# Inappropriate Sinus Tachycardia: Etiology, Pathophysiology and Management

*Ahmed A. et al. 2022. J Am Coll Cardiol.*

## Introduction

The current paper by A. Ahmed and colleagues describes the etiology, pathophysiology, and management strategies of patients with symptomatic IST.[1]

Inappropriate Sinus Tachycardia (IST) is a prevalent and debilitating condition in otherwise healthy younger patients, resulting in significant loss of quality of life. In IST, resting heart rate is abnormally high (>100bpm), which is not always recognized as IST and thus often misdiagnosed with panic attacks and mental disorders.[1] Common symptoms include palpitations, lightheadedness, pre-syncope, syncope, orthostatic intolerance, chest pain/pressure, dyspnea and exercise intolerance.[2] Prevalence of IST, which may be underdiagnosed, is four times likely to occur in females than in males and among those between the ages of 15 to 45 years old.[3]

## Mechanism of IST

Advanced electrophysiological mapping technology has revealed sino-atrial (SA) nodal complexities and distinct dual SA nodal sites with different exits at various heart rates. Causes of IST are multifactorial. SA nodal abnormalities may be driven by autonomic and neurohormonal activation, specifically involving an imbalance of sympathetic and parasympathetic denervation as a key culprit. Other factors including physiological (dehydration, exercise, pain, and others), substance abuse (alcohol, cocaine, tobacco, and others) and medical issues (anemia, Cushing's disease, hyperthyroidism, infection, psychiatric, orthostatic hypotension, and others) may also contribute to the elements of sinus tachycardia.[1]

## Diagnostic Evaluation

When distinguishing between IST and postural orthostatic tachycardia syndrome (POTS), symptom evaluation is critical. A key difference between the two syndromes is POTS patients tend to have a more pronounced degree of postural change in heart rate than those with IST such that in a supine position, the heart rate in POTS patients rarely increases above 100 bpm whereas in IST, resting heart rate is often > 100 bpm. Thus, techniques like sitting or standing, tilt table testing and use of continuous monitoring devices like implantable loop recorders or event monitors can help delineate sinus tachycardia from POTS and other arrhythmias like supraventricular tachycardia. In addition, echocardiography should be considered to rule out structural heart abnormalities.

## Management of IST

When IST is diagnosed, lifestyle modifications are usually in order. Avoiding stimulants like caffeine, nicotine, and alcohol while incorporating yoga, strength training and psychological support are methods to help reduce resting heart rate and blood pressure. Medically, beta blockers and calcium channel blockers remain as first line therapy to decrease parasympathetic tone and neurohormonal imbalance in IST patients, however symptom improvements are often dampened with known pharmacological side effects, particularly fatigue and hypotension.

## Ivabradine

Ivabradine, a hyperpolarization-activated cyclic nucleotide-gated channel blocker traditionally administered to heart failure patients, works to slow heart rate so the heart can pump blood more efficiently through the body. This pharmacological therapy is somewhat efficacious in reducing heart rate and funny current ($I_f$), a key characteristic rhythm of IST, as well as improves symptoms. Ivabradine is, however, contraindicated in pregnant or lactating females.[4]

### Sinus Node Ablation

Conventional sinus node (SN) ablation or modification targets the region of earliest atrial activation in sinus rhythm.[5] This method has offered only moderate success in reducing heart rates and not without procedure-related complications and a high incidence of symptom recurrence.[3] There is also no agreement on optimal technique – modification or ablation via open chest ablation vs minimally invasive approaches with mapping, nor long term improvement of symptoms. And finally, in cases of complete SN obliteration, tachycardia may still originate from other SN sites or from the AV junction.[5]

### Sinus Node Sparing Hybrid Ablation

An alternative to SN ablation is epi-endo- thoracoscopic hybrid ablation which has shown some promise in symptomatic drug refractory or drug intolerant IST patients.[6] This approach involves use of an endocardial mapping catheter to identify location of the SA node. An epicardial lesion set is created along the superior vena cava, inferior vena cava and crista terminalis (CT).[7] Endocardial radiofrequency (RF) lesions are then delivered to complete the gaps in the CT ablation line. This hybrid approach offers a few key advantages over traditional ablation strategies. It is minimally invasive, offers direct tissue visualization of the structures of interest and mitigates collateral damage to adjacent tissues like the esophagus or phrenic nerve, all while simultaneous endocardial activation mapping is conducted to allow for SN identification and precise epicardial ablation.

### Key Takeaways

- IST is a potentially debilitating arrhythmia syndrome that more often affects younger females.
- Although the etiology and mechanism of IST are not entirely known, it seems that an imbalance of autonomic and neurohormonal factors play a large role in driving SA nodal dysfunction.
- Pharmacological regimens like beta blockers and ivabradine have limited effectiveness in controlling elevated heart rate, and while conventional SN ablation approaches demonstrate acute success, symptoms recurrence is common along with the need for repeat ablation.
- Sino-atrial node sparing hybrid ablation may be a viable treatment option among symptomatic IST patients intolerant or refractory to medications.
- The HEAL-IST Trial, currently underway, is a prospective, multi-center, single arm, Bayesian adaptive-designed trial which will evaluate the safety and effectiveness of a hybrid sinus node sparing ablation in up to 142 symptomatic drug refractory or drug intolerant IST patients. Freedom from IST (mean heart rate of ≤ 90bpm or at least a 15% reduction in mean heart rate) will be evaluated at 12 months as compared to baseline in the absence of new or higher dosage of previously failed medications.[8]

***References:***
[1]*Ahmed A. et al. 2022. J Am Coll Cardiol. 79(24): 2450-2462.*
[2]*Khiabani AJ et al. 2019. Annals of Thoracic Surg. 108(4):1162-1168.*
[3]*Olshansky B and RM Sullivan 2019. Europace. 21(2):194-207.*
[4]*Mayo Clinic, online search for Ivabradine.*
[5]*Rodriguez-Manero M. 2017. JACC Clin Electrophysiol. 3(3):253-265.*
[6]*Lakkireddy D et al. 2022. Heart Rhythm. 19(1):30-38.*
[7]*De Asmundis C et al. 2022. J Interv Card Elctrophysiol. 63(3):531-544.*
[8]*HEAL-IST Trial, ClinicalTrials.gov Identifier: NCT05280093.*



AtriCure