

Orthostatic Intolerance Following Infections: Focus on POTS and IOH

Satish R Raj MD MSCI FACC FHRS

**Professor of Cardiac Sciences
Libin Cardiovascular Institute
University of Calgary**

**June 2023 – National Academy of Science &
Engineering Focus on Infection Associated Chronic
Illness**

Satish R Raj - Faculty Disclosure

Consulting/Honoraria

Theravance Biopharma – nOH Consulting
Amneal Pharma – nOH Consulting
Servier Affaires Medicales – POTS Consulting
Regeneron – POTS Consulting
Argenx BV – POTS Consulting
Antag Pharma – POTS Consulting

Associate Editor

Autonomic Neurosciences: Basic & Clinical
(Elsevier)

Research Grants

Canadian Institutes of Health Research
Dysautonomia International
Stand Up To POTS

Long COVID – Focus on Tachycardia

REVIEW

THE AMERICAN
JOURNAL of
MEDICINE®

Post-COVID-19 Tachycardia Syndrome: A Distinct Phenotype of Post-Acute COVID-19 Syndrome



Marcus Ståhlberg, MD, PhD,^a Ulrika Reistam, MD,^a Artur Fedorowski, MD, PhD,^{b,c} Humberto Villacorta, MD,^d Yu Horiuchi, MD,^e Jeroen Bax, MD,^f Bertram Pitt, MD,^g Simon Matskeplishvili, MD,^h Thomas F. Lüscher, MD, PhD,^{i,j} Immo Weichert, MD,^k Khalid Bin Thani, MD,^l Alan Maisel, MD^m

^aCardiology, Heart, Vascular and Neuro Theme, Karolinska University Hospital and Department of Medicine, Karolinska Institutet, Stockholm, Sweden; ^bDepartment of Clinical Sciences, Faculty of Medicine, Lund University, Lund, Sweden; ^cDepartment of Cardiology, Skåne University Hospital, Malmö, Sweden; ^dDivision of Cardiology, Fluminense Federal University, Niterói, Rio de Janeiro State, Brazil; ^eDivision of Cardiology, Mitsui Memorial Hospital, Tokyo, Japan; ^fDepartment of Cardiology, Leiden University Medical Center, The Netherlands; ^gUniversity of Michigan, Ann Arbor; ^hLomonosov Moscow State University Medical Center, Moscow, Russia; ⁱDivision, Royal Brompton & Harefield Hospitals and National Heart and Lung Institute, Imperial College, London, UK; ^jCenter for Molecular Cardiology, University of Zurich, Switzerland; ^kAcute Medicine Department, Ipswich Hospital, East Suffolk and North East NHS Foundation Trust, Ipswich, UK; ^lDepartment of Cardiology, Salmaniya Medical Complex, Manama, Bahrain; ^mDivision of Cardiovascular Medicine, University of California San Diego, La Jolla.

JACC: CASE REPORTS
© 2021 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY-NC-ND LICENSE (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

VOL. 3, NO. 4, 2021

MINI-FOCUS ISSUE: COVID-19

INTERMEDIATE

CASE REPORT: EDUCATION CORNER

Long-Haul Post-COVID-19 Symptoms Presenting as a Variant of Postural Orthostatic Tachycardia Syndrome

The Swedish Experience

Madeleine Johansson, MD, PhD,^{a,b,*} Marcus Ståhlberg, MD, PhD,^{c,d,*} Michael Runold, MD, PhD,^e Malin Nygren-Bonnier, PhD, PT,^{f,g} Jan Nilsson, MD, PhD,^a Brian Olshansky, MD,^h Judith Bruchfeld, MD, PhD,^{i,j,†} Artur Fedorowski, MD, PhD^{a,b,†}

Typical Long COVID Symptoms Similar to POTS Symptoms



- Difficulty breathing or shortness of breath



- Tiredness or fatigue



- Symptoms that get worse after physical or mental activities (also known as post-exertional malaise)



- Difficulty thinking or concentrating (sometimes referred to as "brain fog")

- Cough

- Chest or stomach pain

- Headache



- Fast-beating or pounding heart (also known as heart palpitations)

- Joint or muscle pain

- Pins and needles feeling



- Diarrhea



- Sleep problems

- Fever



- Dizziness on standing (lightheadedness)

- Rash

- Mood changes

- Change in smell or taste

- Changes in menstrual period cycles

Society Position Statement

Canadian Cardiovascular Society Position Statement on Postural Orthostatic Tachycardia Syndrome (POTS) and Related Disorders of Chronic Orthostatic Intolerance

Satish R. Raj, MD, MSCI, FRCPC (Chair),^a Juan C. Guzman, MD, MSc, FRCPC (Co-chair),^b
Paula Harvey, BMBS, PhD,^c Lawrence Richer, MD, MSc, FRCPC,^d
Ronald Schondorf, MD, PhD, FRCPC,^e Colette Seifer, MD, FRCPC,^f
Nicolas Thibodeau-Jarry, MD, MMSc(MedEd),^g and Robert S. Sheldon, MD, PhD, FRCPC^a

^a Department of Cardiac Sciences, Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta, Canada

^b Department of Medicine, McMaster University, Hamilton, Ontario, Canada

^c Department of Medicine, University of Toronto, Toronto, Ontario, Canada

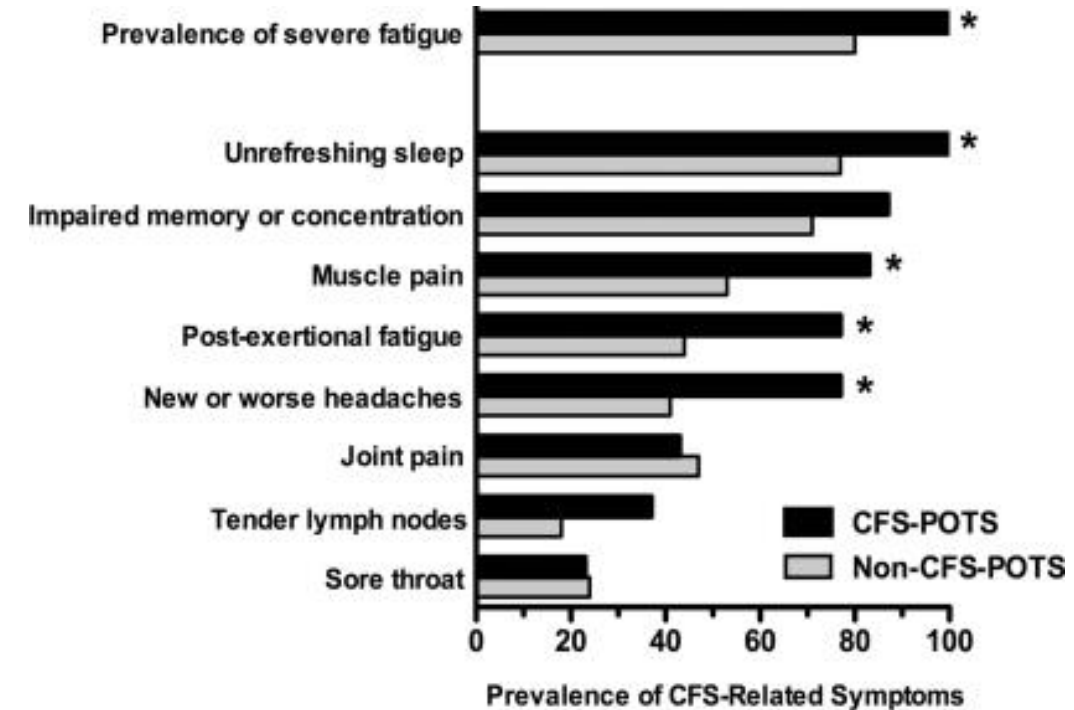
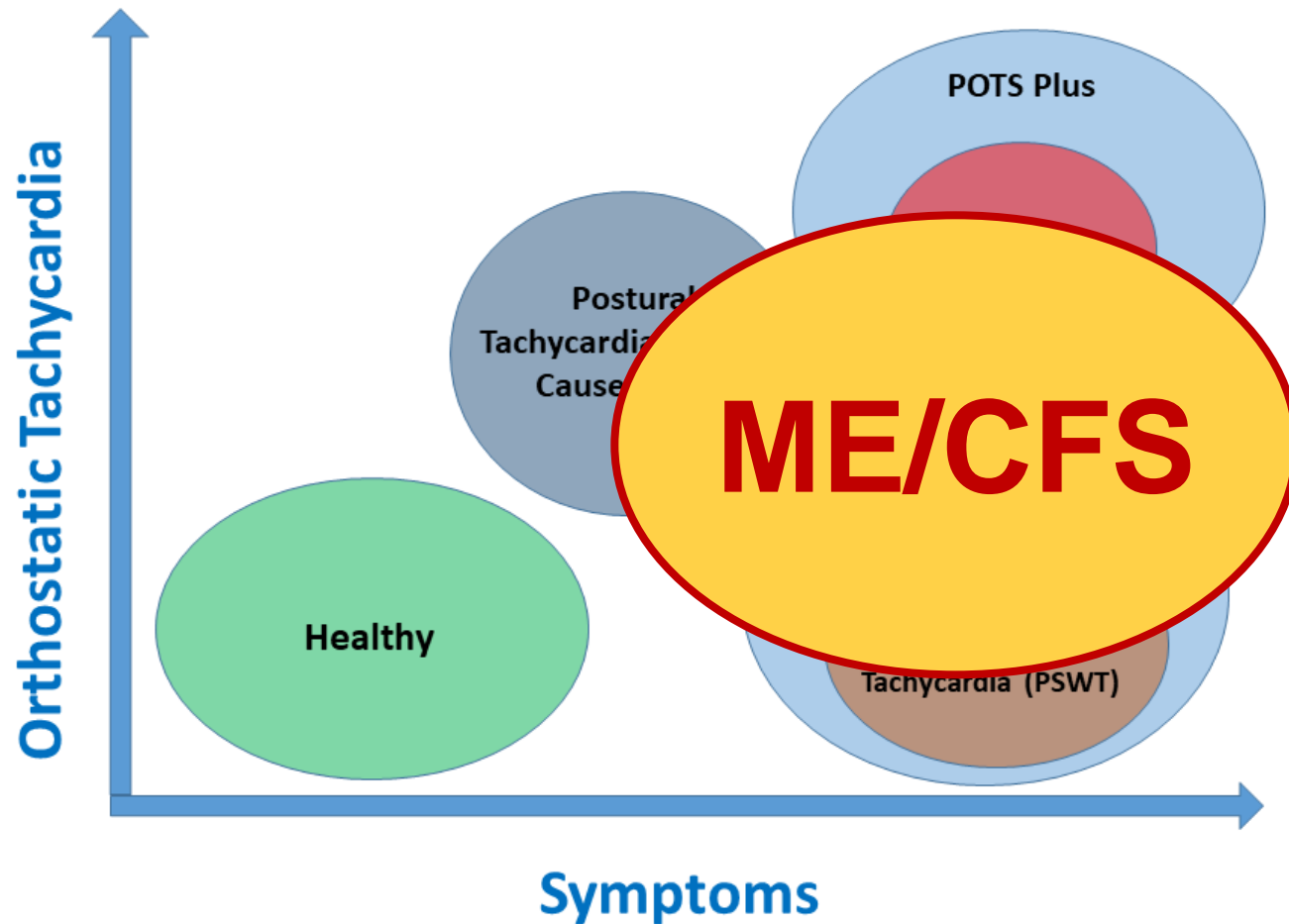
^d Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

^e Department of Neurology, Jewish General Hospital, McGill University, Montreal, Quebec, Canada

^f University of Manitoba, Winnipeg, Manitoba, Canada

^g Department of Medicine (Cardiology), Institut de Cardiologie de Montréal, Université de Montréal, Montréal, Quebec, Canada

CCS 2019 POTS & Orthostatic Intolerance Schema



Postural Tachycardia Syndrome

- Common Criteria

- **Orthostatic tachycardia > 30 bpm**
 - >40 bpm in children
 - **No orthostatic hypotension**
 - Δ BP > 20/10 mmHg
 - **Symptoms with upright posture**
 - sympathetic activation;
 - cerebral hypoperfusion
 - better with recumbence
 - **Chronic symptoms > 3-6 months**
-
- **No other obvious cause for orthostatic tachycardia**

Inappropriate Sinus Tachycardia - Definition

- **Heart Rate Criteria:**
 - Sinus rate > 100 bpm at rest, or
 - A mean 24-hour heart rate >90 bpm
- **Exclude primary causes of sinus tachycardia**
- **Associated with distressing symptoms of palpitations (syndrome)**

Spectrum of Orthostatic Hypotension

Classic Orthostatic Hypotension (cOH)

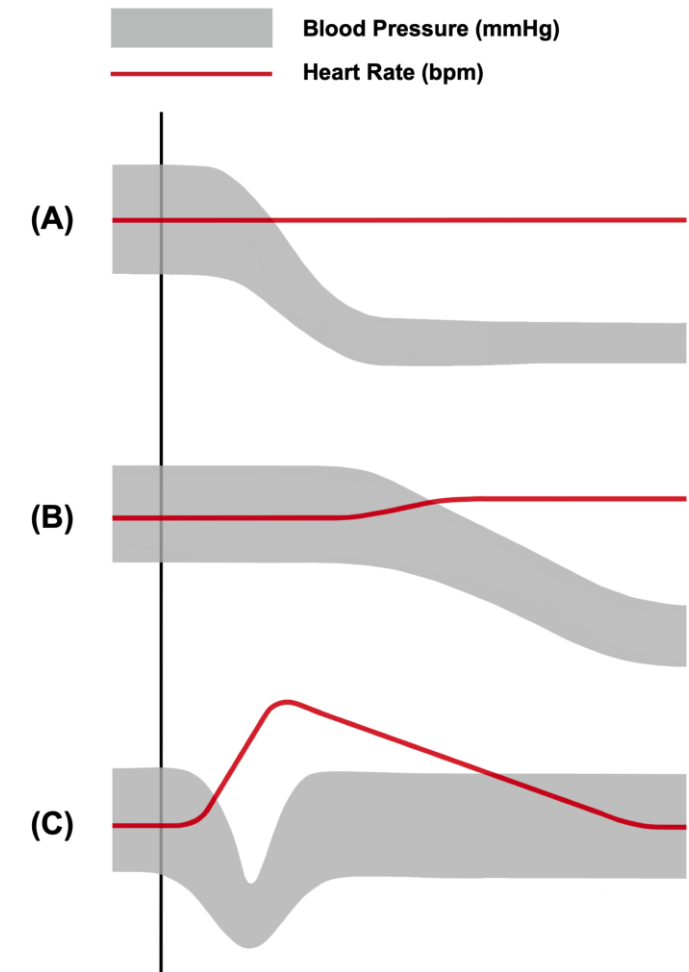
- Sustained drop in SBP ≥ 20 mmHg and/or DBP ≥ 10 mmHg
- Occurs within 30s – 3mins of active stand or HUT

Delayed Orthostatic Hypotension (dOH)

- Drop in SBP ≥ 20 mmHg and/or DBP ≥ 10 mmHg
- Occurs after 3mins of active stand or HUT

Initial Orthostatic Hypotension (IOH)

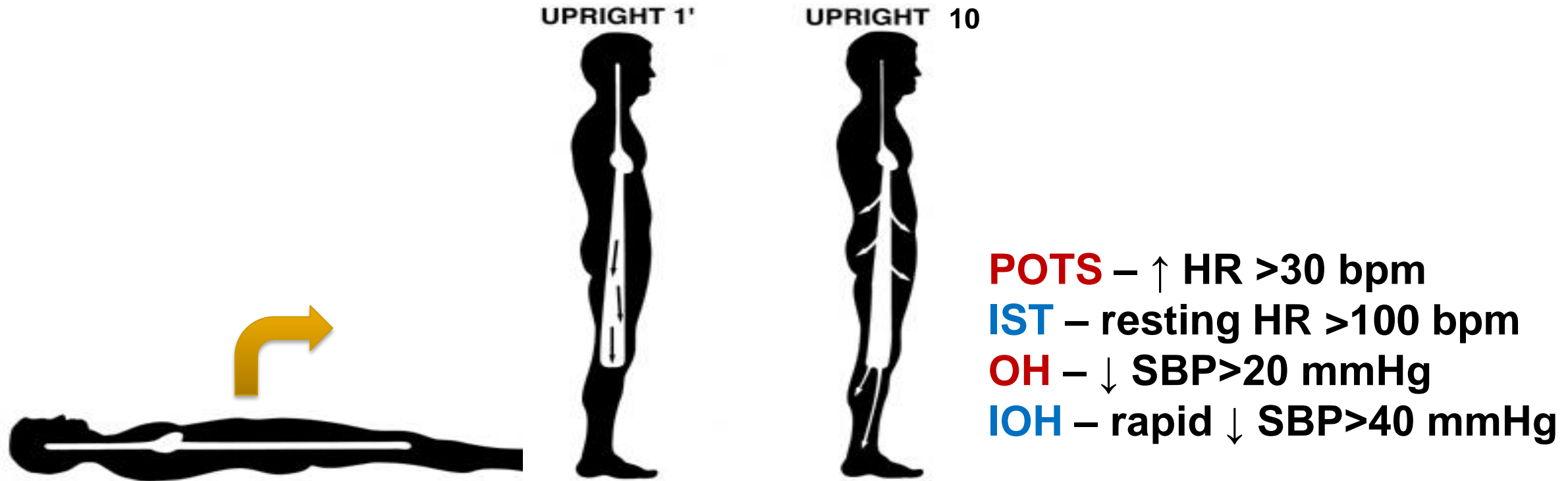
- Drop in SBP ≥ 40 mmHg and/or DBP ≥ 20 mmHg
- Occurs within 15s of active standing



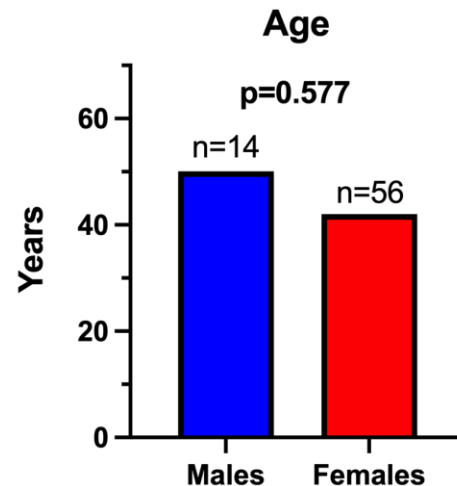
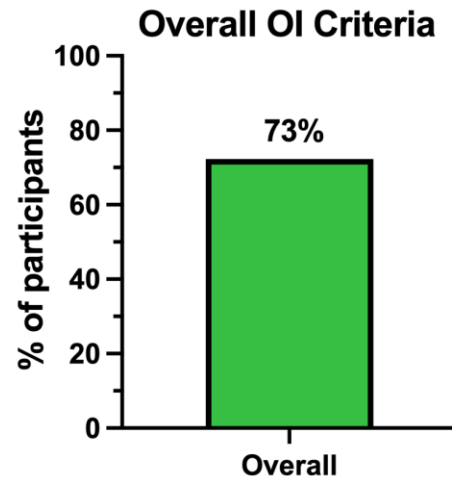
Autonomic Testing in Long COVID (PASC) Syndrome

- Ongoing symptoms >3 months post COVID-19 infn
 - Ages 18-80 years
- Online questionnaire
- Brief Autonomic Testing Battery
- Ongoing – 78 patients (63 F) enrolled to date
- **FUNDED by CIHR**

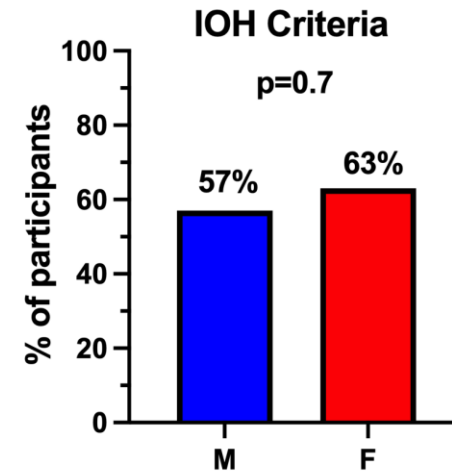
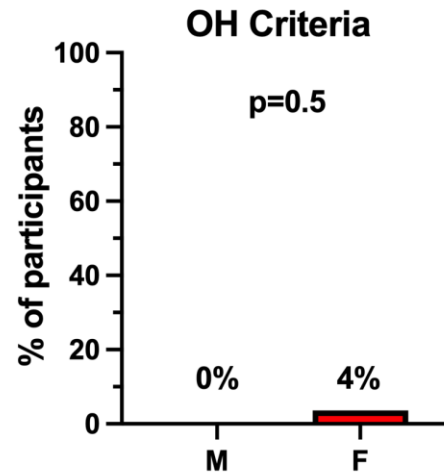
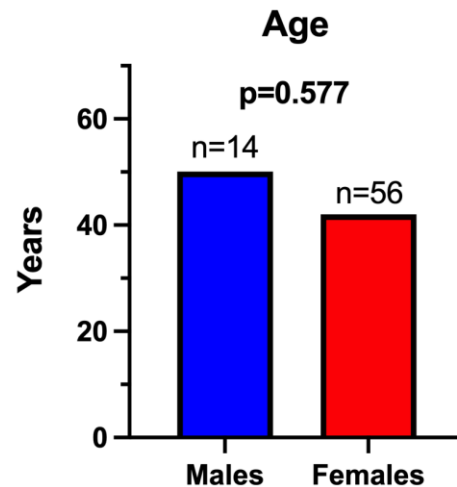
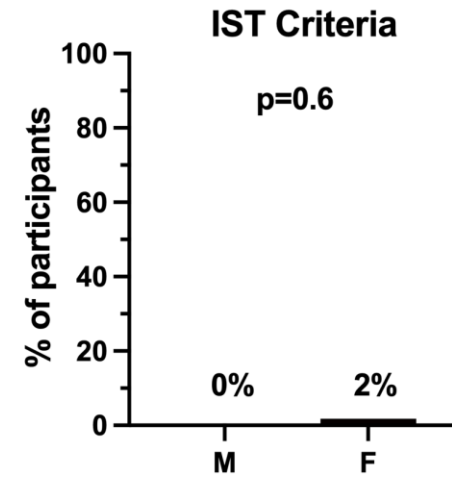
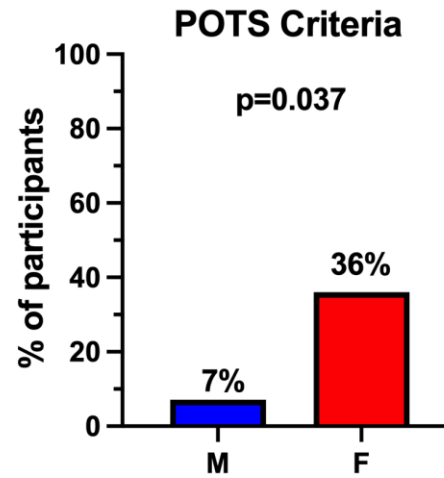
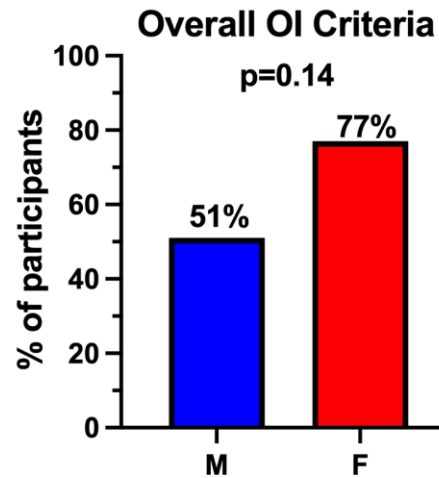
Active Stand Test with Continuous Beat-to-Beat Monitoring



Hemodynamic Autonomic Disorders



Hemodynamic Autonomic Disorders



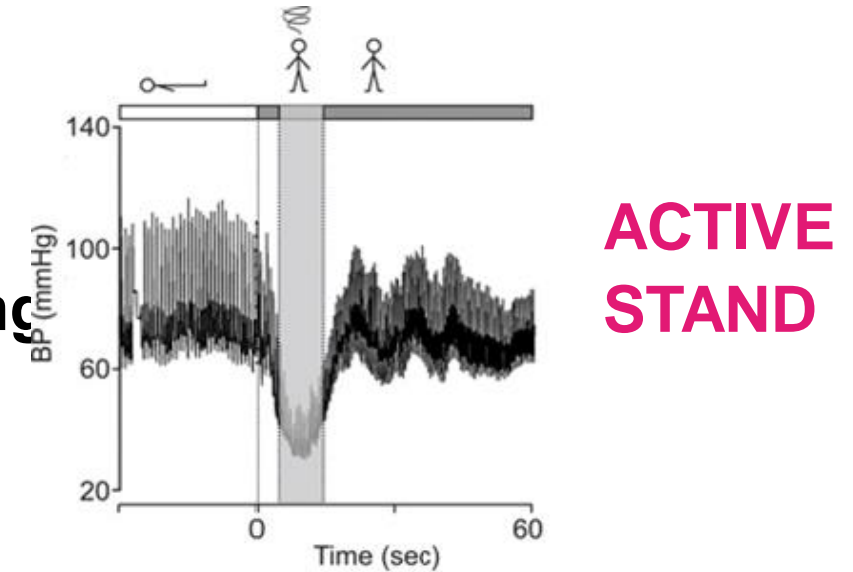
Take Home Messages

- **Autonomic Hemodynamic Disorders are common in PASC/Long COVID**
 - **POTS**
 - **Other Stuff Too**
- **You only find what you look for**
- **Sex Differences Exist in**
 - **Frequency of Specific Disorders**
 - **Symptom Presentation**

Initial Orthostatic Hypotension (IOH)

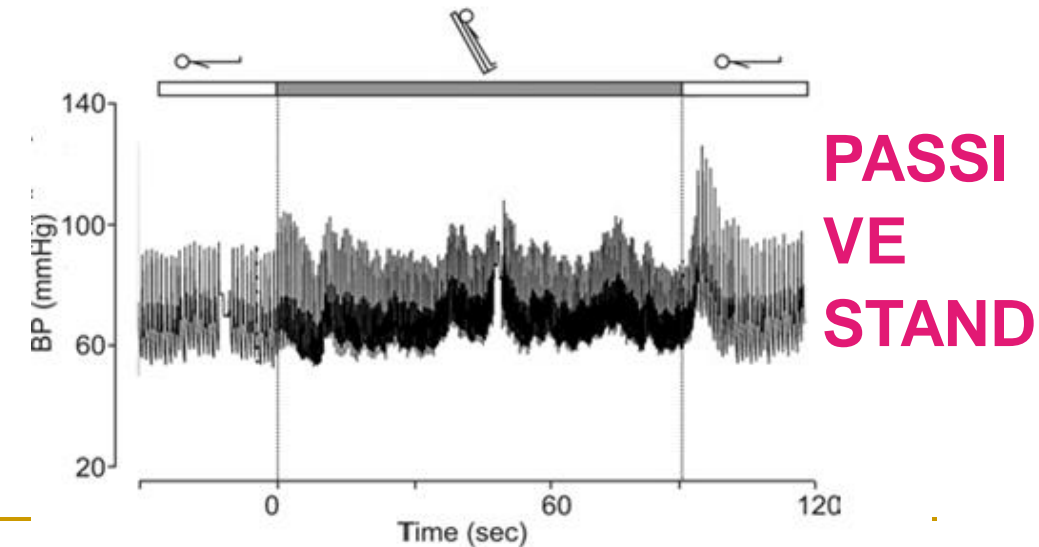
Definition (Wieling)

- Large transient ↓ BP (within 15s) of standing
- Associated with presyncope symptoms
- Occurs during **ACTIVE** stand



Mechanism

- Rapid vasodilation in contracting leg muscles due to brief muscular effort of a stand



Diagnosis of IOH

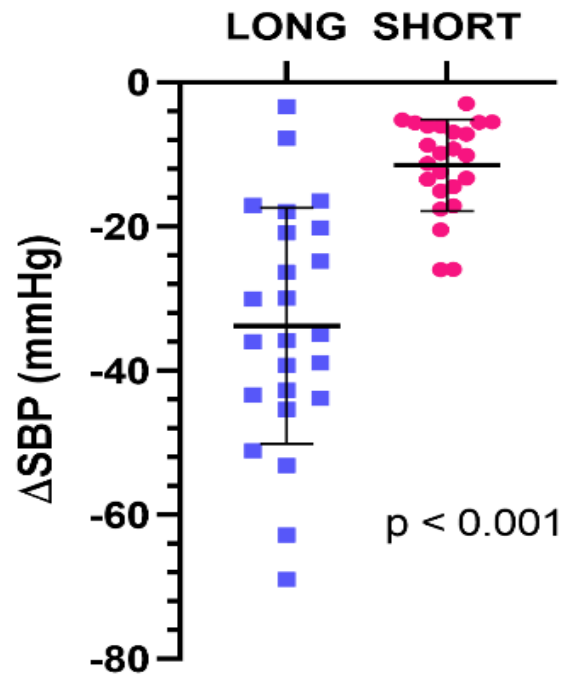
- **Medical History**

- Frequent lightheadedness immediately on standing
- Symptoms get better in <1 min; then can keep walking
- Occasionally – must sit down;
 - symptoms do not recur when standing again after 1-2 min
- Occasional syncope – often at night; in bathroom

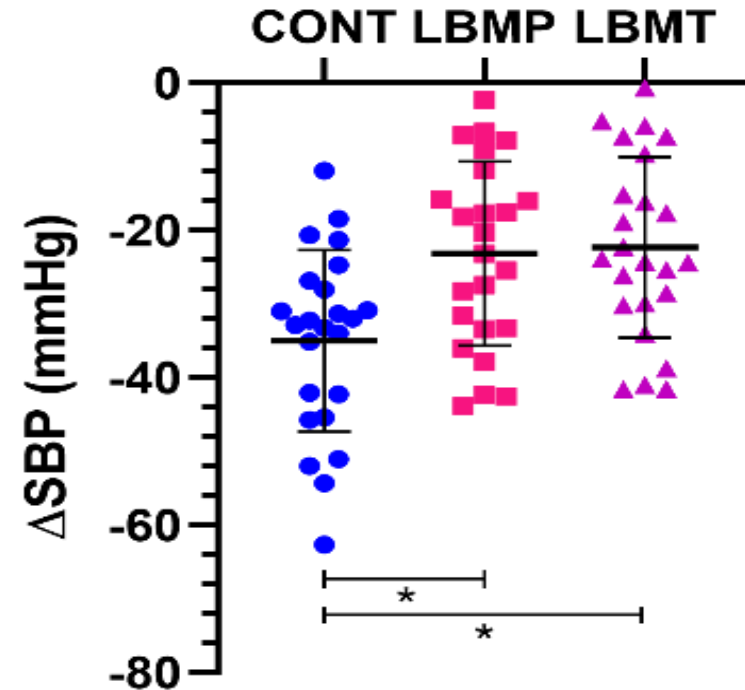
- **Active Stand Test**

- Need beat-to-beat BP monitor
 - Rapid drop and recovery of SBP
-

IOH: Refractory Period & Muscle Pre-Activation (LBMP)



IOH
blunted
with SHORT
sit



IOH Summary

- The reflex underlying IOH has a refractory period <2 minutes
- Both LMBP & LBMT blunt the drop in SBP & improve symptoms of IOH
- IOH affects many aspects of patient life, and should be a more widely recognized disorder
- <https://youtu.be/9M4NqQkcRaM>



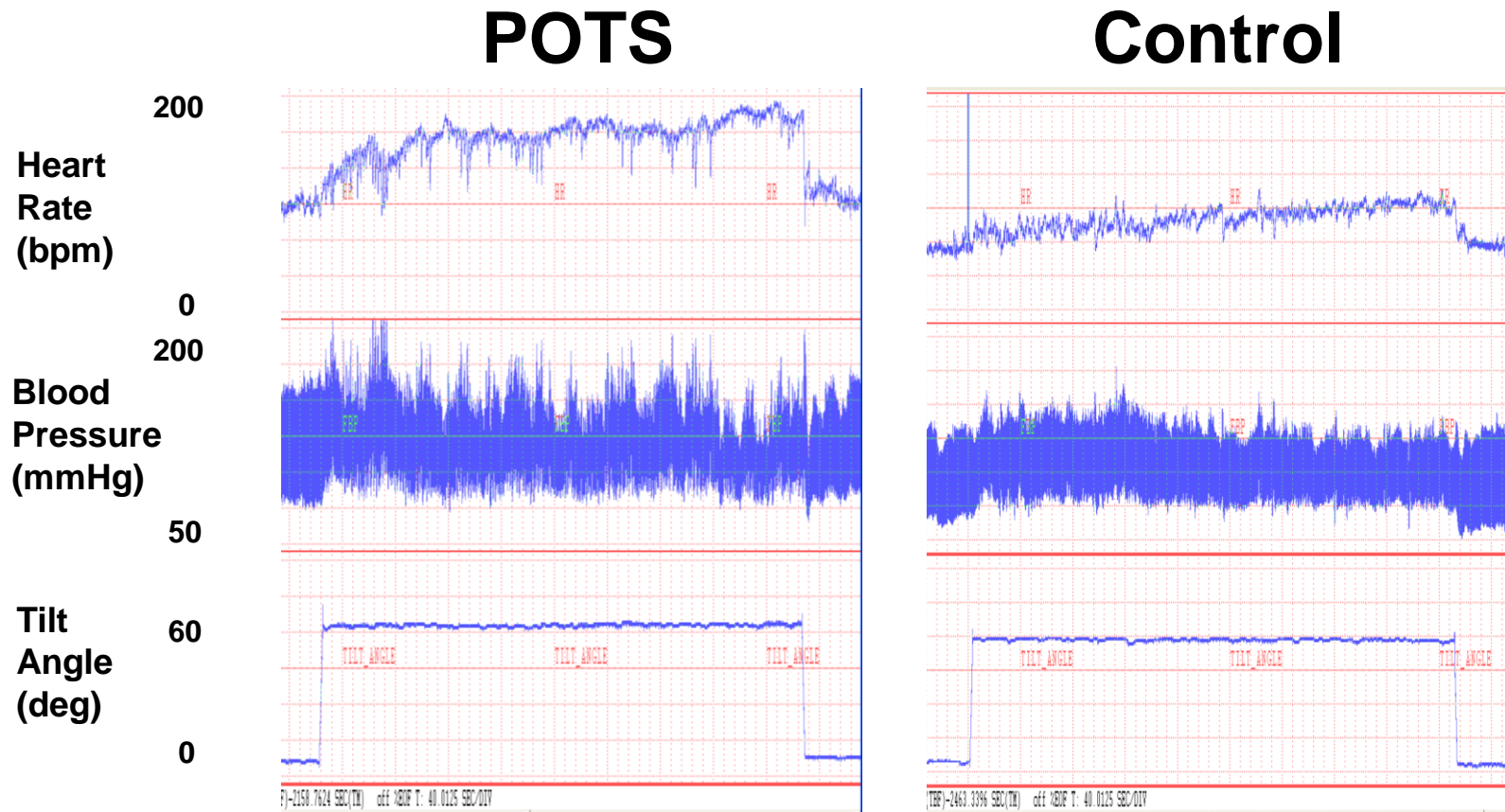
Postural Tachycardia Syndrome - Common Criteria

- **Orthostatic tachycardia ≥ 30 bpm**
 - ≥ 40 bpm required if < 18 years
- **No consistent orthostatic hypotension**
 - $\Delta BP \geq 20/10$ mmHg
- **Orthostatic Symptoms**
 - Worse upright; better recumbent
- **Chronic symptoms ≥ 3 months**

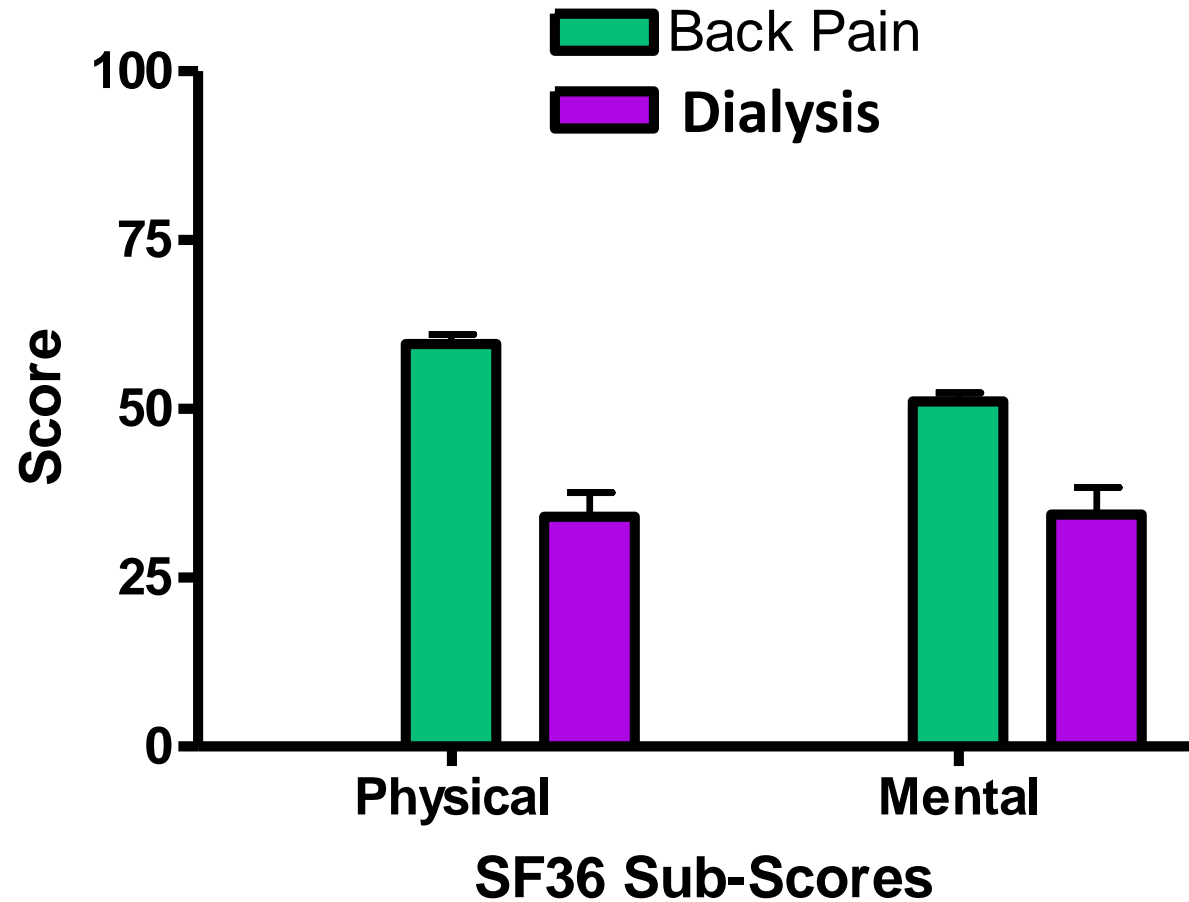


Phillip Low MD
Mayo Clinic

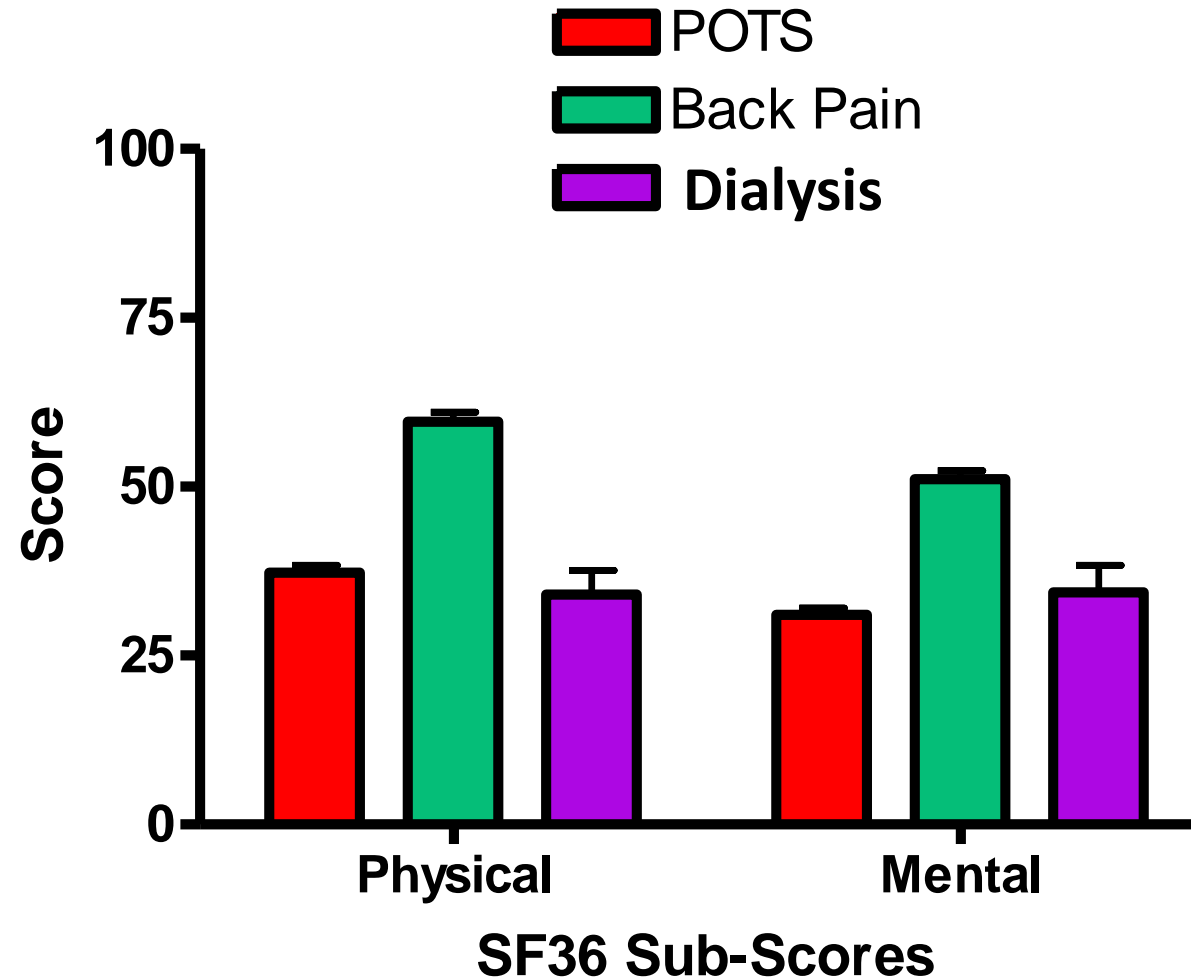
Tilt Testing



Health Related Quality of Life (SF-36) – Chronic Illnesses



Health Related Quality of Life (SF-36) – Chronic Illnesses



POTS – Treatment

POTS: Treatment Approaches

■ Non-Pharmacological

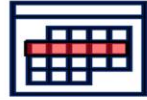
- ❑ Dietary Salt
- ❑ Diet
- ❑ Compression Garments
- ❑ Exercise – may not apply to patients without tachycardia

■ Pharmacological

- ❑ Propranolol
- ❑ Ivabradine
- ❑ Pyridostigmine
- ❑ DDAVP

Dietary Salt in POTS: Summary

One Week



Sodium Intake

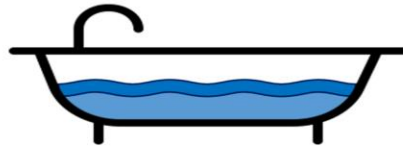


↓ Na⁺

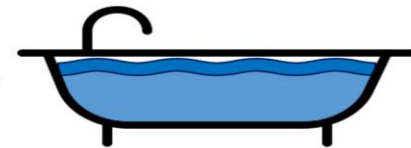


↑ Na⁺

Blood Volume



↓ Volume

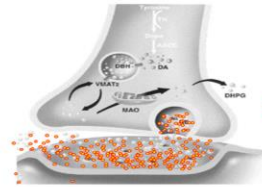


↑ Volume

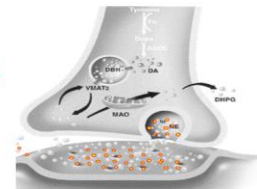
+

+

Standing Norepinephrine

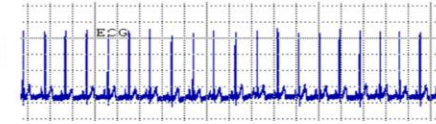


↑ NE

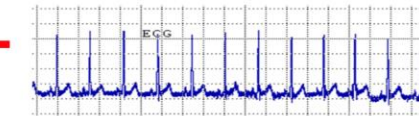


↓ NE

Standing Heart Rate



↑ HR



↓ HR

Dietary Salt in POTS: Practical Tips

■ Target

- Water - 3L/day (water bottle)
- Salt - 8-10g/day

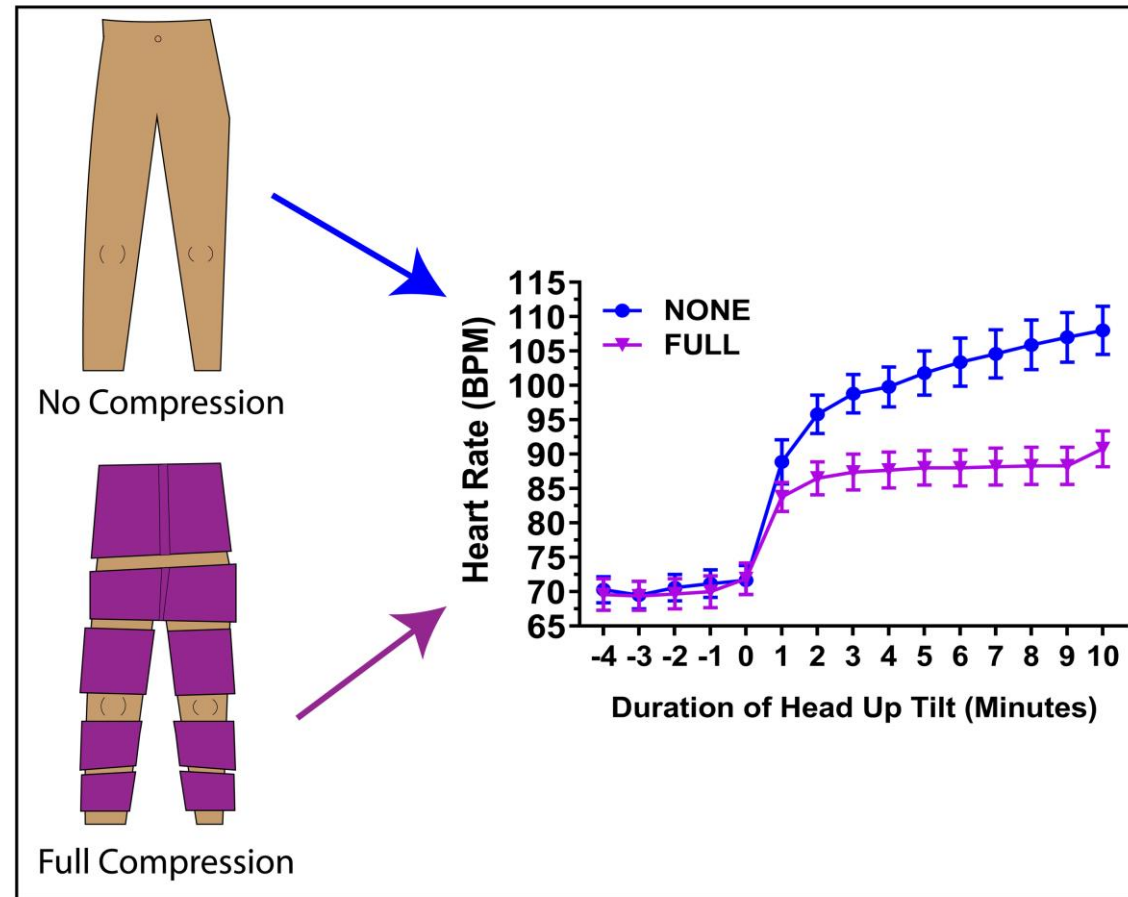
■ Teaspoon Approach

- 2 teaspoons of salt in zipped snack bag in AM
- Get this ingested through the day
 - Most add it to foods
 - “Salt Water” Shots

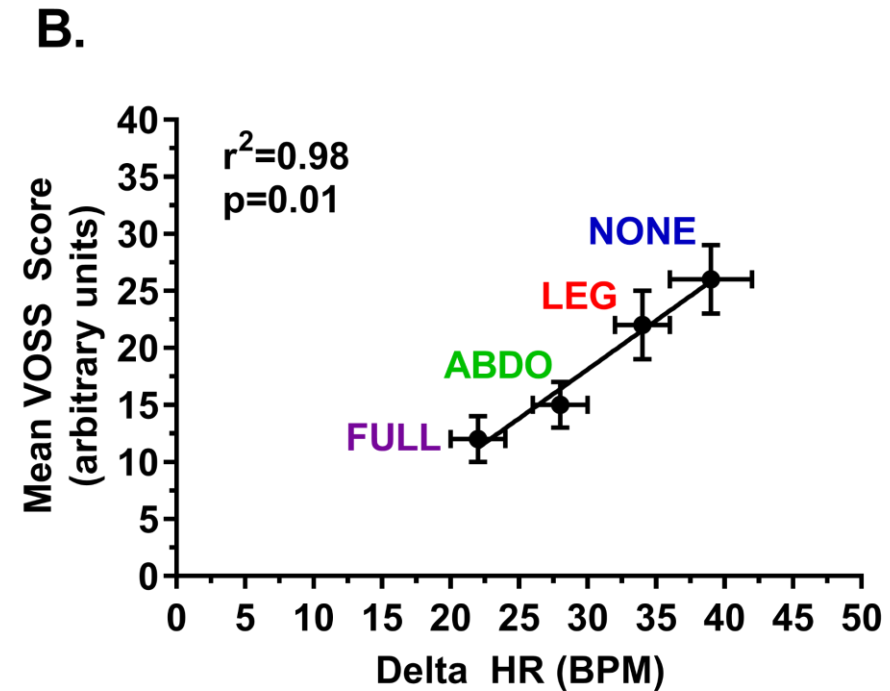
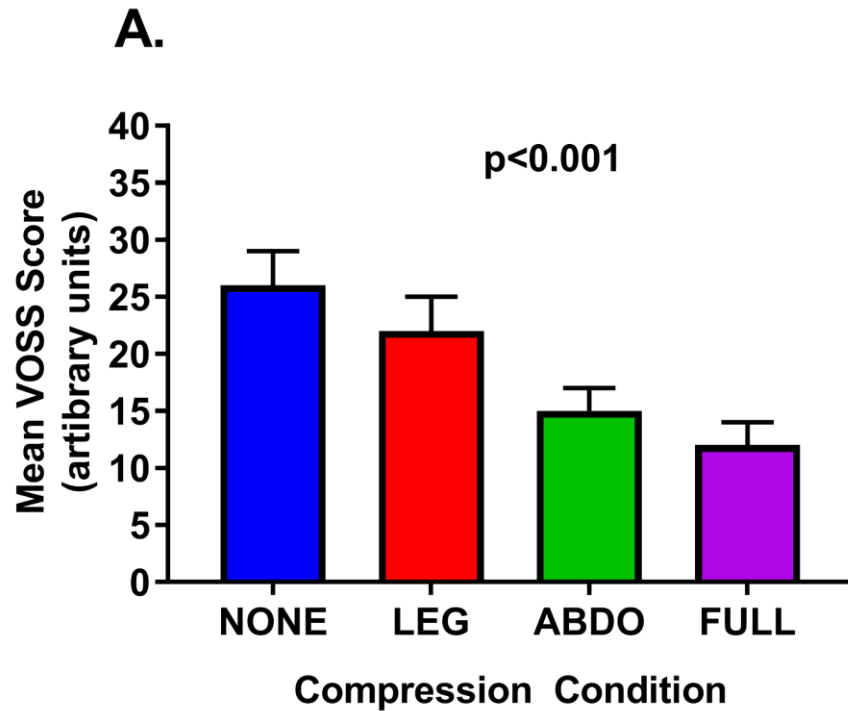
■ Salt Tablets – only if diet not tolerated

- Regular - lots of nausea; fairly inexpensive
- Gel Coated (“Vitassium”) – better tolerated; can get expensive

Compression Garments – They Work



Compression Garments – Symptoms Improve



POTS: Treatment Approaches

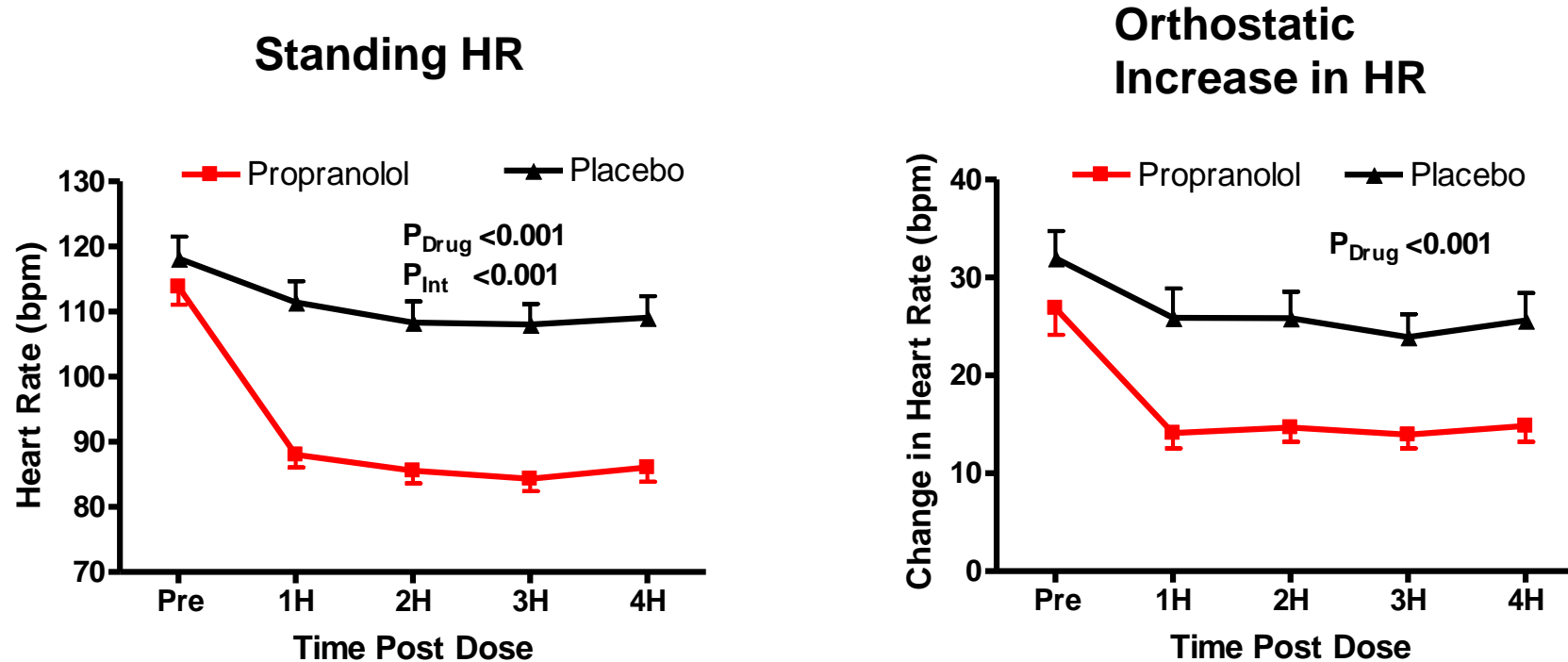
■ Non-Pharmacological

- ❑ Dietary Salt
- ❑ Diet
- ❑ Compression Garments
- ❑ Exercise — may not apply to patients without tachycardia

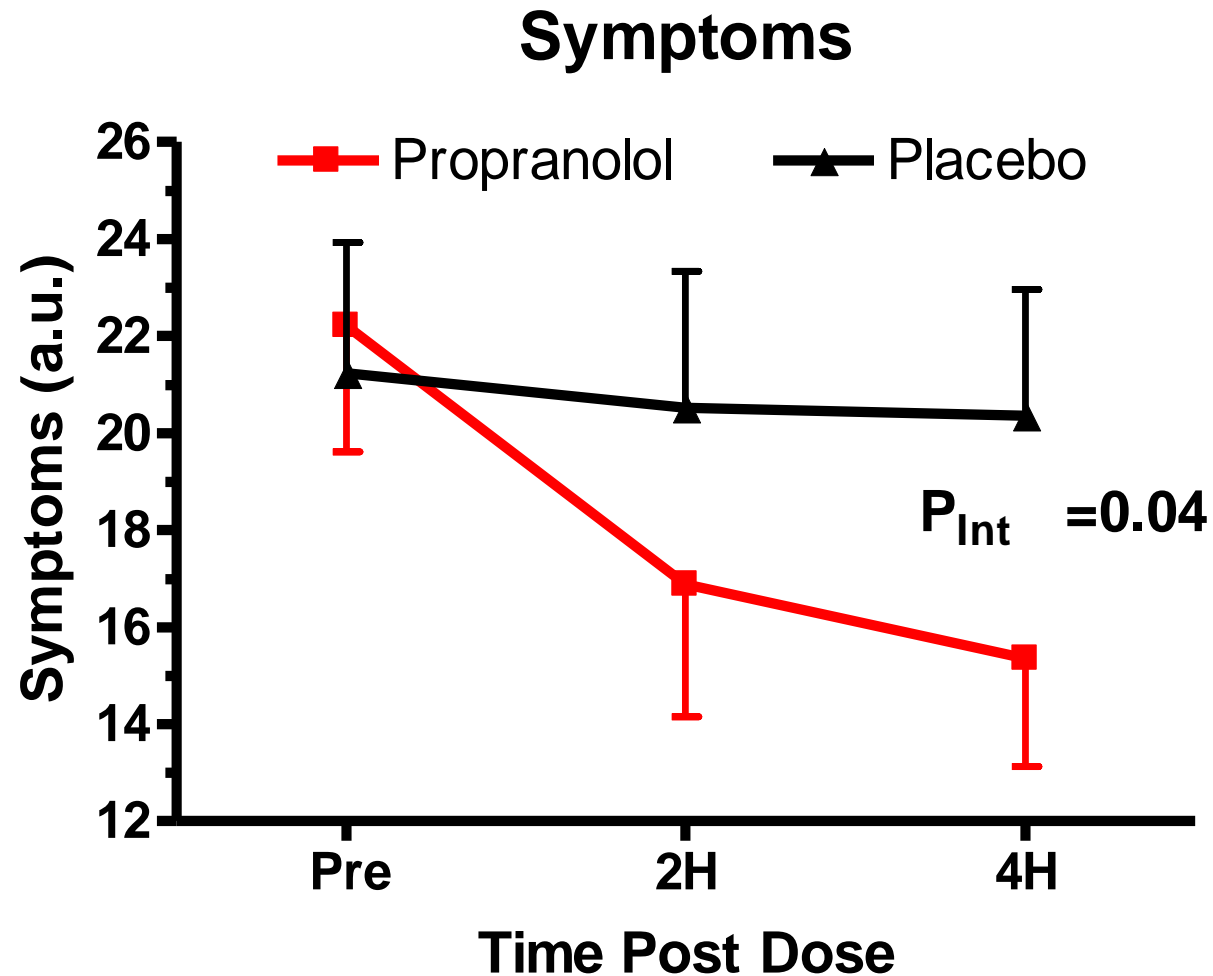
■ Pharmacological

- ❑ Propranolol
- ❑ Ivabradine
- ❑ Pyridostigmine
- ❑ DDAVP

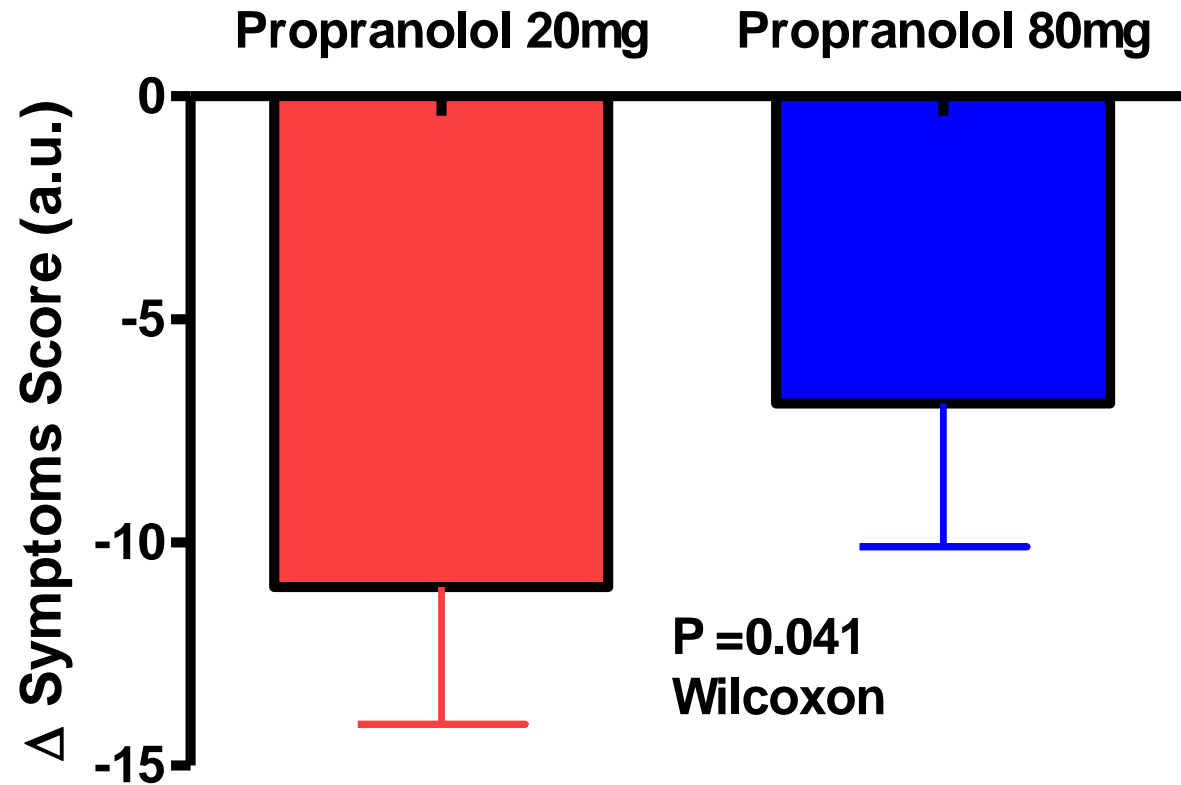
Propranolol 20mg lowers Orthostatic Tachycardia



Propranolol Improves Symptoms...



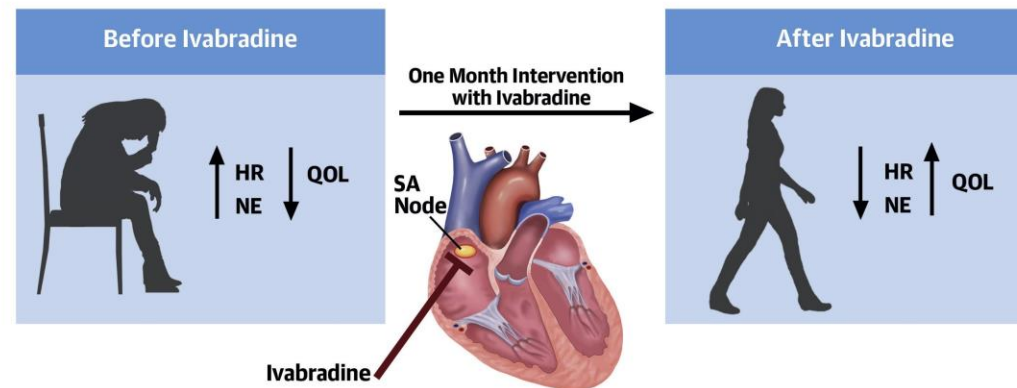
...but Less is More



Just a little bit!

Ivabradine in POTS – Crossover RCT

CENTRAL ILLUSTRATION: Ivabradine Improves Heart Rate, Quality of Life, and Norepinephrine Levels in Hyperadrenergic Postural Orthostatic Tachycardia Syndrome

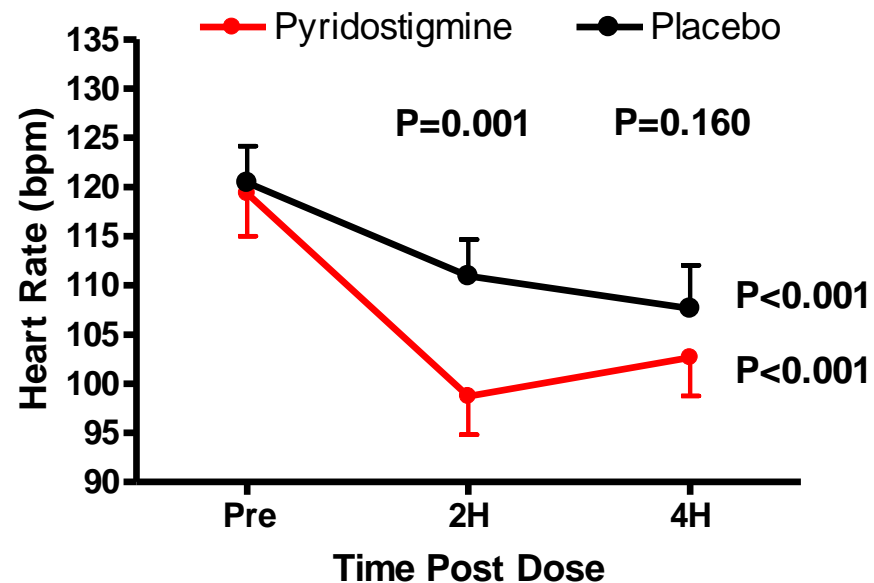


Heart Rate (HR)	Quality of Life (QOL)	Norepinephrine (NE)
Ivabradine significantly lowered: <ul style="list-style-type: none">• HR compared to placebo• Change in HR from supine to standing	Compared to placebo, ivabradine significantly improved: <ul style="list-style-type: none">• Physical functioning• Social functioning	Ivabradine decreased: <ul style="list-style-type: none">• Change in NE from supine to standing

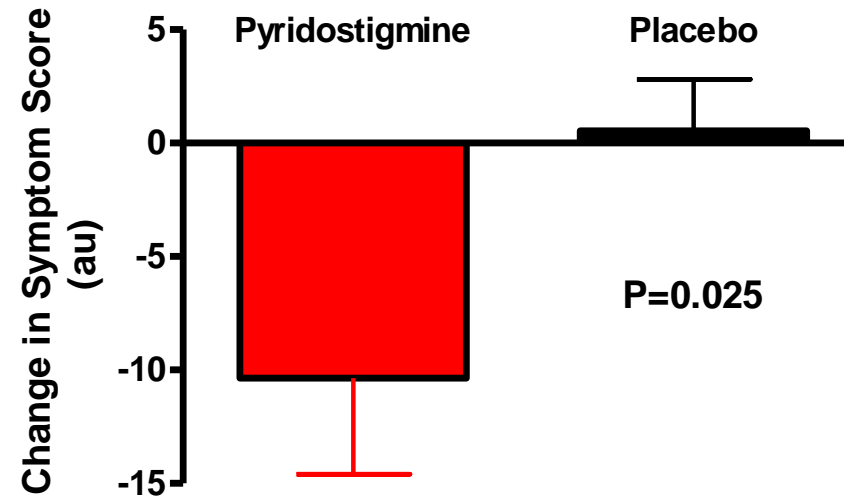
Taub, P.R. et al. J Am Coll Cardiol. 2021;77(7):861-71.

Pyridostigmine (AChE inhibitor)

Standing Heart Rate



Symptoms



Avoid with diarrhea

Calgary Autonomic Investigation & Management Clinic: POTS Patient Brochures



- **Clinical Referral:**
 - **Arrhythmia Clinic**
- **Research Referral:**
 - Autonomic.research@ucalgary.ca

Take Home Messages

- **Chronic disorders associated with significant disability**
 - **Cure is not readily available**
 - **These disorders can be treated**
-

Questions?



UNIVERSITY OF
CALGARY



Satish R Raj MD MSCI
Satish.raj@ucalgary.ca