



Postural Orthostatic Tachycardia Syndrome

D. Elizabeth Le, MD, FACC, FASE, FAHA

Associate Professor of Medicine

April 10, 2025

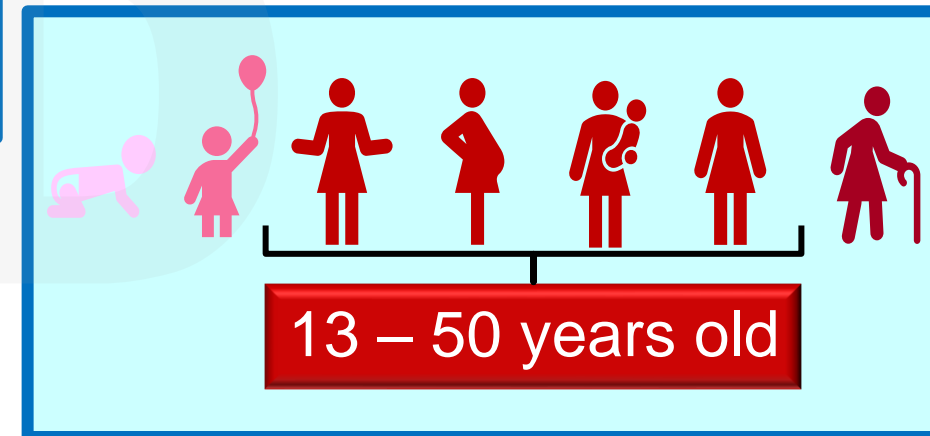
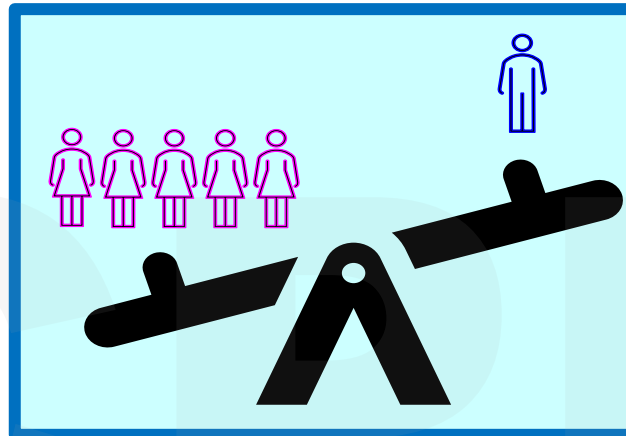
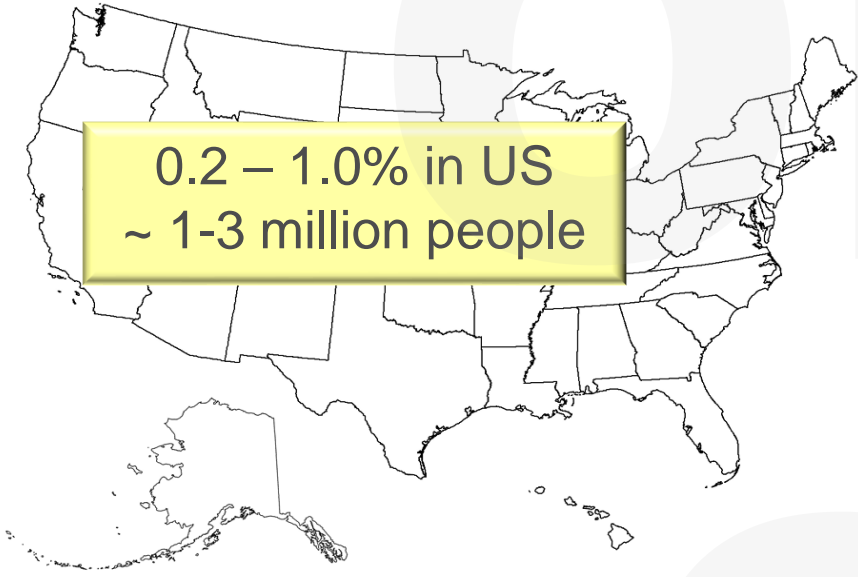
Disclosures

- No actual or potential conflicts of interest in relation to this program or presentation to disclose.
- There are **NO** FDA-approved medications for POTS
- All medications discussed are for off-label use but have been studied in clinical trials.
- The contents do not represent the views of the U.S. Department of Veterans Affairs or the U.S. government.

Objectives

- Recognize the criteria to diagnose postural orthostatic tachycardia syndrome (POTS)
- Select the appropriate nonpharmacologic and pharmacologic treatment for POTS

Demographics



In the News.....

The Washington Post

Breaking News

Trending Now

5 minutes ago

A mysterious condition is striking young, highly trained athletes

First described more than 150 years ago, POTS has proliferated since the coronavirus pandemic. The syndrome tends to strike suddenly, leaving previously healthy people unable to function, with no clear cause. In recent years, doctors have noticed a curious and disproportionate subset of patients: female athletes at peak fitness.

They're young and athletic. They're also ill with a condition called POTS.

Since covid-19, diagnoses have increased, researchers and doctors report



By Ariana Eunjung Cha

April 10, 2024 at 5:00 a.m. EDT

TODAY ON THE SHOW SHOP OLYMPICS WELLNESS PARENTS FOOD LIFE TODAY PLAZA **TODAY all day**

Katie Ledecky opens up about POTS diagnosis and how she manages it when competing

The swimmer opened up about her diagnosis in her recent memoir, "Just Add Water."

Katie Ledecky talks record Paris run, family, plans for LA Olympics 04:10



LONDON 2012 RIO 2016 TOKYO 2021 PARIS 2024

[Katie Ledecky POTS: What to Know About Her Symptoms and Treatment \(today.com\)](#)



Prevalence – Long COVID

11/2024



- > 776.8 million cases
- 7.1 million deaths
- ~ 47 million long COVID (6%)

12/2024



- ~ 103 million cases
- ~ 1.12 million deaths
- ~ 15.7 million Long COVID (14-18%)

- 2-14% of survivors developed POTS
- 9-61% experienced POTS-like symptoms within 6-8 months
- POTS rate 5-fold higher with infection than with vaccination
- Women > Men
- Whites + Hispanics > Blacks and Asians
- Lower prevalence in higher educated and higher income groups

WHO; CDC

Narasimhan B et al. Vascular Health and Risk Management 2023;19:303-316.

Ormiston CK et al. Heart Rhythm 2022;19:1180-1889.

Kwan AC et al. Nature Cardiovasc Res 2022;1:1187-1194

Why is POTS a challenging diagnosis?

- Heterogeneous presentation
 - Underdiagnosed or misdiagnosed
- Atypical features overlap with other medical conditions
- Co-existing psychiatric conditions
 - Attributed to chronic anxiety or panic disorders
- Lack of clinician familiarity with the condition
- Multiple mechanisms



POTS – Patients' Experience

Self-reported patient survey from UK, N=4,835

Patients saw an average of 7 physicians before POTS diagnosis

Average of 4 years before correct diagnosis of POTS is made

2 out of 3 patients report at least 10 different symptoms

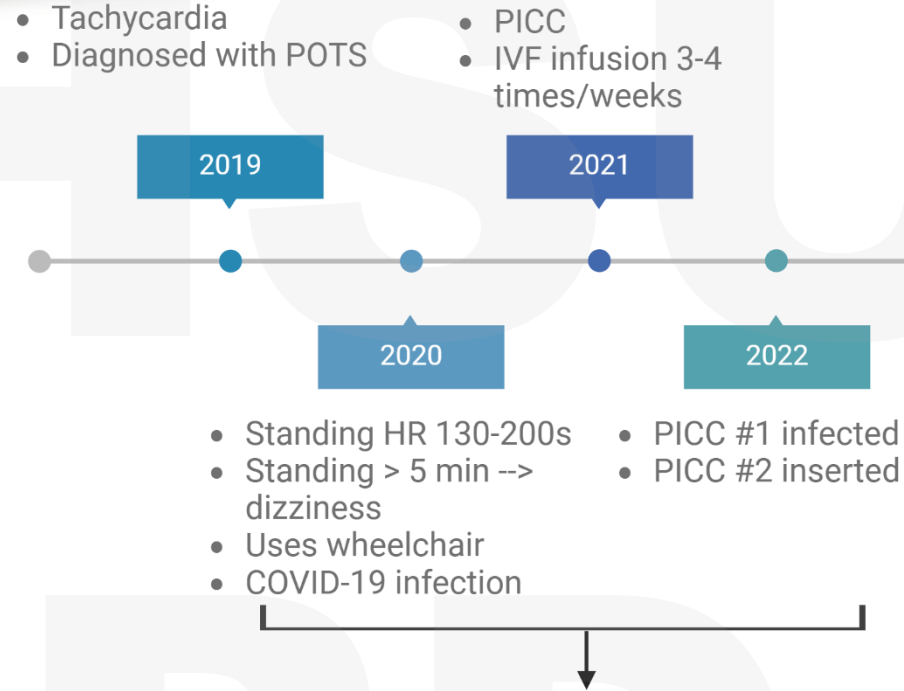
- Median time to diagnosis ~ 6-72 months
- 27% saw >10 physicians
- 83% given psychiatric diagnosis before POTS diagnosis

Can be debilitating and negatively affect quality of life
Challenging diagnosis but can be helpful if confirmed



Case - History

23 yo female with history of migraine and POTS diagnosed in 2019, referred to general cardiology clinic for management of POTS.



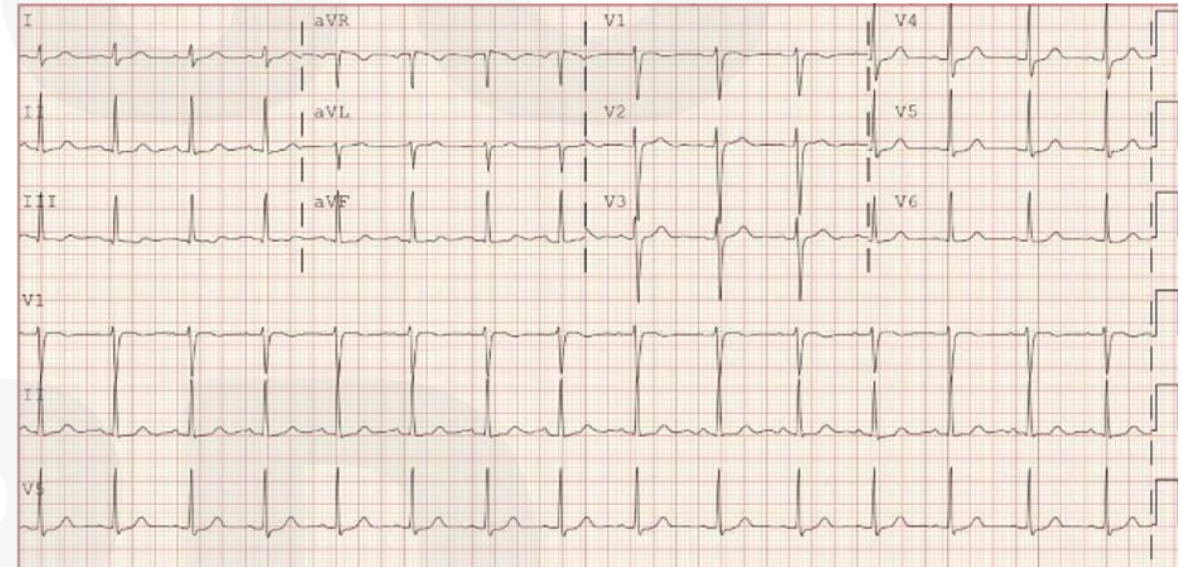
Did not tolerate

- Fludrocortisone (4/2021) --> low HR and BP
- Midodrine (8/2021) --> low HR, felt strange
- Pyridostigmine --> hypotension, diarrhea, coughing
- Metoprolol tartrate --> not effective
- Nortryptiline --> for migraine but worsened dizziness
- Venlafaxine --> for migraine but worsened dizziness

Case - History

Vitals

- Sitting: Pulse 88 BP 125/70
- Standing: Pulse 133 BP 130/65
- Standing > 3min Pulse 88 BP 133/68
- Exam: no murmur, PIC in right UE with erythema around bandage
- ECG: NSR
- 24hour Holter Monitor: Mean HR 83, range 56-83 bpm, sinus arrhythmia, no ectopy
- TTE: normal



Historical Perspective

~1860
(Da Costa)

- Irritable heart syndrome

1918 (Lewis)
1941 (Wood)

- Soldier's heart
- Da Costa syndrome

1982
(Rosen and Cryer)

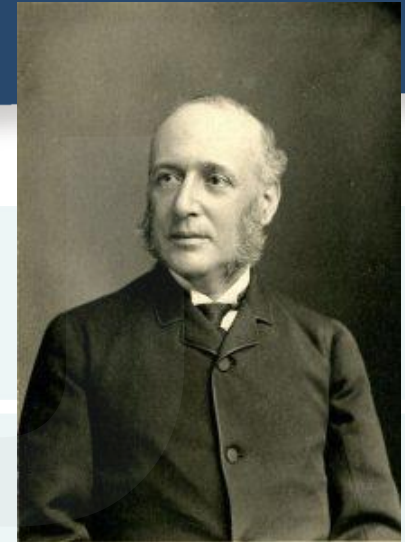
- Postural tachycardia syndrome
- Disabling tachycardia upon standing without orthostatic hypotension

1986
(Fouad)

- Idiopathic hypovolemia
- Small degree of hypotension

1993
(Schondorf and Low)

- Current definition of POTS



Dr. Jacob M. Da Costa
<https://www.civilwarmed.org/irritableheart/>

Symptom Characteristics

- Palpitations or tachycardia onset
 - 12.5% Acute (<1 month)
 - 13.8% Subacute (1-3 months)
 - 5.9% Insidious (>3 months)
- Frequency
- Impact on function and quality of life

Symptoms

Postural Cardiac Symptoms

- Lightheadedness (99%)
- Tachycardia (97%)
- Presyncope (94%)
- Shortness of breath (88%)
- Palpitations (87%)
- Chest discomfort

Noncardiac Symptoms

- Mental clouding (brain fog)
- Tremulousness
- Blurred or tunnel vision
- Nausea

Observed with chronic autoimmune disease

- Headache
- Sleep disturbances
- Malaise
- Abdominal pain, heartburn, diarrhea, constipation (last hours, multiple times/week)

Symptoms Context

Triggers

- Infection
 - COVID-19 (22%)
- Vaccination
 - HPV
- Surgery (12%)
- Trauma
- Pregnancy (9%)
- Childbirth
- Prolonged period of inactivity

Exacerbation

- Heat
- Fever
- Dehydration
- Morning hours
- Non-dippers
- Strong emotions
- Alcohol
- Menstruation
 - Worse pre or early cycle when estrogen and progesterone are low or decreasing

Dietary and Exercise Habits & Culprit Medications

Diet and Functional Status

- Diet
 - Amount of salt and volume of water intake
 - Size of meals
- Exercise tolerance
 - Quantify amount of activity and reduction of activity over a period of time
 - List physical activities that no longer can be performed

Medications that can exacerbate POTs

- Antidepressants
 - Serotonin-norepinephrine reuptake inhibitors
 - Monoamine oxidase inhibitors
- Antipsychotics (phenothiazines)
- Anticholinergics
- ADHD medications
- Diuretics
- Vasodilators and venodilators
- Oral contraceptive pills that contain antimineralocorticoid (drospirenone)
- Stimulants (caffeine, nicotine)

Detailed Autonomic Review of Systems

Musculoskeletal

Muscle fatigue

Weakness

Pain

Gastrointestinal

Nausea

Bloating

Dysmotility

Gastroparesis

Diarrhea

Constipation

Pain

Irritable bowel syndrome

Weight loss

Nervous System

Headache

Migraine

Cognitive impairment

Brain fog

Photophobia

Phonophobia

Blurred vision

Neuropathic pain

Sleep disorder

Involuntary movement

Respiratory

Short of breath

Hyperventilation

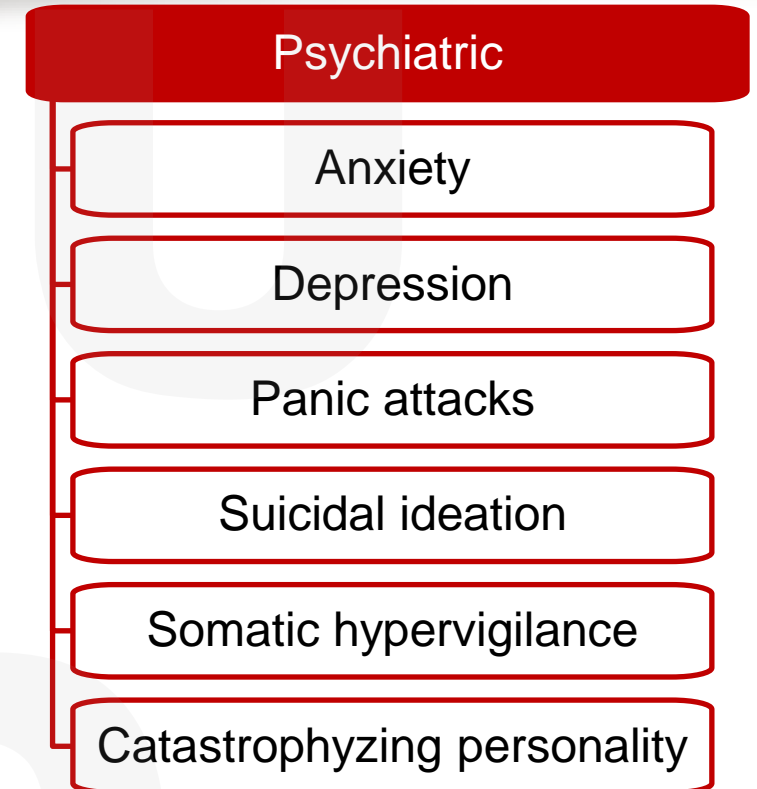
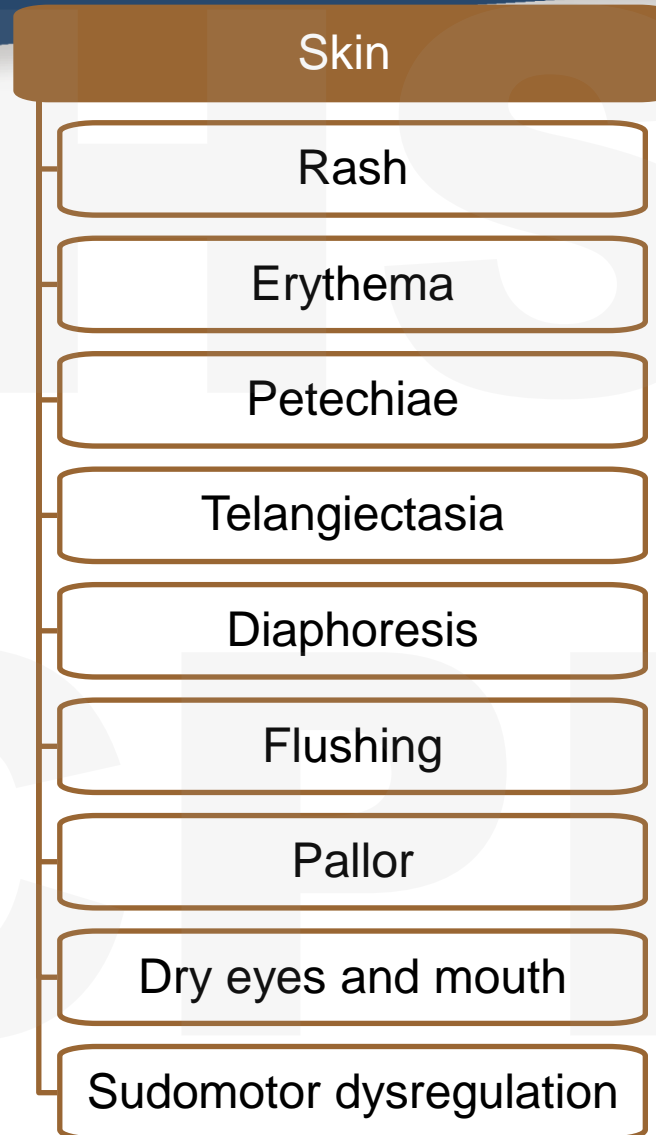
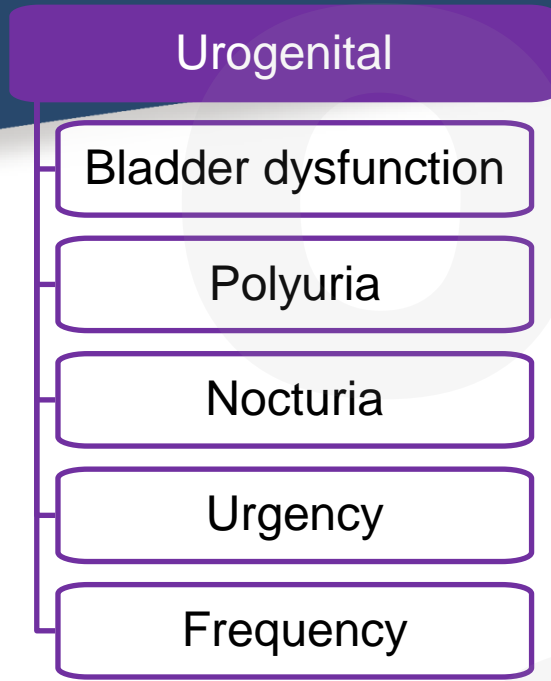
Bronchial asthma

Aboseit DO et al. Cleveland Clinic
J Med. 2023;90:439-477.

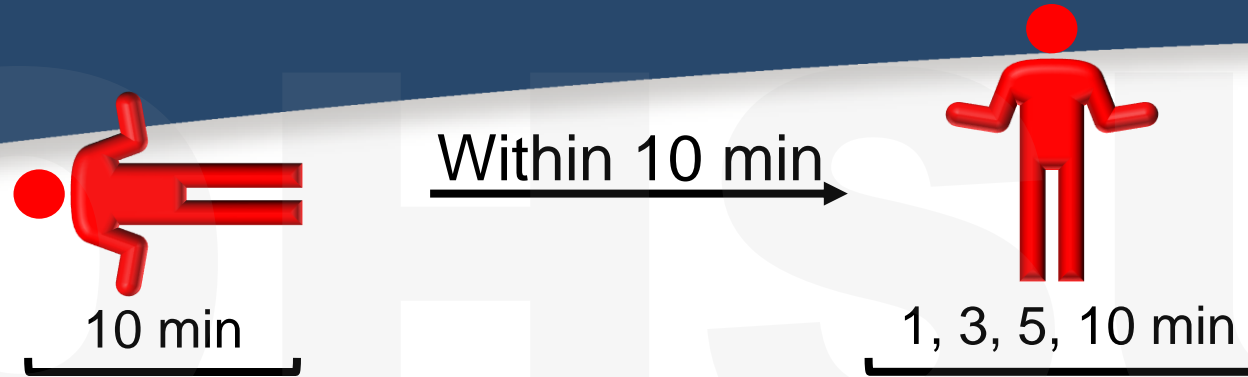
Sebastian SA et al. Curr Prob
Cardiol. 2022;47:1-24



Detailed Autonomic Review of Systems



POTS vs. Postural Tachycardia



Upright Tachycardia

- ≥ 30 bpm >19 years old
- ≥ 40 bpm 12-19 years old
- Sustained tachycardia >30 s
 - 2 measurements at least 1 min apart
- No orthostatic hypotension ($\downarrow \geq 20/10$ mmHg by 3 min)

+

Chronic

- ≥ 6 months
- >3 months
 - Canadian CV Society

+

Associated with Symptoms

Orthostatic

- Lightheadedness
- Palpitations
- Tremulousness
- Atypical chest discomfort

Not orthostatic

- Fatigue
- Blurred vision
- Pre-syncope
- Bloating, diarrhea, constipation
- Headache
- Brain fog
- Exercise intolerance

+

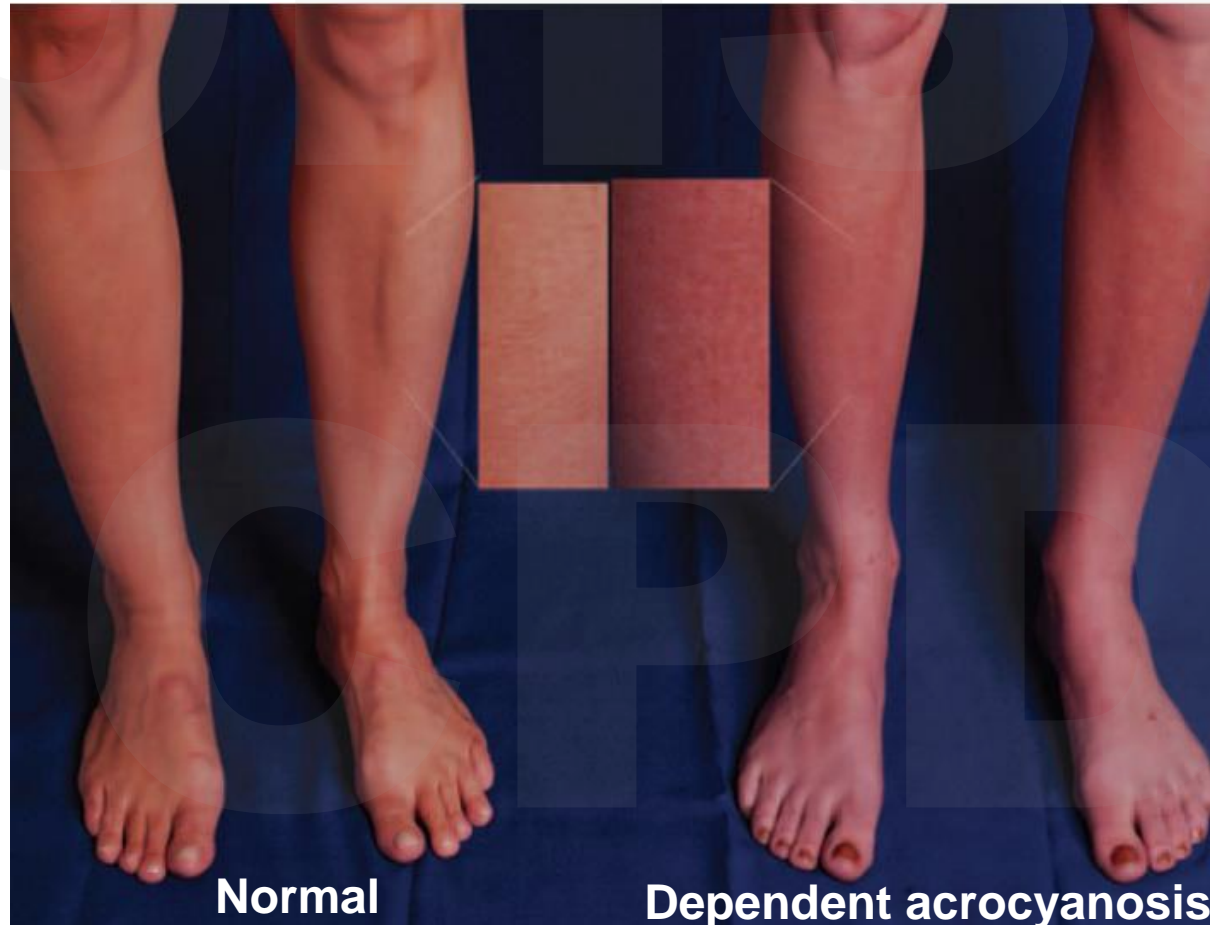
Absence of other conditions

- Acute dehydration
- Infection
- Anemia
- Hyperthyroidism
- Pheochromocytoma
- Medications-induced effects
- Recreational drugs effects
- Sustained bed rest
- Anxiety or panic attacks

Physical Exam

“POTS feet”

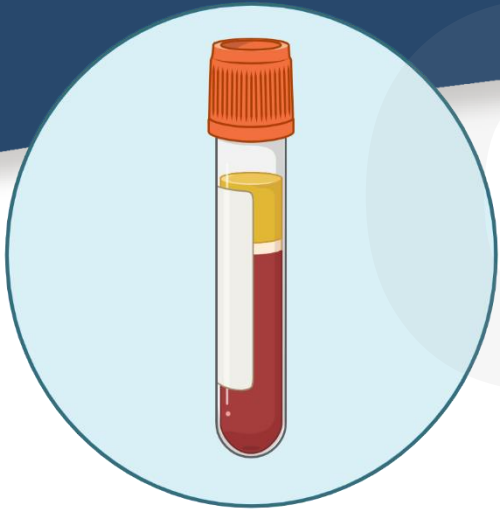
Acrocyanosis (dark, red-blue discoloration of lower legs that is cold to touch (~50%))



Normal

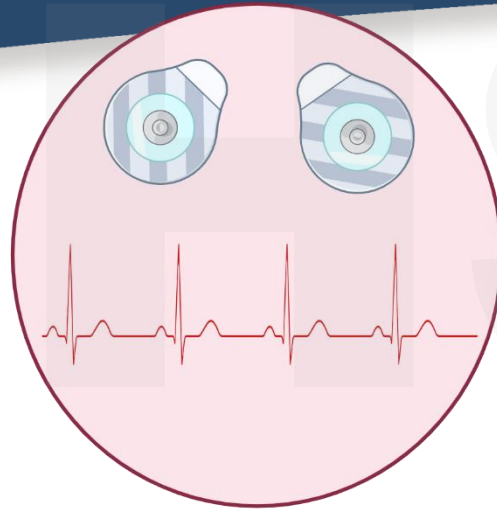
Dependent acrocyanosis

Basic Laboratory and Other Tests



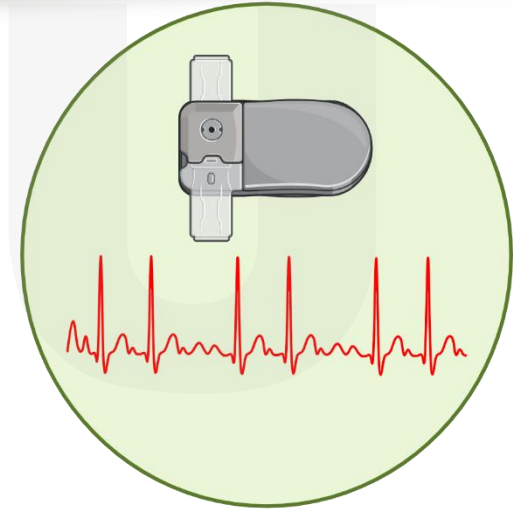
LABS

- CBC
- Basic metabolic panel
- TSH, free T4
- Ferritin
- AM cortisol



ECG

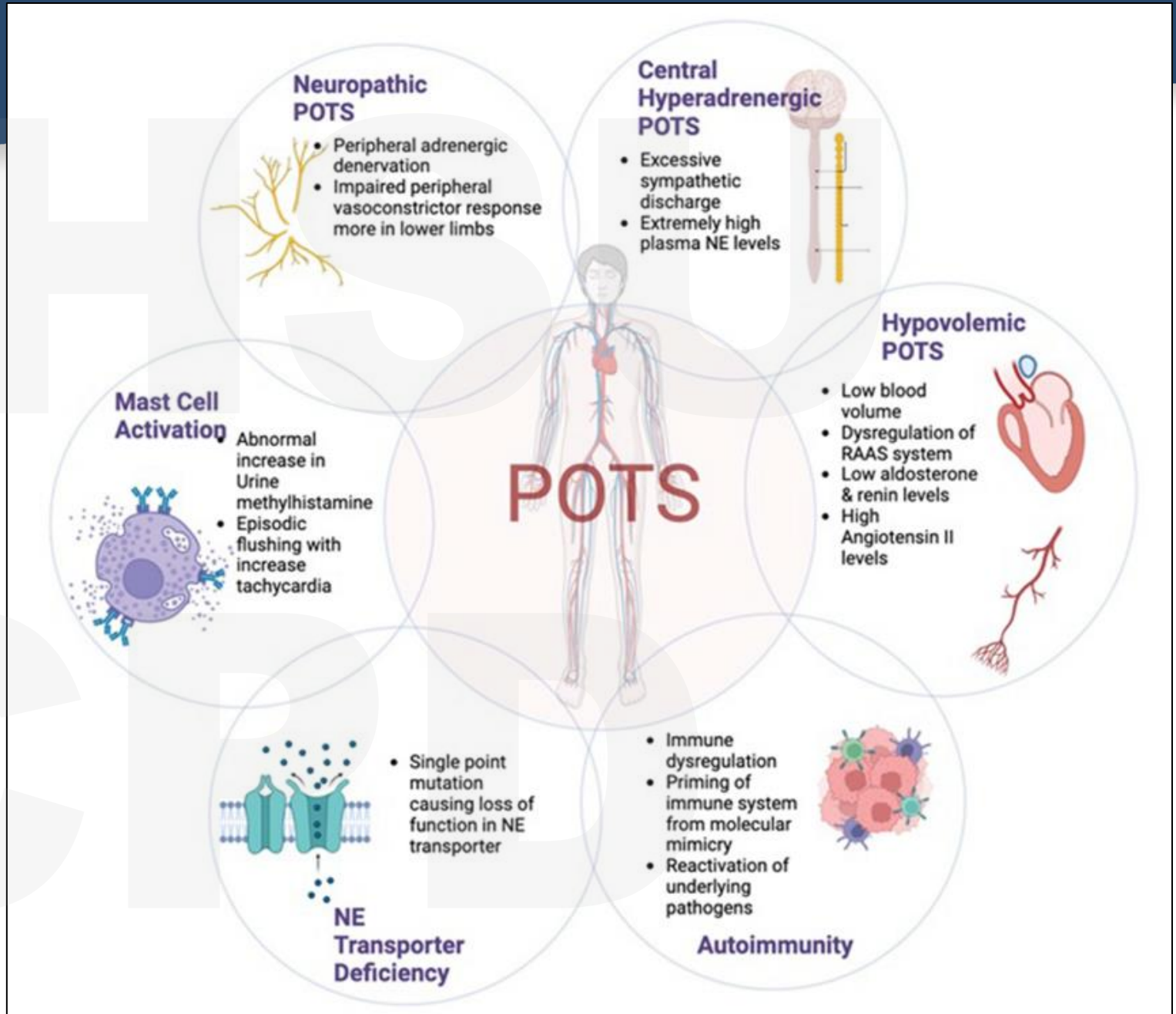
- Sinus tachycardia
- Atrial tachycardia
- Multifocal atrial tachycardia



CONTINUOUS MONITOR

- Arrhythmia
- Inappropriate sinus tachycardia
 - >100 bpm at rest supine and standing
 - Mean 24-hour rate >90 bpm and associated with palpitations

POTS Subtypes

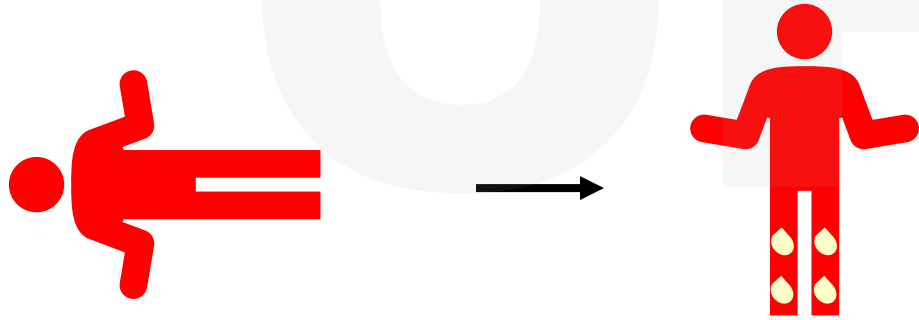


POTS Downward Spiral



Hypovolemic POTS

~ 70% prevalence



Significant ↑ heart rate
and norepinephrine level

Normal

60%
Plasma

40%
RBC + WBC + platelets

POTS

52%
Plasma (↓13%)

48%
RBC + WBC + platelets

Blood pooling

↓ Cardiac output

Tachycardia

Impaired renin-angiotensin-
aldosterone regulation

↓ Sodium retention

Hypovolemia



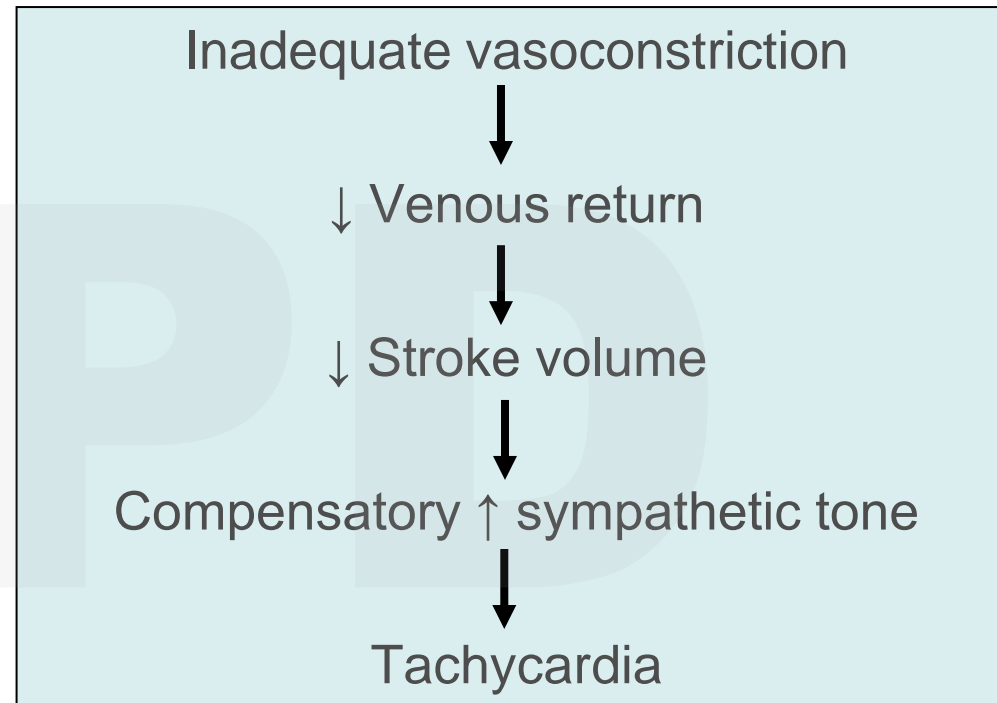
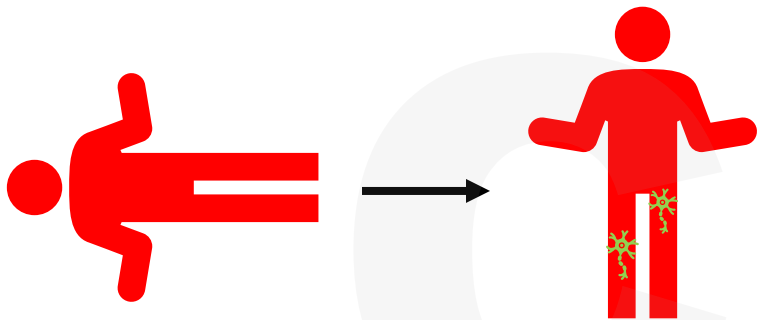
Neuropathic POTS

~ 50% prevalence

Sympathetic denervation, lower limbs

Lower supine/standing heart rate

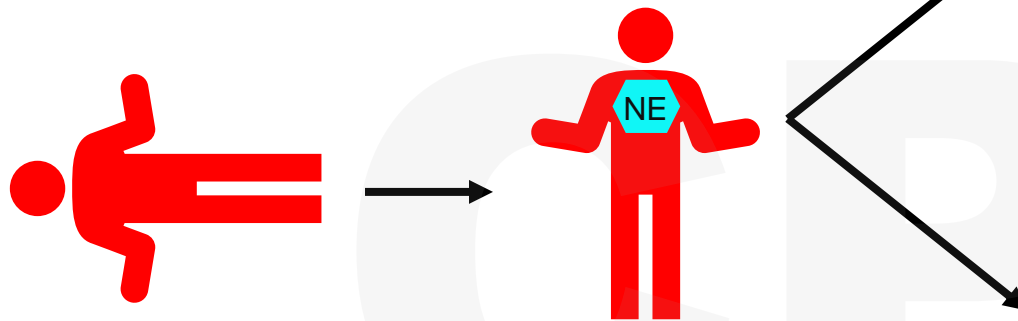
Less anxiety and depression



Hyperadrenergic POTS

~ 50% prevalence

Palpitations, anxiety, tremulousness,
hyperhidrosis



Tricyclic antidepressant (nortriptyline)
Serotonin-norepinephrine reuptake inhibitors (bupropion)
Attention-deficit disorder medications (methylphenidate)

High standing norepinephrine levels
($\geq 600 - 1,000$ pg/mL)

↑ Systolic blood pressure ≥ 10 mmHg
within 10 min of standing

↓ Norepinephrine transporter density
(rare genetic mutation)

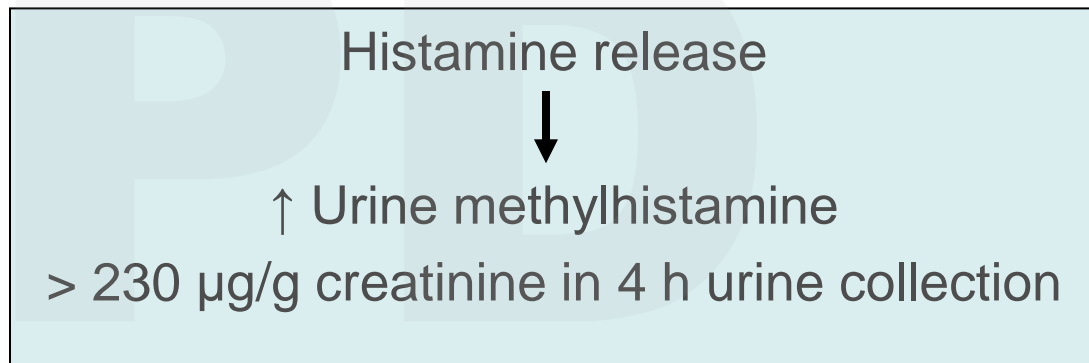
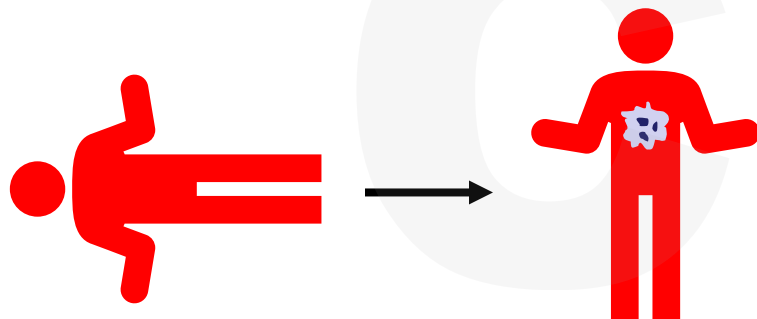
↓ Norepinephrine clearance of synaptic
norepinephrine

↑ Sympathetic nerve activation

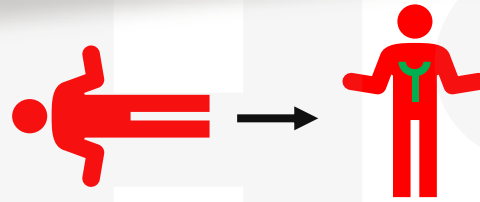
Mast Cell Activation Syndrome

9% prevalence

- Strong allergic symptoms
- Food sensitivities
- Dermatographism
- Frequent urticaria
- Severe Flushing
- Shortness of breath
- Neuropathy



Autoimmune POTS



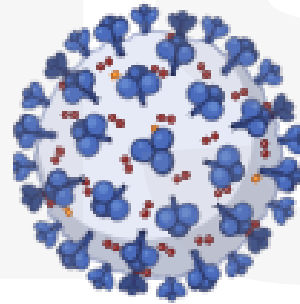
16% prevalence

- Preceding viral illness
- 7% Antiphospholipids antibodies
- 6% Hashimoto thyroiditis
- 3% Celiac disease
- 3% Sjögren syndrome
- 2% Rheumatoid arthritis
- 2% SLE

- 87% prevalence auto antibodies to M1, M2, and M3 muscarinic receptors
- 25% prevalence antinuclear antibodies
- Cardiac lipid-raft-associated proteins (cardiac dysautonomia)
- Adrenergic G-protein coupled receptors antibodies
 - α_1 -adrenergic receptors
 - B_1 - and β_2 -adrenergic receptors
- Angiotensin II type 1 receptor antibodies

Possible Underlying Mechanism of Long COVID-19 and POTS

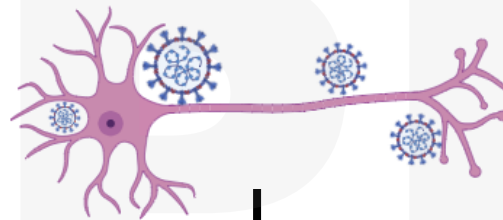
Long COVID-19



↓ Blood Volume &
Deconditioning of the heart



Neural propagation of
COVID-19



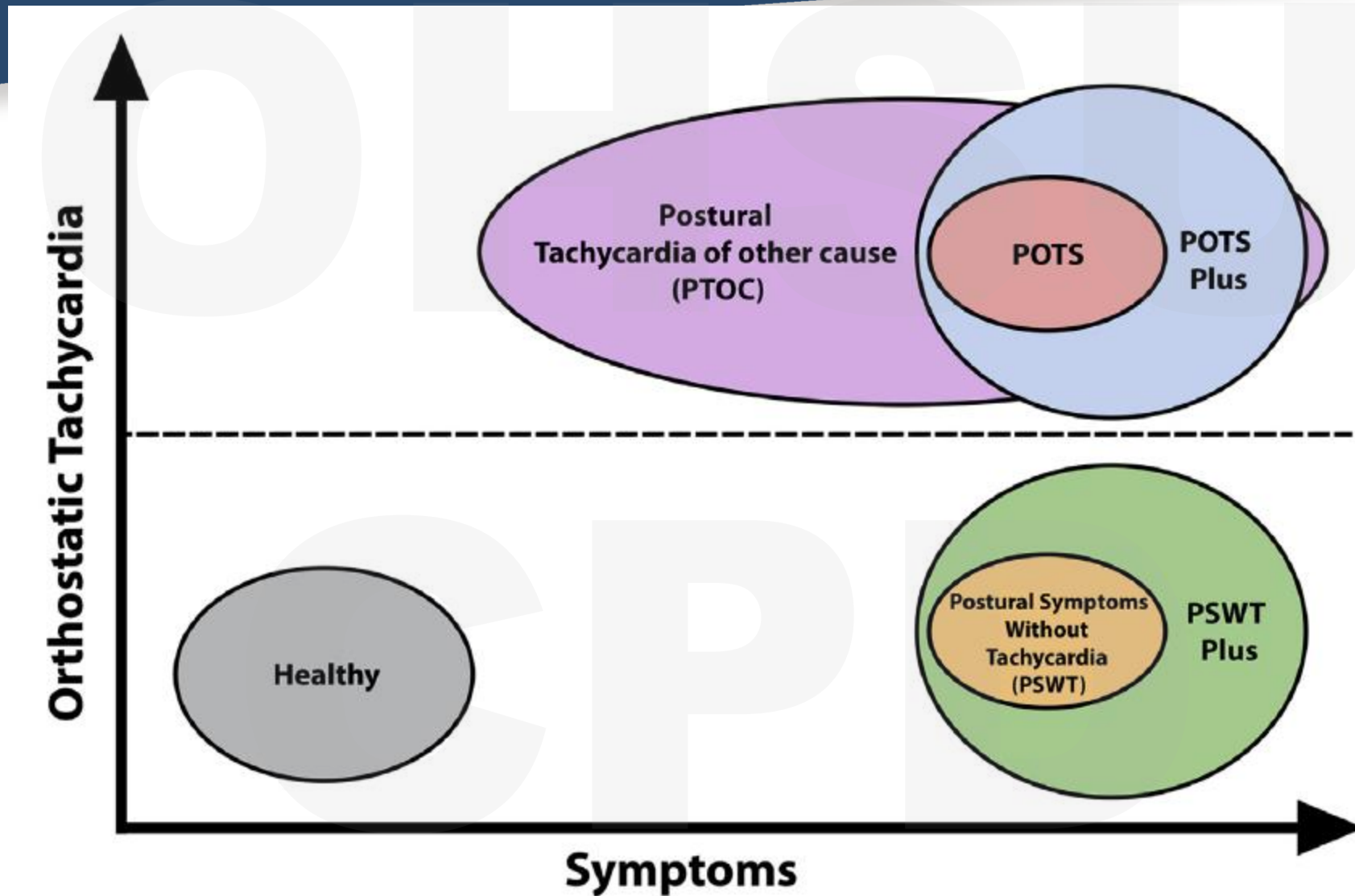
Inflammatory &
Autoimmunity



Dysautonomia

POTS

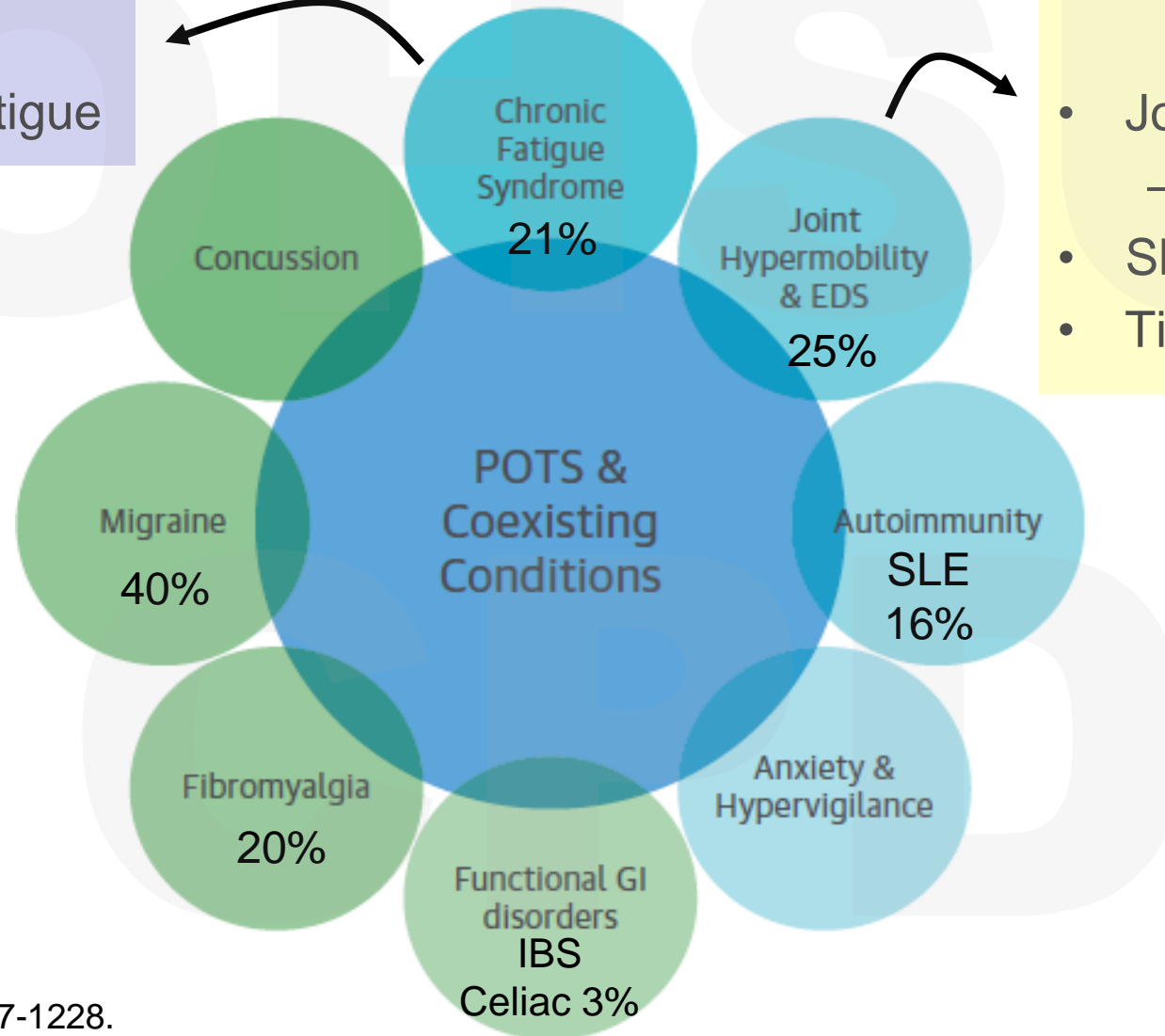
POTS and Related Disorders



Co-existing Conditions with POTS

Chronic Fatigue Syndrome

- 75% of POTS – fatigue



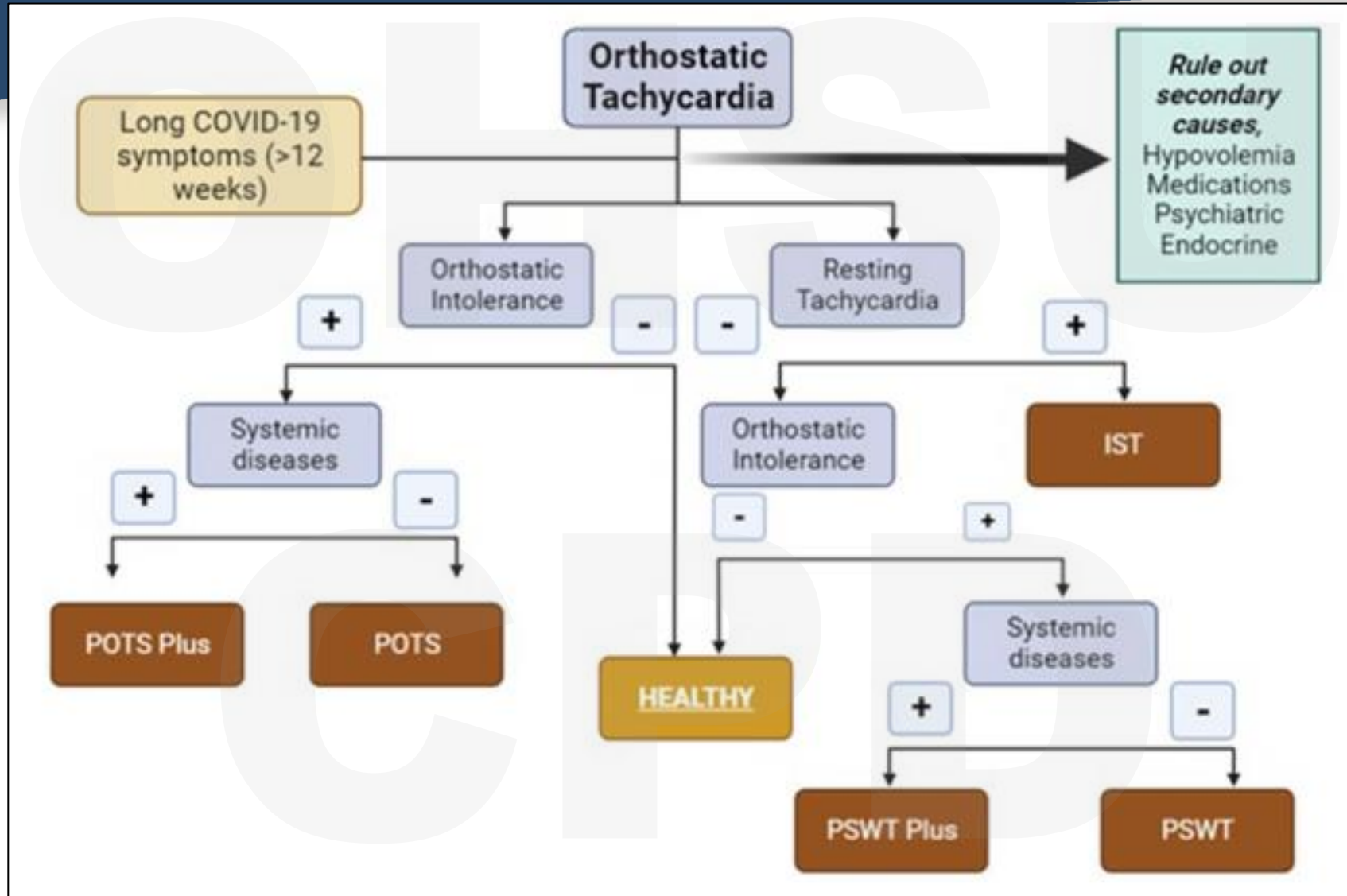
Type III Ehlers-Danlos Syndrome

- Joint hypermobility
 - Autonomic dysregulation
- Skin hyperextensibility
- Tissue fragility

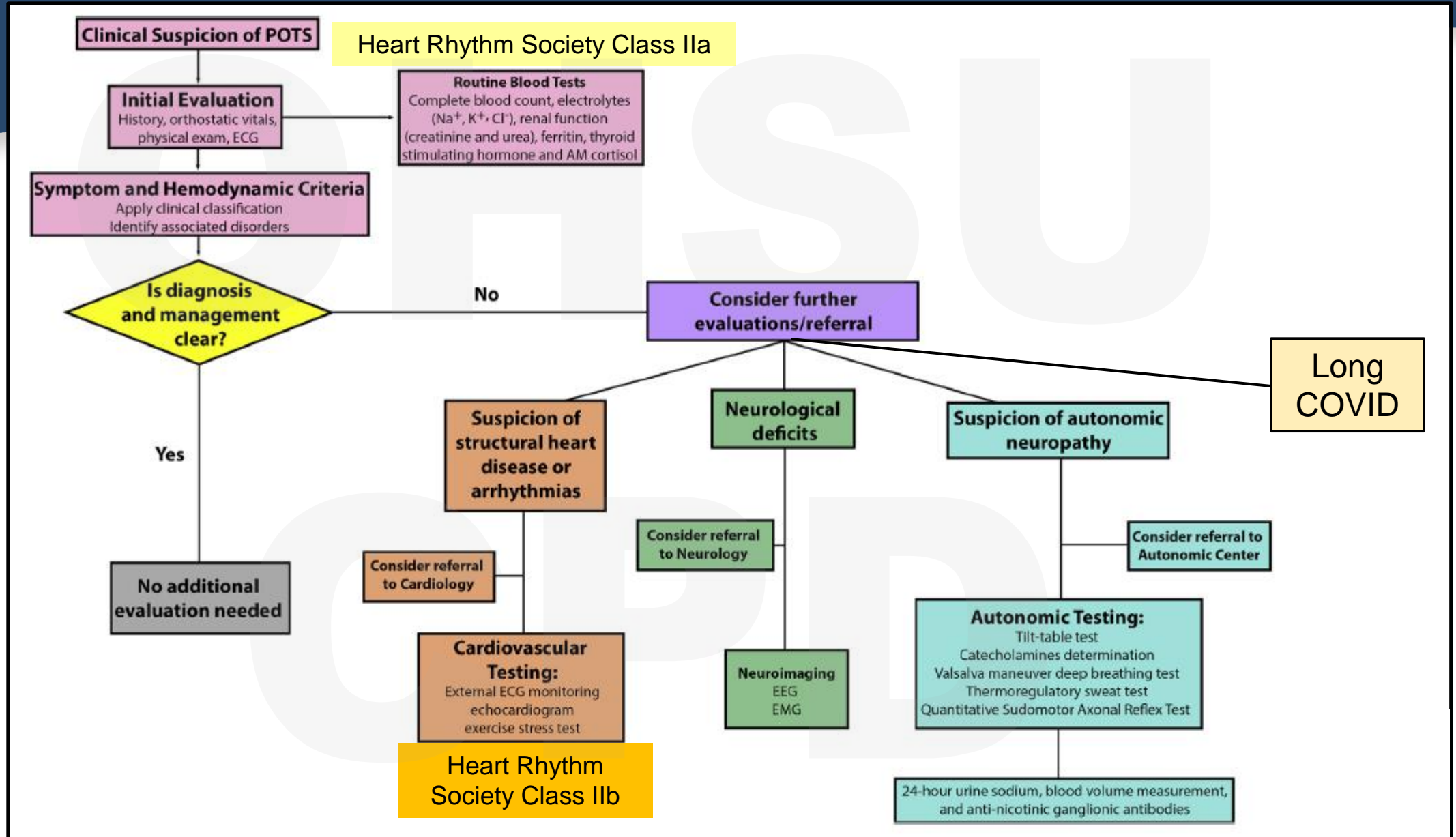
Differential Diagnoses

- Hyperthyroidism
- Infection
- Pheochromocytoma
 - Palpitations, lightheadedness, flushing while supine
 - Plasma norepinephrine higher than POTS
 - ↑ Metanephrines
- Inappropriate sinus tachycardia
 - $HR \geq 100$ bpm at rest
 - Mean 24-hour heart rate ≥ 90 bpm
 - Associated with palpitations
- Acute dehydration
- Exercise
- Physical deconditioning
- Panic attacks
- Pain
- Alcohol
- Caffeine
- Medication-induced or exacerbated

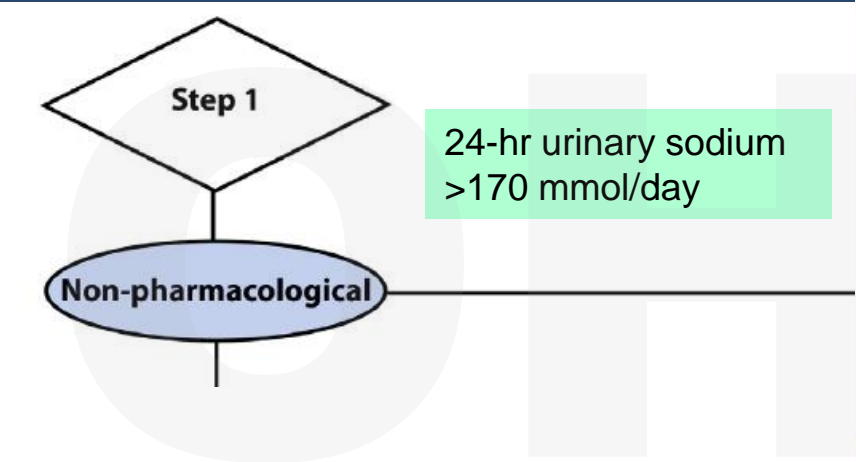
Diagnostic Algorithm


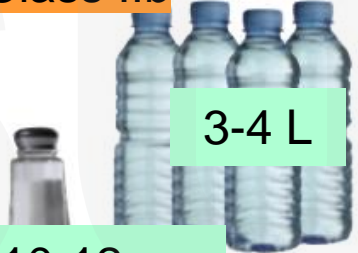

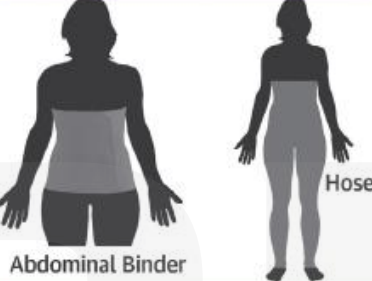
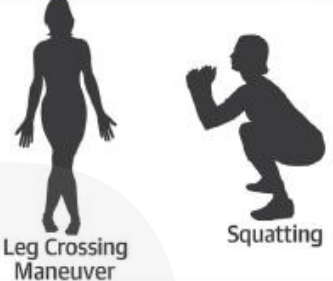






Diagnostic Algorithm – Referral?



Nonpharmacologic Treatment Options



Avoid Situations That Can Exacerbate Symptoms	Liberal Intake of Salt and Water	Sleep With Head of Bed Elevated
 <p>Large/Heavy Meals</p> <p>Heat Exposure</p> <p>Alcohol Intake</p>	<p>Class IIb</p>  <p>3-4 L</p> <p>10-12 gm</p>	<p>>10%</p>  <p>Head posts should be elevated 4-6 inches</p>
Use of Compression Garments	Physical Counter Maneuvers	Drinking Water Before Getting Up In The Morning
 <p>Abdominal Binder</p> <p>Hose</p>	 <p>Leg Crossing Maneuver</p> <p>Squatting</p>	<p>Drinking a 16 oz glass of water quickly before getting out of bed in the morning or prolonged standing to minimize orthostatic symptoms</p> 
Class IIa Strategies to Avoid Upright Exercise		
 <p>Seated Rower</p>	 <p>Swimming</p>	 <p>Recumbant Bicycle</p>

Raj SR et al. Can J Cardiol. 2020;36:357-372.
Bryarly M et al. JACC. 2019;73:1207-1228.
Sebastian SA et al. Curr Prob Cardiol. 2022;47:1-24

Case - Management

- Tachycardia
- Diagnosed with POTS

- PICC
- IVF infusion 3-4 times/weeks

- Propranolol changed to metoprolol succinate 50 mg BID
- Metop tartrate 12.5 mg QID prn
- Removed PICC #2
- Compression stockings
- Physical therapy

2019

2021

2023

2020

2022

Did not tolerate

- Fludrocortisone (4/2021) --> low HR and BP
- Midodrine (8/2021) --> low HR, felt strange
- Pyridostigmine --> hypotension, diarrhea, coughing
- Metoprolol tartrate --> not effective
- Nortryptiline --> for migraine but worsened dizziness
- Venlafaxine --> for migraine but worsened dizziness

- Standing HR 130-200s
- Standing > 5 min --> dizziness
- Uses wheelchair
- COVID-19 infection

- PICC #1 infected
- PICC #2 inserted

Nonpharmacologic Therapies

Therapy	Dosage	Pathologic mechanisms addressed	Potential drawbacks	Comments
Exercise	≥ 30 min at least 3 times a week	All	Worsened symptoms at the outset, prolonged fatigue	Gradually progress from non-upright to upright endurance and resistance exercises
Dietary fluid	2–3 L per day	All	Hyponatremia	
Dietary salt	10–12 g per day	All	Difficult to augment sufficiently through diet alone	Supplement with sodium chloride tablets, if necessary
Compression stockings	Waist high 30 40 mmHg	All	Difficult to put on	
Sleep with head elevation	4-6 inches	All		
Salt tablets	1 g tablet 3 times daily	Hypovolemia	Poor taste, nausea, dyspepsia	Recommended for use after meals
Acute intravenous normal saline	1 L over 1–3 hours	Hypovolemia	Inconvenient, medical setting required	Heart Rhythm Society Consensus Statement class IIa recommendation (benefit probably exceeds risk)
Chronic intravenous normal saline	1 L every 2 days	Hypovolemia	Access complications and infection with central line	Heart Rhythm Society Consensus Statement class III recommendation (recommends against)

Compression Garments

N= 26 female

Age: 16-54 years old

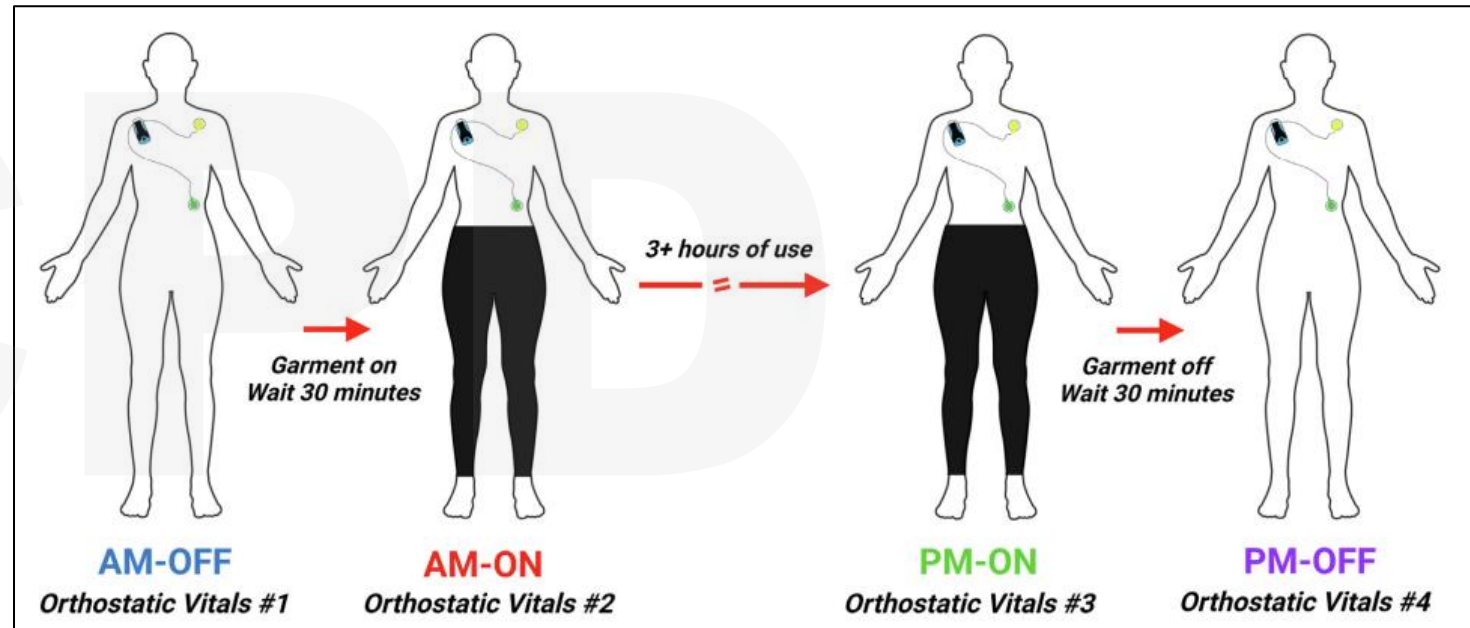
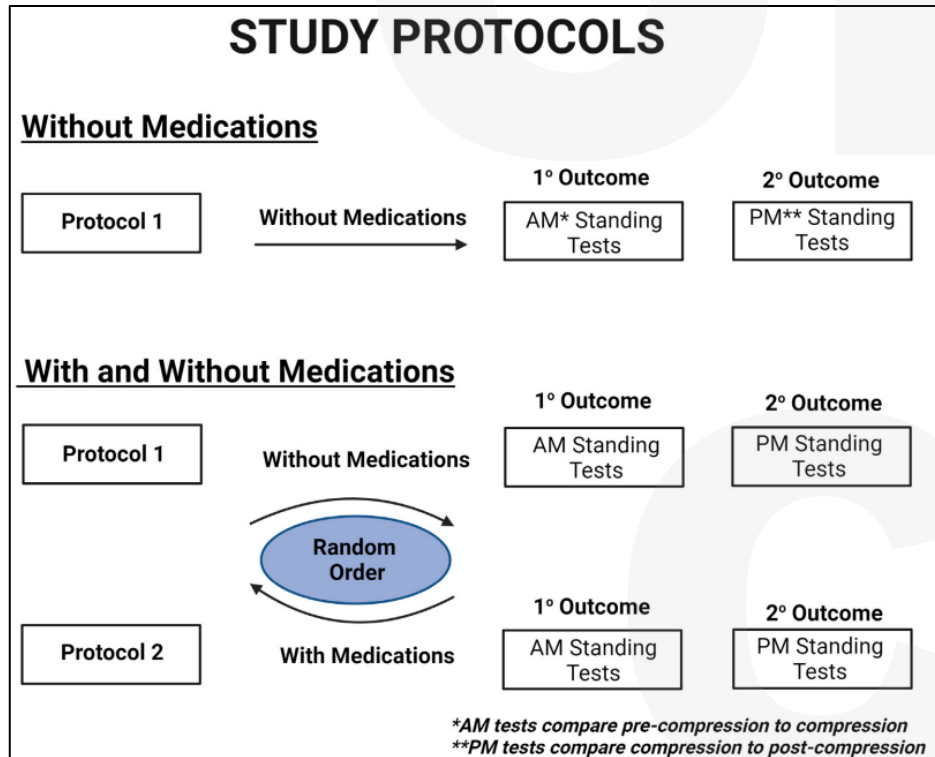
Race: White n=21; South Asian n=1; Indigenous n=1, Multiple n=3

Meds:

- Beta-blockers (71%, n=17)
- Midodrine (31%, n=8)
- Pyridostigmine (12%, n=3)

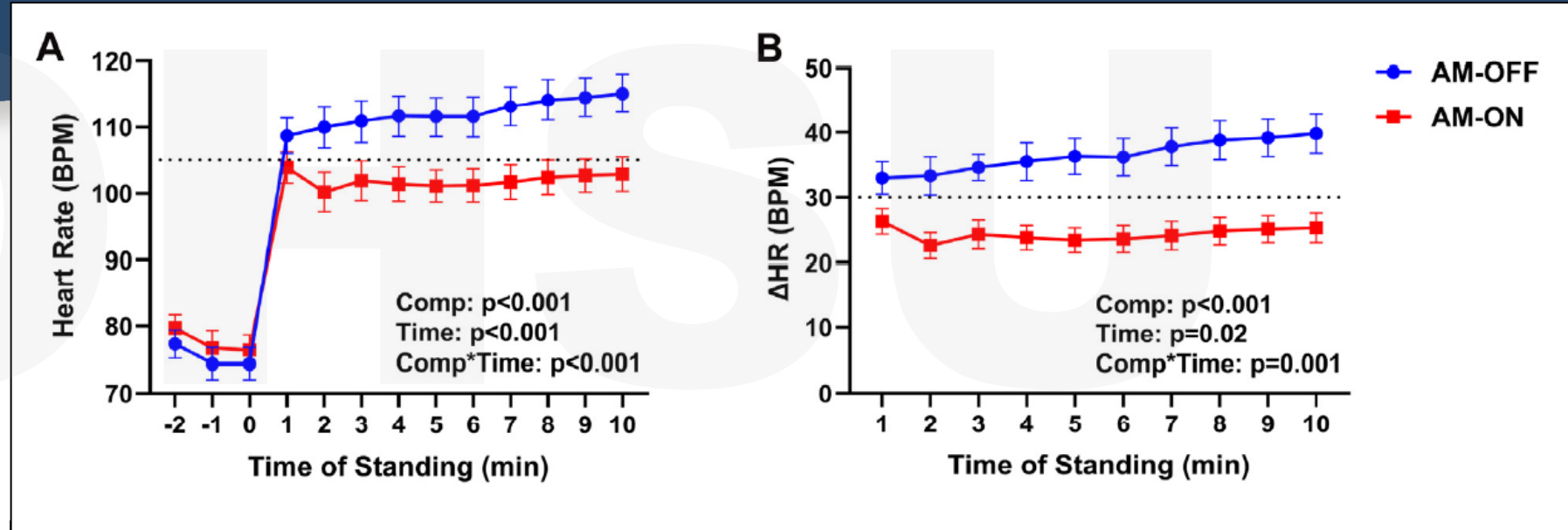
Commercial medical compression garment (65%, n=17)

Athletic style (17%, n=4)

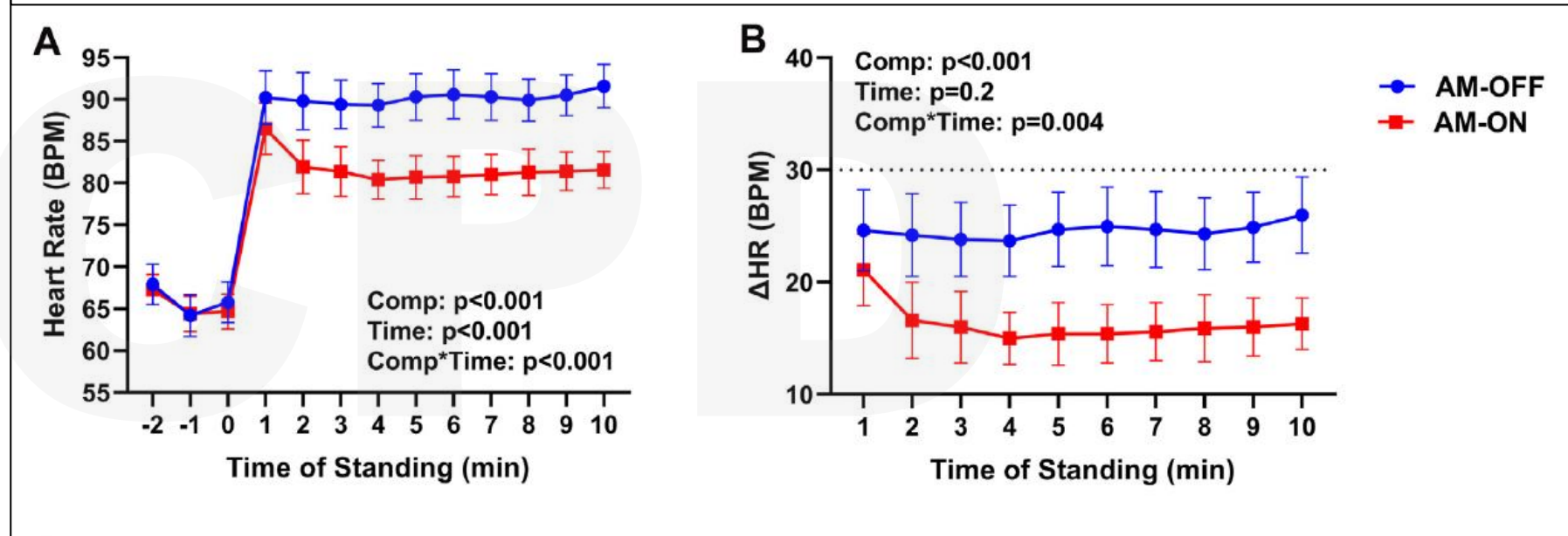


Compression Garments

NO MEDICINE



WITH MEDICINE



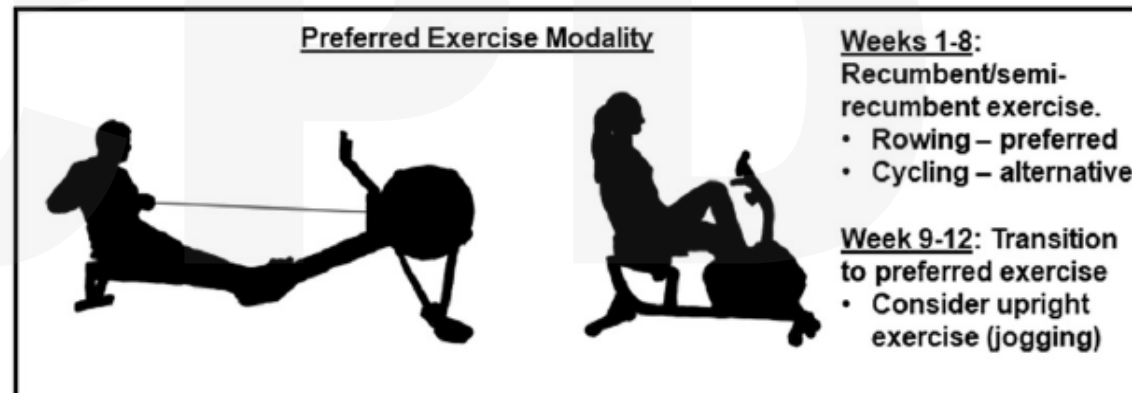
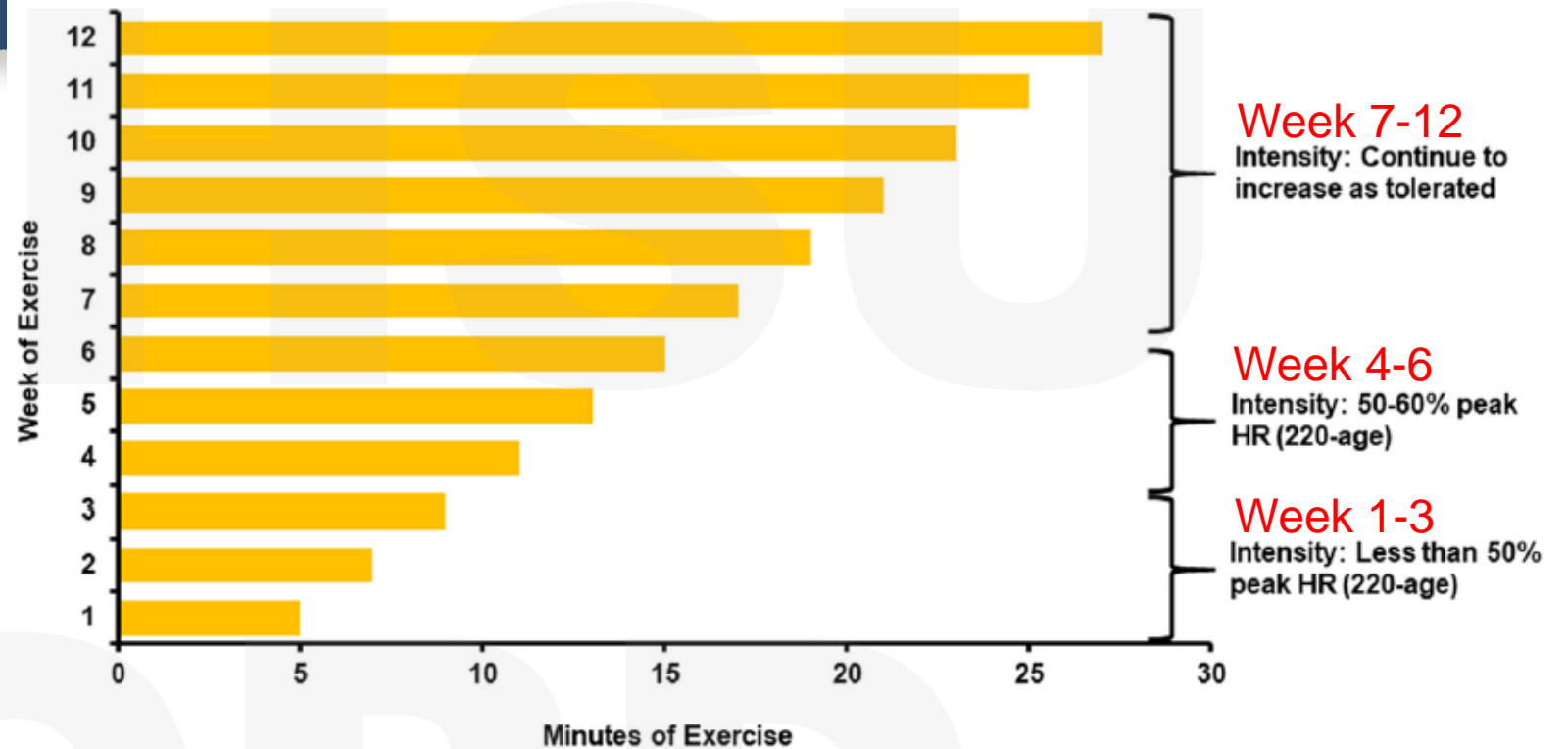
Exercise Prescription

Endurance:

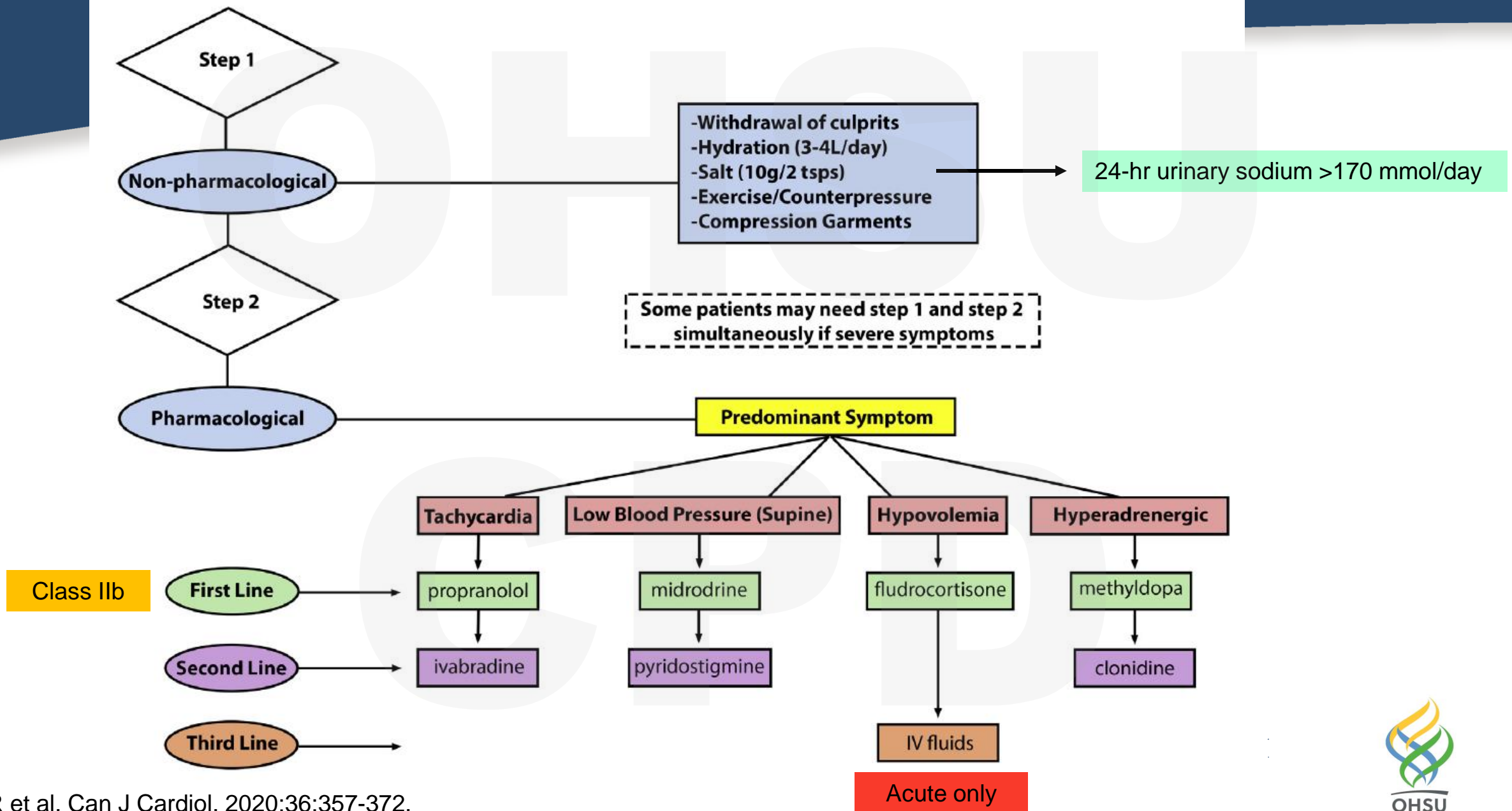
- 5 min warm-up, 5 min cool-down
- Recumbent
 - 3-4 times/week for 25-30 min for 2 months
- Upright bike or walking on treadmill
 - 5-6 times/week for 45-60 min

Resistance

- Weight-lifting once/week, 15-20 min/session
- Increase 2 times/week, 30-40 min/session



Treatment Algorithm - Pharmacotherapy



Pharmacologic Therapies

**NO medication has been FDA-approved specifically for POTS.
The following medications have been studied in clinical trials**

Therapy	Dosage	Pathologic mechanism addressed	Potential drawbacks	Comments
Blood volume expanders				
Fludro-cortisone IIb	0.05–0.1 mg twice daily	Hypovolemia	Hypokalemia, hypertension, fatigue, headache, fluid retention, edema	
Desmopressin	0.1–0.2 mg 3 times daily	Hypovolemia	Hyponatremia, headache, edema	Only for occasional use; must monitor blood sodium, 1x/week
Erythro-poietin	2,000–3,000 IU subcutaneously 1–3 times per week	Hypovolemia	High cost, requires injection, risk of vascular complications	Reserved for patients with symptoms refractory to more common treatments
Heart rate-lowering agents				
Propranolol IIb	10–20 mg 3–4 times daily	All	Hypotension, fatigue, drowsiness, wheezing	Not well tolerated at higher dosages
Ivabradine	5–7.5 mg twice daily	All	Palpitations, headache, dizziness, constipation	

Pharmacologic Therapies

Therapy	Dosage	Pathologic mechanism addressed	Potential drawbacks	Comments
Clonidine	0.05–0.2 mg twice daily	Hyperadrenergic	Mental clouding, fatigue, drowsiness, constipation	Can be associated with rebound hypertension and tachycardia
Methyldopa	125 mg once or twice daily	Hyperadrenergic	Hypotension, fatigue, headache, drowsiness, constipation	Rare lupus-like syndrome reported
Other drugs				15-30 min before getting out of bed in AM
Midodrine IIb	2.5-15 mg every 4 hours, 3 times daily only	Neuropathic	Hypertension, goose bumps, urinary retention	Not recommended for use within 4-5 hours of sleep
Pyridostigmine IIb	30–60 mg 3 times daily	All	Abdominal cramping, diarrhea, increased sweating	May increase gastrointestinal motility
Droxidopa	100–600 mg 3 times daily	All	Nausea, palpitations, urinary symptoms	May worsen tachycardia
Modafinil	100–200 mg twice daily	"Brain fog"	Headache, dizziness, anxiety, insomnia	May improve cognitive symptoms
H₁ and H₂ histamine receptor blockers			Avoid concomitant beta-blocker	Drowsiness, dizziness

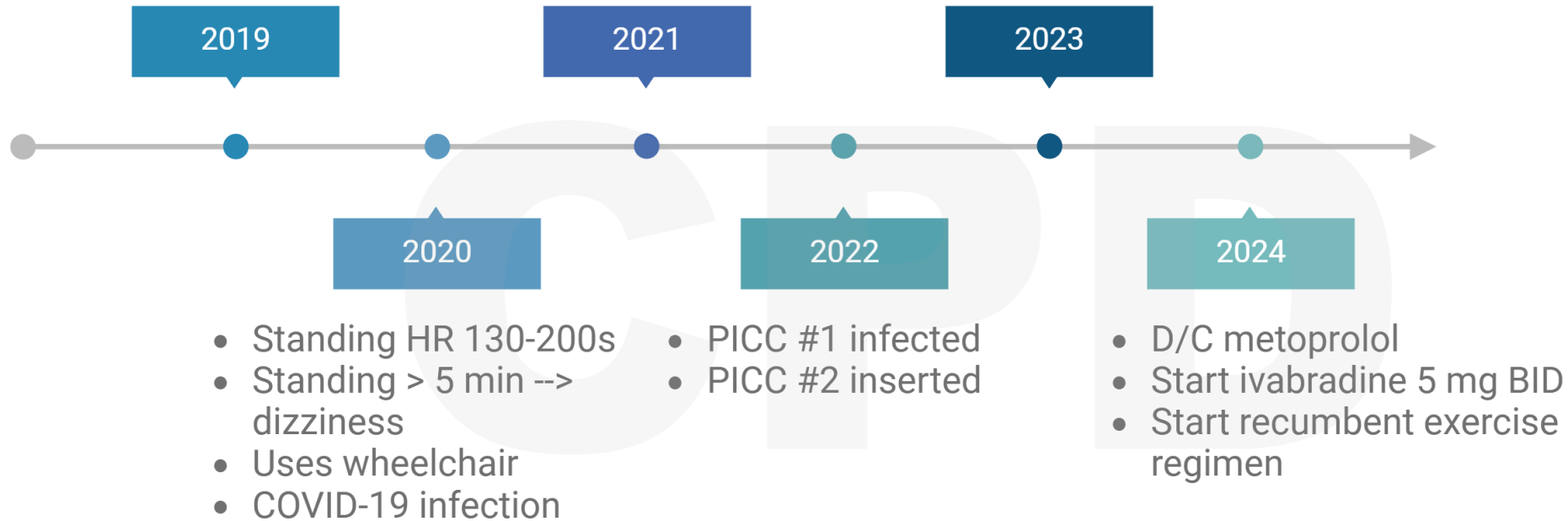


Case - Management

- Tachycardia
- Diagnosed with POTS

- PICC
- IVF infusion 3-4 times/weeks

- Propranolol changed to metoprolol succinate 50 mg BID
- Metop tartrate 12.5 mg QID prn
- Removed PICC #2
- Compression stockings
- Physical therapy



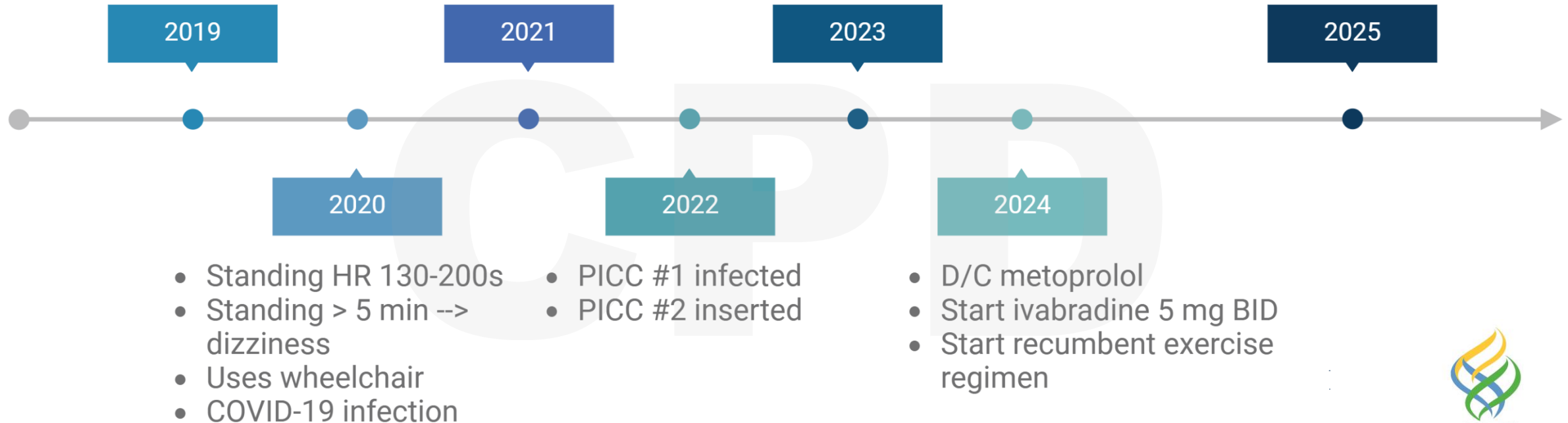
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- Advance recumbent exercise regimen
- Liberal fluid intake
- Waist-high compression garment
- Ivabradine 5 mg BID



Key Points

- Heterogeneous presentation
- Features overlap with other conditions
- 80% occur in premenopausal women
- Etiology and pathophysiology of POTS are not fully understood
- Clinical diagnosis: history, exam, basic diagnostic tests
- Graded treatment:
 - Avoid known triggers
 - Optimize fluid and salt intake
 - Compression garments
 - Regimented exercise program
 - Pharmacotherapy for refractory symptoms
 - Personalize medication according to POTS subtype