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Findings from the 2015 HRS Expert Consensus Document on Postural Tachycardia Syndrome (POTS) and Inappropriate Sinus Tachycardia (IST)

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2015 Heart Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope

the American Autonomic Society (AAS),
the American College of Cardiology (ACC),
the Asia Pacific Heart Rhythm Society (APHRS),
the European Heart Rhythm Association (EHRA),
the Pediatric and Congenital Electrophysiology Society (PACES) and
the Latin American Society of Cardiac Pacing and Electrophysiology. The document will be published in the online edition of Heart Rhythm, the official journal of HRS, on May 13, 2015.

Objectives:

- Establish a working criteria for the diagnosis of POTS and IST.
- Provide guidance and recommendation on their assessment and management.
- Identify key area in which knowledge is lacking.

Outlines

- Background
- Pathophysiology
- Diagnosis modalities
- Treatment options

Epidemiology: POTS

- The prevalence of POTS is approximately 0.2%
- Ages of 15 and 25 years
- More than 75% are female

Definition: POTS

1-Frequent symptoms that occur with standing such as lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue.

2-An increase in heart rate of >30 bpm when moving from a recumbent to a standing position held for more than 30 seconds (or >40 bpm in individuals 12 to 19 years of age); and

3-The absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure).

Symptoms: POTS

CARDIOVASCULAR	GASTROINTESTINAL	NEUROLOGICAL
Lightheaded	Nausea	Headaches
Dizziness	Diarrhoea	Tremulous
Rapid Heart rate	Abdominal cramps	
Palpitations	Constipation	
Near fainting or fainting	Bloating	
Short of breath		
Chest Pain		
MUSCULAR SKELETAL	**GENERAL**	**OTHER**
Restless Leg syndrome	Fatigue	Excess Sweating
Myofascial pain	Tiredness	Loss of sweating
Neuropathic pain	Weakness	Bladder problems
	Exercise intolerance	Sleep disturbance

Pathophysiology of POTS

- Peripheral Autonomic denervation
- Hypovolemia
- Hyperadrenergic POTS
- Deconditioning
- Anxiety and Hypervigilance

Diagnosis: POTS

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

Diagnosis: POTS

- Thermoregulatory sweat test.
- Supine and upright plasma epinephrine and norepinephrine level tests.
- A 24-hour urine sample.
- A complete psychological assessment.

Treatments: POTS

- The treatment of POTS is difficult; there are no therapies that are uniformly successful, and combinations of approaches are often needed.

- Non-pharmacological. Pharmacological, and invasive

Treatments: POTS

- Drugs to avoid:

  ACEI, α- and β-B, CCB, diuretics, MOI, TCA and phenothiazines.

- Aggravating factors such as dehydration, extreme heat and excess consumption of alcohol should be avoided

Treatments: POTS

- Diet: increasing fluid salt intake small meals, increasing sodium intake by taking salt tablets , IV NS

- Exercise: In a number of studies, exercise has been reported to be beneficial both in alleviating POTS symptoms, as well as playing a role in curing the condition eg swimming, cycling, aerobic exercise

Treatments: POTS

Major pathophysiological mechanisms of POTS	Pathophysiology	Treatments	Mechanism of therapy
Partial autonomic neuropathy	Partial autonomic neuropathy in lower extremities	Midodrine (Jacob et al., 1997; Hoeldtke et al., 2006; Lai et al., 2009; Ross et al., 2014)	An alpha-1 agonist that increases peripheral vasoconstriction
	Abnormal splanchnic blood flow and pooling	Octreotide (Hoeldtke and Davis, 1991; Hoeldtke et al., 2006)	A somatostatin analog that decreases splanchnic blood flow
Perturbed renin-angiotensin aldosterone system and hypovolemia	Inappropriately low levels of renin and/or aldosterone	Exercise (Fu et al., 2011)	Precise mechanism unclear, but increases renin:aldosterone ratio
	Low blood and/or plasma volume	Exercise (Fu et al., 2011)	Increases plasma volume
		Fludrocortisone (Freitas et al., 2000)	A mineralocorticoid that increases sodium and water retention
		Erythropoietin (Hoeldtke et al., 1995; Kanjwal et al., 2012)	A hormone that increases blood volume
		Saline Infusions (Jacob et al., 1997)	Acutely increases plasma volume
		DDAVP (Coffin et al., 2012)	An ADH analog that increases intravascular volume
Hyperadrenergic State	Increased secretion and clearance of norepinephrine	Propranolol (Raj et al., 2009; Fu et al., 2011);	A non-selective beta-blocker that impairs sympathetic activation
		Pyridostigmine (Raj et al., 2005b; Singer et al., 2006; Kanjwal et al., 2011)	An acetylcholinesterase inhibitor that increases parasympathetic activity and slows heart rate

Treatments: POTS

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Case Report:

Potentially New Indication of Ivabradine: Treatment of a Patient with Postural Orthostatic Tachycardia Syndrome

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INTRODUCTION

The present report describes a female aged 25 years with postural orthostatic tachycardia syndrome (POTS). Her symptoms of weakness, palpitations, and tingling and coldness in her feet were completely alleviated with Ivabradine.

A woman aged 25 years who is otherwise healthy presented to our emergency department (ED) with a 2-week history of fatigue, palpitations and severe weakness on standing, which began after a febrile viral illness. She reported that after she stands she feels a racing of her heart followed by fatigue, numbness and tingling and coldness in her feet. On several occasions she fell to the floor without losing conciseness. Her physical examination was unrevealing: her baseline heart rate (HR) was 80 bpm and supine blood pressure (BP) was 130/76mmHg. Baseline blood analysis, thyroid function test and electrocardiogram, and echocardiogram were normal. In the ED, the patient was asked to stand, and after 3 minutes she felt weak and tingling and a cold sensation in her feet. Her HR rose to 139 her BP was 125/70 mmHg (Fig. **1**). The patient laid down prior to collapsing from lower limb weakness. Head up Tilt table test was performed: after 5 minutes her HR increased from 75 to 140 without postural hypotension and recurrence of her symptoms was noted, the test was terminated. Her HR after

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CLINICAL RESEARCH
Syncope and Implantable Loop Recorders

Single centre experience of ivabradine in postural orthostatic tachycardia syndrome

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Aims Postural orthostatic tachycardia syndrome (POTS) is associated with tachycardia on orthostasis. Patients frequently report palpitations, presyncope, and fatigue. Conventional therapy is effective in less than 60%. Case reports suggest ivabradine (a selective sinus node blocker, with no effect on blood pressure) may alleviate POTS-related symptoms. This is a retrospective case-series.

Methods and results Postural orthostatic tachycardia syndrome patients prescribed ivabradine were identified from the pharmacy database. Case notes were reviewed and participants completed a symptom assessment tool. Twenty-two patients were identified. Data were available from 20. Eight patients reported reduced tachycardia and fatigue and four reported only reduced tachycardia. The most common reason for discontinuing ivabradine was lack of efficacy (n ¼ 6). Five patients reported side-effects resulting in two discontinuing treatment.

Conclusion This retrospective case series indicates that 60% of patients treated with ivabradine report a symptomatic improvement. A randomized controlled trial accessing the efficacy of ivabradine in POTS is indicated, particularly in patients resistant to, or intolerant of, conventional therapy.

Keywords Postural orthostatic tachycardia syndrome † Ivabradine † Fatigue

Treatments: POTS

Recommendations—Treatment for POTS	Class	Level
A regular, structured, and progressive exercise program for patients with POTS can be effective.	IIa	B-R
It is reasonable to treat patients with POTS who have short-term clinical decompensations with an acute intravenous infusion of up to 2 L of saline.	IIa	C
Patients with POTS might be best managed with a multidisciplinary approach.	IIb	E
The consumption of up to 2–3 L of water and 10–12 g of NaCl daily by patients with POTS may be considered.	IIb	E
It seems reasonable to treat patients with POTS with fludrocortisone or pyridostigmine.	IIb	C
Treatment of patients with POTS with midodrine or low-dose propranolol may be considered.	IIb	B-R
It seems reasonable to treat patients with POTS who have prominent hyperadrenergic features with clonidine or alpha-methyldopa.	IIb	E

Treatments: POTS

Drugs that block the norepinephrine reuptake transporter can worsen symptoms in patients with POTS and should not be administered.	III	B-R
Regular intravenous infusions of saline in patients with POTS are not recommended in the absence of evidence, and chronic or repeated intravenous cannulation is potentially harmful.	III	E
Radiofrequency sinus node modification, surgical correction of a Chiari malformation type I, and balloon dilation or stenting of the jugular vein are not recommended for routine use in patients with POTS and are potentially harmful.	III	B-NR

Inappropriate Sinus Tachycardia (IST)

- **Definition:**

HR >100 bpm at rest (with a mean 24-hour heart rate >90 bpm not due to primary causes) and is associated with distressing symptoms of palpitations.

Epidemiology: IST

- IST prevalence was 1.2% (7 of 604 patients),
- Including both symptomatic and asymptomatic patients.
- Little has been reported on long-term outcomes.
- IST is believed to be a chronic condition.

Pathophysiology of IST

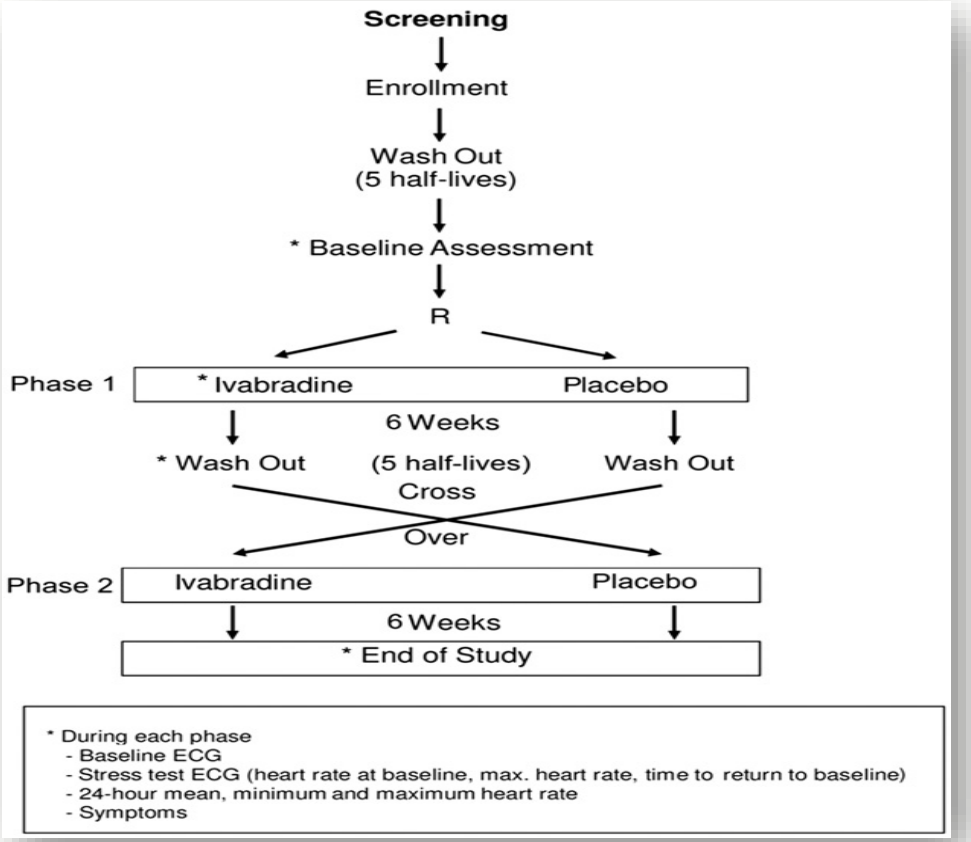
- Increased sinus node automaticity,
- Beta-adrenergic hypersensitivity,
- Decreased parasympathetic activity,
- Impaired neurohumoral modulation.

Diagnosis: IST

Recommendations—Investigation of IST	Class	Level
A complete history, physical exam, and 12-lead ECG are recommended.	I	E
Complete blood counts and thyroid function studies might be useful.	IIa	E
A 24-hour Holter monitoring might be useful.	IIb	E
Urine/serum drug screening might be useful.	IIb	E
It might be worth considering autonomic testing.	IIb	E
It might be worth considering treadmill exercise testing.	IIb	E

Clinical Efficacy of Ivabradine in Patients With Inappropriate Sinus Tachycardia

A Prospective, Randomized, Placebo-Controlled, Double-Blind, Crossover Evaluation



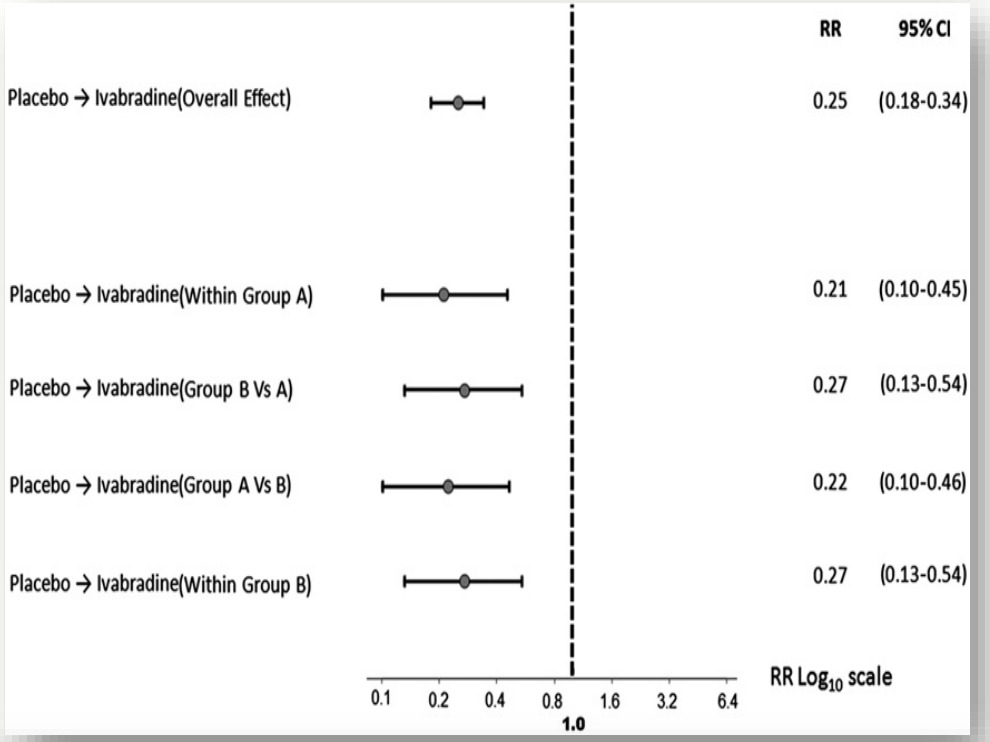


Figure 2 Comparative Assessment of Symptoms in Patients With Inappropriate Sinus Tachycardia Receiving Placebo Versus Patients Receiving Ivabradine

Treatments: IST

Recommendations—Treatment for IST

	Class	Level
Reversible causes of sinus tachycardia should be sought and treated.	I	E
Ivabradine can be useful for treating patients with IST.	IIa	B-R
Sinus node modification, surgical ablation, and sympathetic denervation are not recommended as a part of routine care for patients with IST.	III	E

Conclusions from the 2015 HRS consensus document on POTS and IST

- Provided a uniform criteria for diagnosis of POTS and ITS.
- Highlighted gap in our knowledge of natural history and assessing patients with these syndromes.
- No effective therapy for any of these syndromes.

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Thank you