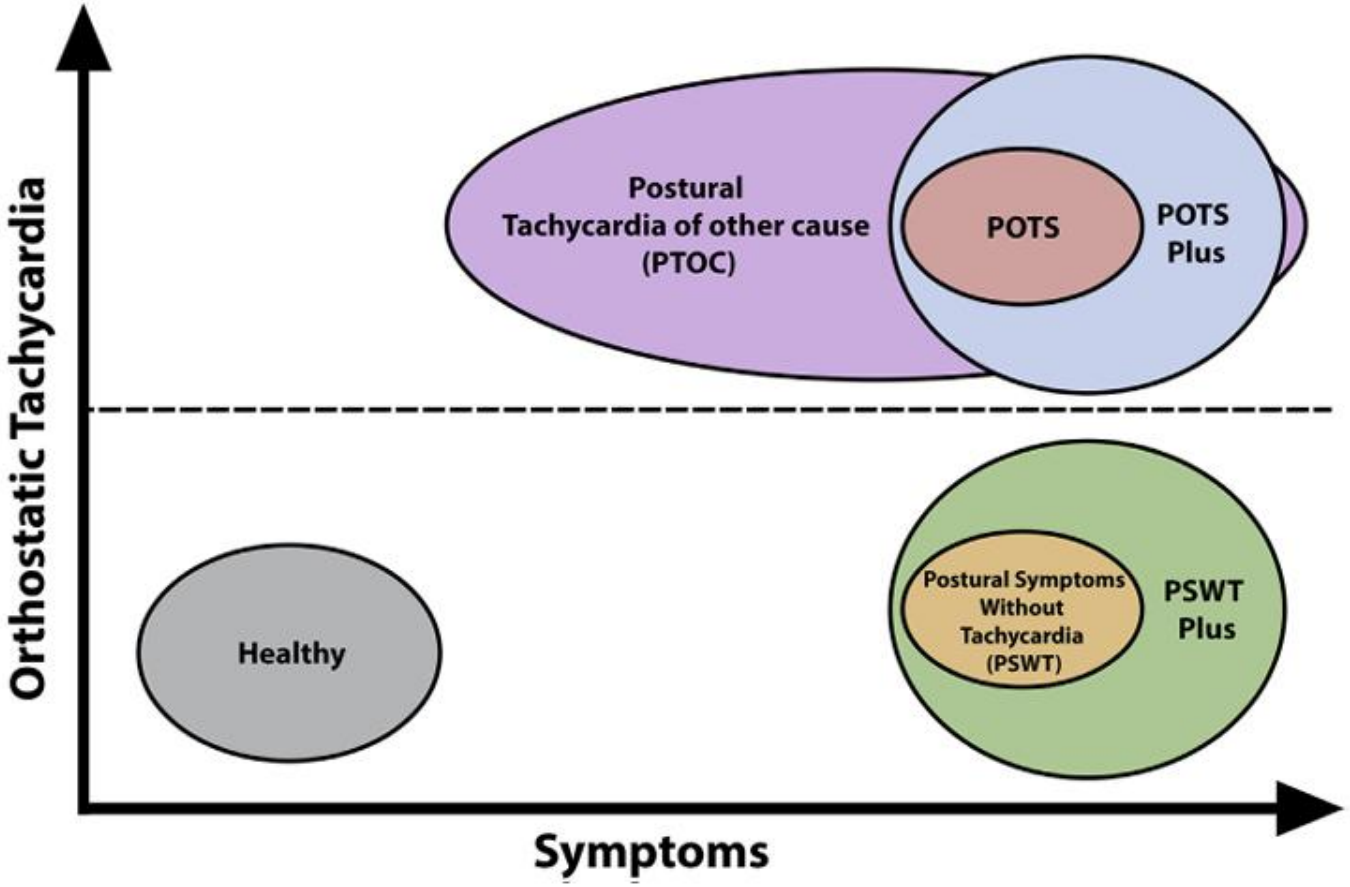
Frequent symptoms that occur with standing and are relieved substantially by recumbency

Symptoms may reflect

Decreased central blood volume	Sympathetic hyperactivity
• Presyncope, generalized weakness, lightheadedness	• Palpitations, tremor, jitteriness

Robbins et al., Neurol Clin Pract, 2026

What is the significance of the tachycardia?



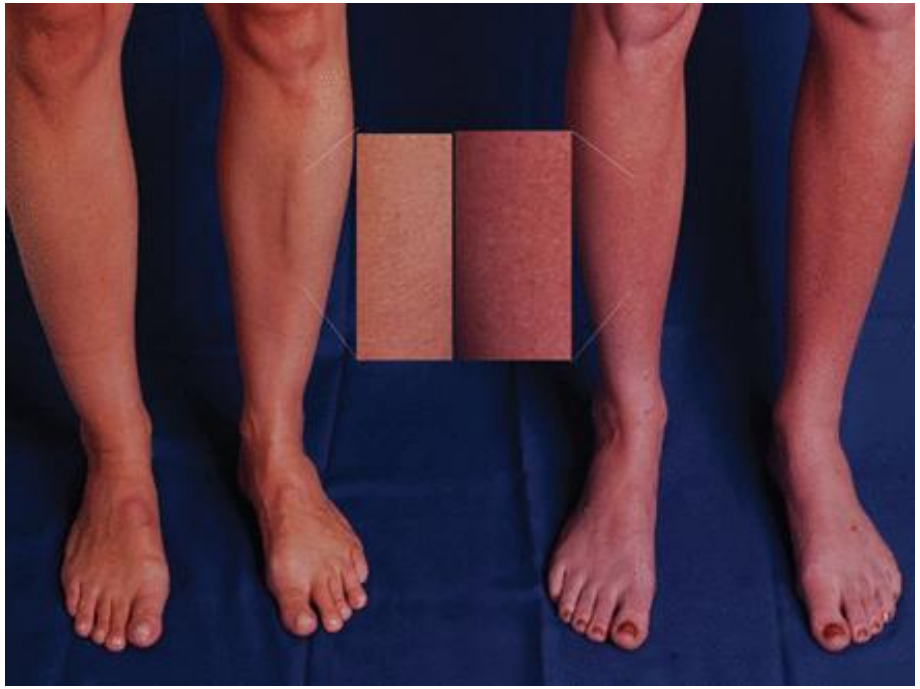
Raj et al., Can Journal Cardiol, 2020

Comorbidities

- Hypermobility spectrum disorder and hEDS
- Chronic fatigue syndrome/myalgic encephalomyelitis
- Migraine
- Fibromyalgia
- Functional gastrointestinal disorders
- Mast cell activation and chemical sensitivities
- Autoimmune disorders
- Studies vary re: whether anxiety/depression is more prevalent. May be misdiagnosed with psychiatric disorders.

Case

- 21-year-old female college athlete presents for evaluation of dizziness.
- Contracted mononucleosis and missed 3 weeks of workouts.
- Spent a lot of time in bed due to fatigue.
- Markedly reduced exercise tolerance upon return, becomes presyncopal.
- Palpitations and dizziness when walking across campus.
- Looks like blood is pooling in her feet



Raj SR, *Indian Pacing Electrophysiol J*., 2006.

POTS diagnosis

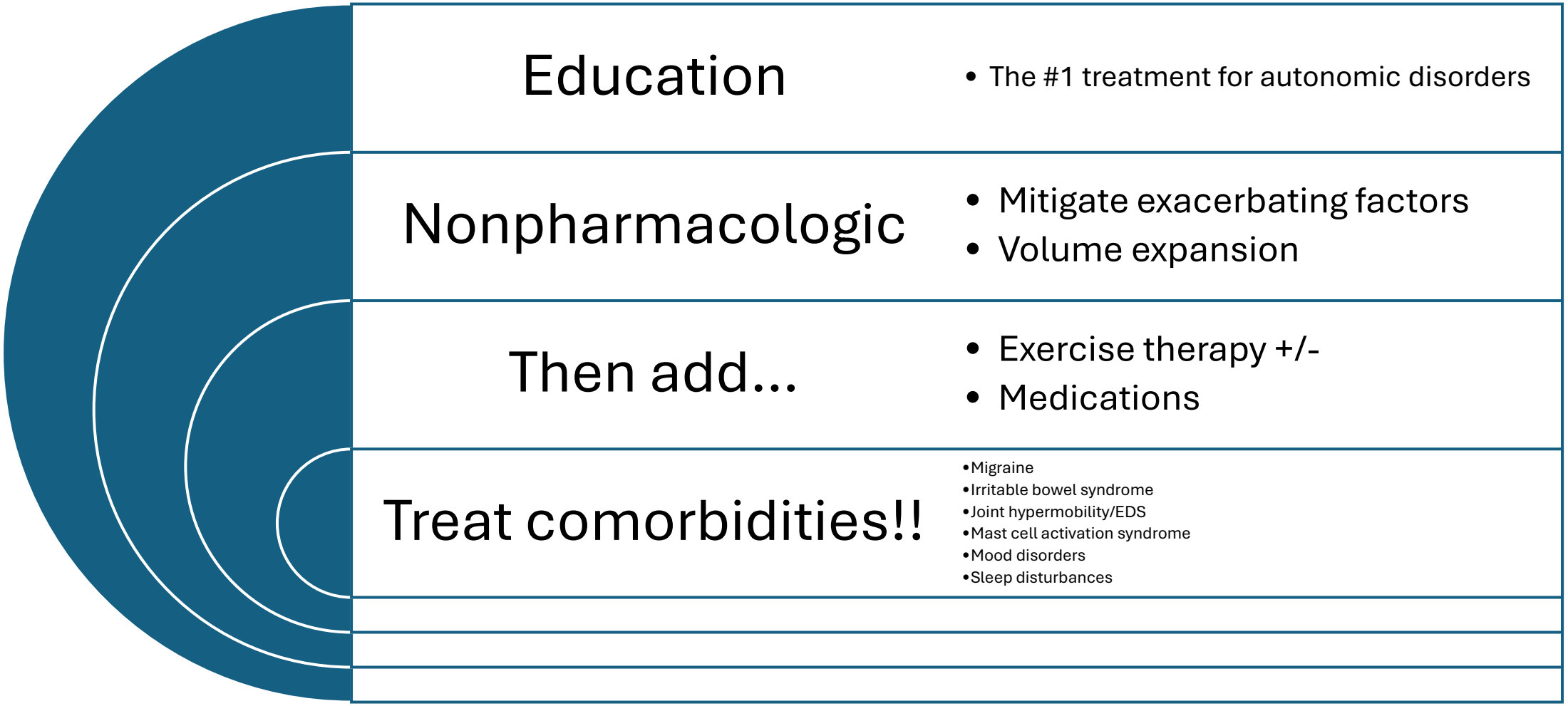
- History is key
  - Demographics
  - Orthostatic intolerance
  - Clinical context
- Orthostatic vitals
- 12-lead ECG
- Basic labs

	Blood pressure	Heart rate
Supine 5 minutes		
Standing 1 minute		
Standing 3 minutes		
Standing 5 minutes		
Standing 7 minutes		
Standing 10 minutes		

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

Sheldon et al., HRS Expert Consensus Document on POT/IST/VVS, 2015.

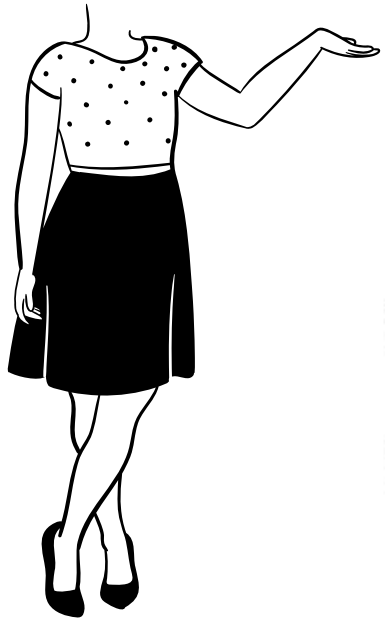
POTS management

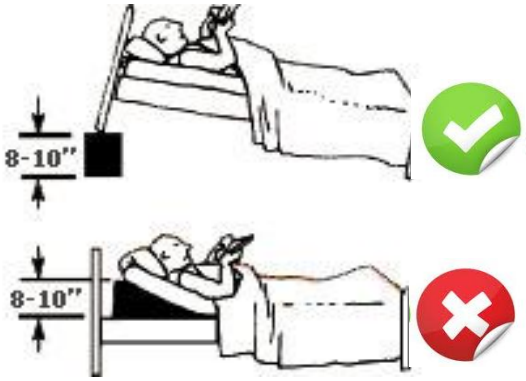


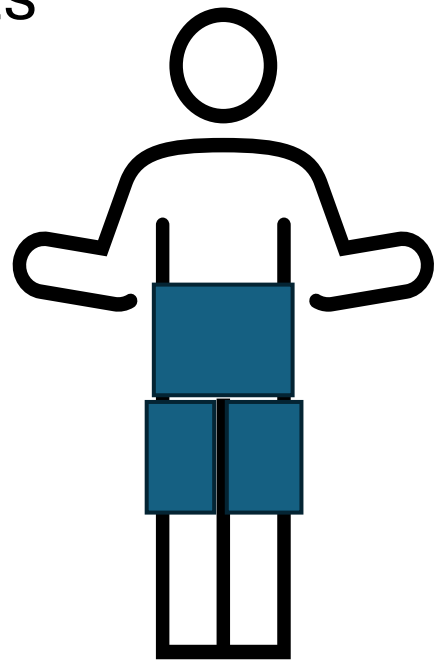
Non-pharmacologic management

- Identify exacerbating factors
  - Morning, heat, large meals, post-exercise
- Fluid intake
  - 2-3 L water daily
- Salt intake
  - 7-10 g if no contraindication
- Bolus water drinking
  - 12-16 oz rapid water consumption mitigates orthostatic tachycardia

- Elevate head of bed
  - Extrapolated from nOH literature
- Physical countermaneuvers
- Compression garments
  - Thigh to waist







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Exercise

- Best evidence support for treatment of POTS
- Only intervention to date that can really reverse some of the pathophysiology
- Cardio workouts targeted to heart rate zones for conditioning
- Start recumbent, gradually add upright exercise
- Strength training for core and lower body
- 3 months in the original research protocol
- Can be performed on own or with gui

Link to full protocol in Bryarly et al., *JACC*, 2019.

Other exercise protocols

- Gibbons' pragmatic protocol
- Utah Autonomic Disorder adaptive Physical Therapy (ADaPT) program
- Flexible, customized approach
  - Frequency
  - Intensity
  - Time
  - Type of exercise

Cardiovascular exercise as a treatment of postural orthostatic tachycardia syndrome: A pragmatic treatment trial

Christopher H. Gibbons, MD, MMSc, Gustavo Silva, MD, Roy Freeman, MD

From the Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.

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1443-9506/25/$36.00
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Postural Orthostatic Tachycardia Syndrome: A State-of-the-Art Review

Dennis H. Lau, MBBS, PhD [a,b,c,*], Artur Fedorowski, MD, PhD [d,e], Satish R. Raj, MD, MSCI [f,g], Caelum Schild, BAppSc [a], Laura A. Pace, MD, PhD [h,i], Svetlana Blitshteyn, MD [j], Vidya Raj, MB ChB [k], Jeffrey R. Boris, MD [l], Lesley Kavi, MBChB [m], Marie-Claire Seeley, RN, PhD [a,b,n,o], Celine Gallagher, RN, PhD [a,b,n,o]

Adaptive Approaches to Exercise Rehabilitation for Postural Tachycardia Syndrome and Related Autonomic Disorders

Lauren Ziaks, PT, DPT, ATC [a,1], Kathryn Johnson, PT, DPT [b,c,1], Kelsi Schiltz, PT, DPT [d], Ryan Pelo, PT, DPT, PhD [d], Guillaume Lamotte, MD, MSc [b], Claudia Dal Molin, DO, RMSK [e], Tae Chung, MD [f], Melissa M. Cortez, DO [b]

Medications

- Midodrine
  - Alpha-1 agonist→Vasoconstrictor
  - Used for hypotension/near syncope
- Propranolol
  - Beta blocker
  - For palpitations/tachycardia—low doses tolerated better
- Pyridostigmine
  - Ach-esterase inhibitor→increases Ach availability
  - Particularly helpful with comorbid constipation
- Fludrocortisone
  - Mineralocorticoid→Volume expansion
  - Tachyphylaxis, hypokalemia, headache, concerns about long term use
- Ivabradine
  - Inhibits SA nodal “funny channels”→slows heart rate
  - Photopsias common, women MUST use contraception
- Clonidine/guanfacine
  - Alpha-2 agonist→central sympatholytic
  - Particularly helpful for hyperadrenergic sx
- NS bolus 1-2 L
  - Rapid volume expansion, huge salt load
  - Effective rescue therapy, avoid as long-term solution



Robbins et al., Neurol Clin Pract, 2026


NOTS
And what-nots....

Case

- 22 yo F presents for evaluation of POTS
- Had influenza A last year, never felt the same
- Fatigued, feels she is “hypoglycemic”
- Had to quit her job in retail, couldn’t stay on her feet
- Transitioned to online classes, does all her work from bed, feels better there

	Blood pressure	**Heart rate**
Supine 5 minutes	100/70	65
Standing 1 minute	90/60	70
Standing 3 minutes	100/70	72
Standing 5 minutes	95/65	70
Standing 7 minutes	95/60	72
Standing 10 minutes	100/70	69

Feels weak and dizzy the duration of the stand test

Chronic orthostatic intolerance

- Symptoms of orthostatic intolerance but without the accompanying tachycardia, “PSWT”
- Why it matters:
  - Won’t meet criteria for POTS research studies
  - Similar management to POTS, though rate-lowering agents may not be helpful

Case

- 18 yo F referred for POTS
- Several years of dizziness upon standing
- Often presyncopal first thing in the morning, has to sit back on her bed
- Fainted once standing up and walking out after class
- Once she is up for a couple of minutes she is fine, can be on her feet for hours

	Blood pressure	**Heart rate**
Supine 5 minutes	95/65	65
Standing 1 minute	90/60	85
Standing 3 minutes	100/70	75
Standing 5 minutes	95/65	75
Standing 7 minutes	95/60	72
Standing 10 minutes	100/70	69

Initial orthostatic hypotension

- Drop in SBP >=40 mmHg or DBP >=20 mmHg within 15 sec standing, with spontaneous correction within 30-60 seconds
- Transient vasodilation in activating leg muscles
- Can occur in otherwise healthy individuals
- Why it matters:
  - Only diagnosed with beat-to-beat BP monitor on an ACTIVE stand
  - Mainstay of therapy is non-pharmacologic with hydration and physical countermaneuvers

Case

- 25 yo policeman was directing traffic for an afternoon event in August
- He was on his feet for 3 hours, wasn't drinking much
- He started to feel lightheaded, nauseated, shaky. Vision tunneled and he blacked out.
- Shook for a few seconds, regained consciousness after 30 seconds or so.
- Passed out in high school choir, and when he was a groomsman.

	Blood pressure	**Heart rate**
Supine 5 minutes	120/80	60
Standing 1 minute	110/85	70
Standing 3 minutes	120/85	75
Standing 5 minutes	120/85	70
Standing 7 minutes	120/80	72
Standing 10 minutes	120/80	70

Vasovagal syncope

- AKA neurocardiogenic syncope, reflex syncope, the common faint
- Common comorbidity of POTS, but often occurs in isolation
- Why it matters:
  - First line therapy is non-pharmacologic: education, hydration, and physical countermaneuvers.
  - May add specific medications if non-pharmacologic management is insufficient
    - Fludrocortisone
    - Midodrine
    - SSRIs
    - Atomoxetine? TBD

Giambusso et al., Expert Rev of Clin Pharm, 2025.

Case

- 30 yo M, previous marathon runner, referred for POTS
- Acute EBV infection last year, has never been the same since
- Chief complaint is fatigue
- Feels poorly when up on his feet
- Feels achy and flu-like if he ever tries to exercise, or even does regular chores
- Unrefreshing sleep

	Blood pressure	**Heart rate**
Supine 5 minutes	120/80	60
Standing 1 minute	110/85	70
Standing 3 minutes	120/85	75
Standing 5 minutes	120/85	70
Standing 7 minutes	120/80	72
Standing 10 minutes	120/80	70

Chronic fatigue syndrome/myalgic encephalomyelitis

- Often follows an infectious illness
- Diagnostic criteria from IOM 2015:
  - >=6 months of profound, functionally-limiting fatigue
  - Post-exertional malaise
  - Unrefreshing sleep
  - Plus one of: cognitive impairment or **orthostatic intolerance**
- Pathophysiology involves defects in energy generation and metabolism and immune dysregulation
- May also be comorbid with POTS
- Why it matters:
  - Pushing the exercise is not helpful and may be detrimental
  - Current recommendations are for activity pacing

Bateman et al., Mayo Clin Proc. 2021

Case

- 45 yo F referred for POTS
- Had COVID 6 months ago and has never been the same
- Overwhelming fatigue
- Dyspnea with any exertion
- Chest pain and palpitations with walking across the room

	Blood pressure	Heart rate
Supine 5 minutes	120/80	80
Standing 1 minute	110/85	90
Standing 3 minutes	120/85	95
Standing 5 minutes	120/85	90
Standing 7 minutes	120/80	92
Standing 10 minutes	120/80	90

Long COVID

- Infection-associated chronic condition (IACC) that occurs after SARS CoV-2 infection
  - Present for at least 3 months
  - Continuous, relapsing and remitting, or progressive disease affecting one or more organ systems (NASEM 2024)
- Why it matters:
  - Heterogeneous disease entity
  - Most Long COVID is NOT POTS (Bryarly et al., JACC, 2025)

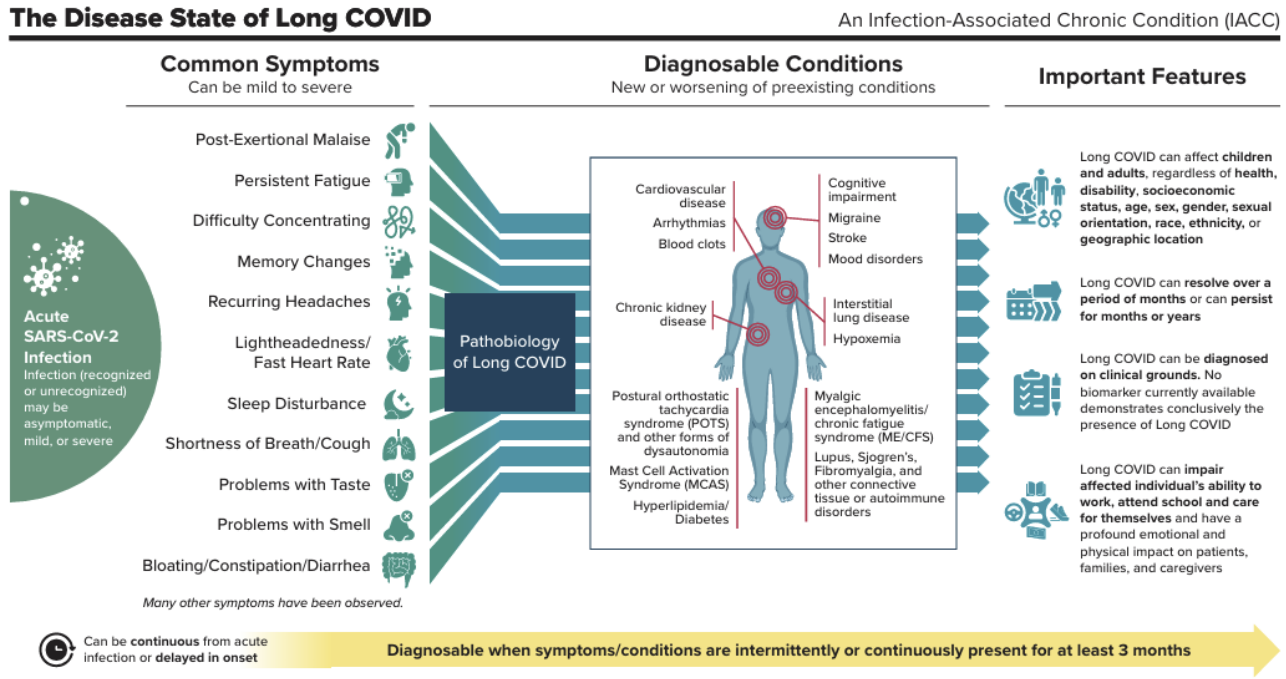


FIGURE 1 2024 NASEM Long COVID Definition.

Long_COVID_Definition_Highlights.pdf

Case

- 75 yo F referred for POTS
- 5 years of progressive fatigue
- Used to cook elaborate holiday meals, now can barely stand long enough to throw together a pot of soup
- Fainted this past summer while out gardening
- Feels ok as long as she is sitting or lying down

	Blood pressure	**Heart rate**
Supine 5 minutes	170/90	80
Standing 1 minute	150/80	80
Standing 3 minutes	110/70	85

Neurogenic orthostatic hypotension

- Drop in SBP >=20 mmHg or DBP >= 10 mmHg within 3 minutes of standing
- Lack of heart rate increment
- This is autonomic failure!
- Why it matters:
  - Should trigger a workup for the underlying cause
  - Reach for pressors if non-pharmacologic management is inadequate

Case

- 22 yo F referred for spells, question of POTS
- Spells from any posture
- Hot feeling, heart racing, general tremulousness, and loss of ability to interact with her surroundings, sometimes with loss of awareness
- Lasts 2-3 minutes and she is tired afterwards
- No limitation in orthostatic tolerance

	Blood pressure	**Heart rate**
Supine 5 minutes	100/70	65
Standing 1 minute	90/60	70
Standing 3 minutes	100/70	72
Standing 5 minutes	95/65	70
Standing 7 minutes	95/60	72
Standing 10 minutes	100/70	69

Spell captured on vEEG with no electrographic correlate, and telemetry with no arrhythmia

Functional Neurologic Disorder

- “Symptoms and signs of genuinely experienced alterations in motor, sensory, or cognitive performance that are distressing or impairing,” caused by dysfunction of brain networks rather than structures (Hallett et al., 2022)
- Is POTS a form of FND?
  - Norcliffe-Kaufmann et al.—anticipatory tachycardia
  - This does not explain the well-established cardiovascular and hemodynamic changes described in POTS
- Though they are not the same, they may be comorbid
  - Not well studied—6% in one series
  - Possible mechanistic link? Disrupted interoception in both





Questions?

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