

Epidemiology and definition of inappropriate sinus tachycardia

Cara N. Pellegrini^{1,2} · Melvin M. Scheinman²

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Abstract Inappropriate sinus tachycardia (IST) is a clinical syndrome lacking formal diagnostic criteria. It is generally defined as an elevated resting heart rate (HR; >90–100 bpm) with an exaggerated response to physical or emotional stress and a clearly sinus mechanism. Clinical manifestations are broad from a complete lack of symptoms to incapacitating incessant tachycardia. Now understood to be relatively prevalent, it is observed to have a generally benign prognosis, though symptoms may persist for years. Whether IST is a single discrete entity or a heterogeneous condition with overlap to other syndromes such as postural orthostatic tachycardia syndrome remains a matter of debate.

Keywords Inappropriate sinus tachycardia · Epidemiology · Clinical syndrome · Postural orthostatic tachycardia syndrome

Inappropriate sinus tachycardia (IST) was first described in 1979 as a clinical syndrome of a persistent, nonparoxysmal increase in the resting sinus heart rate (HR) [1]. Still somewhat vaguely defined, IST lacks a strict definition or agreed upon diagnostic criteria. Most studies have utilized an average daytime HR of greater than 95–100 bpm and 24-h average HR of more than 90–95 bpm (Table 1). There is often an exaggerated response to exertion and/or postural change, the HR increase is unrelated to or out of proportion to the level of physical or

emotional stress, and the HR recovery tends to be prolonged. By definition, there is no physiologic provocation such as fever or hyperthyroidism, nor do patients typically have associated heart disease (Table 2). Medications and substance use must be reviewed in detail to ensure tachycardia is not due to a stimulant, such as the increasingly prevalent Adderall. Importantly, the P wave must be consistent morphologically with a sinus mechanism on 12-lead electrocardiogram.

Clinical manifestations range from patients who are totally asymptomatic to suffering incapacitating incessant tachycardia. Common complaints include palpitations, lightheadedness, presyncope, syncope, orthostatic intolerance, chest pain/pressure, dyspnea, and exercise intolerance. Non-cardiac symptoms are frequent as well, such as anxiety, depression, abdominal discomfort, myalgia, and headache. In many patients, the history will have functional overtones, with symptoms disproportionate to the severity of the tachycardia, and difficult to temporarily relate to periods of more elevated HR. Efforts to treat the tachycardia alone often do not ameliorate symptoms.

IST has traditionally been thought to be a rare condition of young women, with health professionals overrepresented. This characterization may better define the group afflicted with IST who are most symptomatic and/or most likely to seek medical attention, rather than the full cohort of those who met criteria for IST. Still and colleagues utilized OPERA (Oulu

Table 1 Defining characteristics of inappropriate sinus tachycardia

Daytime heart rate (average) >95–100 bpm
24-h heart rate (average) >90–95
Exaggerated response to exertion/postural change/emotion
Prolonged heart rate recovery
No secondary cause
P wave morphology consistent with sinus mechanism

✉ Cara N. Pellegrini
cara.pellegrini@va.gov

¹ San Francisco VA Medical Center, 4150 Clement Street, 111C, San Francisco, CA 94121, USA

² University of California San Francisco, San Francisco, CA, USA

Table 2 Potential etiologies of sinus tachycardia that must be excluded for diagnosis of inappropriate sinus tachycardia

Medications/substances	Medical conditions	Physiologic contributors
Anticholinergics	Anemia	Pain
Decongestants	Infection/fever	Dehydration
Albuterol	Pulmonary embolus	Exercise
Adderall	Pericarditis	Anxiety
Alcohol	Myocardial infarction	Hypoglycemia
Caffeine	Aortic or mitral regurgitation	
Tobacco	Pneumothorax	
Cocaine, methamphetamines	Hyperthyroidism	
B-blocker withdrawal	Diabetic neuropathy	
	Cushing's disease	
	Pheochromocytoma	
	Carcinoid	

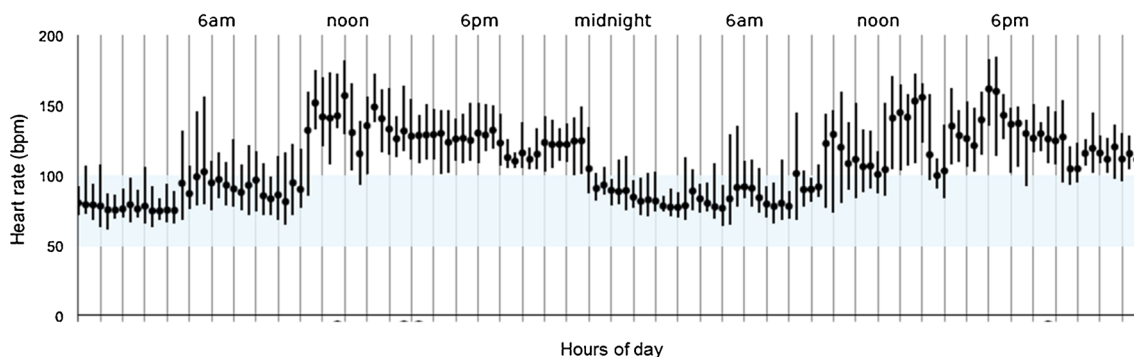
Project Elucidating Risk of Atherosclerosis), a population-based case-control study of middle-aged people that was looking for risk factors of cardiovascular disease, to study the prevalence of IST. They found more than 1 % of the 604 middle-aged subjects met HR criteria for IST, without a gender difference [2]. Of note, this exceeds reported prevalence for all other supraventricular tachycardias combined. There were no significant differences in echocardiographic, laboratory, or heart rate variability measurements between those with and without IST, though hypertension was overrepresented among those with IST. IST has been reported in older individuals as well [3].

The onset of symptoms may be abrupt or insidious. Inciting factors such as ablation of another arrhythmia or addition of a medication may play a role. IST following atrial fibrillation ablation targeting the ganglionated plexi, purposefully or otherwise, has been reported, concordant with the idea of a dysautonomia contributing to IST [4, 5]. IST has also been reported following radiofrequency ablation or cryoablation of AV nodal tachycardia (only in the setting of fast pathway ablation) and para-Hisian accessory pathways [6–8]. In the majority of cases, the IST

is short-lived, though ivabradine has been used successfully in a more persistent case [7].

Additionally, SVT ablation may in some cases unmask an already present IST. For this reason, it is important to obtain 24-h ambulatory monitors for patients with known supraventricular tachycardias to exclude coexistence of IST, which will remain even following a successful supraventricular tachycardia ablation, to the disappointment of the patient. On the flip side, electrophysiology study is not necessary for the diagnosis of IST, the diagnosis of which should rely on assessment of the clinical picture and ambulatory monitoring; we have seen isoproterenol infusion that was meant to provoke a stress response lead only to clinically irrelevant atrial tachycardias and a more confused clinical picture.

Data are consistent that the condition of IST is generally benign, perhaps due to the HR typically slowing somewhat during sleep [9] (Fig. 1). While individual cases of tachycardia-induced cardiomyopathy have been reported [10], the risk of tachycardia-induced cardiomyopathy appears to be quite small. Symptoms may persist for years, but do not tend to progress, and may eventually fade away. After a mean follow-up of 6 years in the study by Stills et al., there was no

**Fig. 1** Typical diurnal variation in heart rate in a patient with inappropriate sinus tachycardia, with reduction in heart rate while sleeping

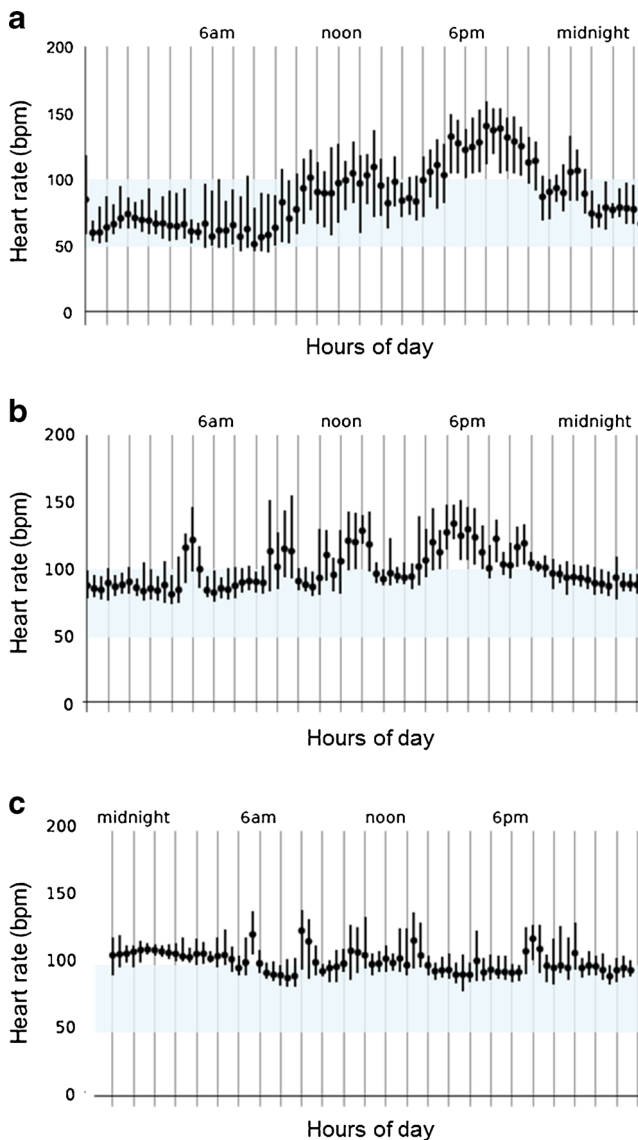


Fig. 2 Heart rate trends from ambulatory monitoring of patients with inappropriate sinus tachycardia. **a** Normal heart rate at rest but excessive response to physiologic demand, **b** moderately elevated heart rate at rest with disproportionate response to demand, and **c** markedly elevated baseline heart rate with disproportionate response to demand

significant change in average HR overall and most subjects still complained of moderate symptoms, though notably only 4 of 11 subjects continued to fulfill the combined diagnostic criteria of IST [2]. Despite this, given human and animal data that link HR and life expectancy, concern persists for some minor increase in mortality which together with the frequently troublesome symptoms motivates therapy.

IST encompasses a heterogeneous population, many of whom have extra-cardiovascular manifestations, which can make the diagnosis difficult. Confusion with IST and postural orthostatic tachycardia syndrome (POTS) can occur, as they are syndrome complexes with many symptoms in common [11]. Further, many patients with IST have inappropriate HR

response during orthostatic stress and patients with POTS may have persistent elevation of HR in the recumbent position. In general, IST patients have a more persistently elevated HR than those with POTS, though variability in heart rate patterns that constitute the cohort of IST patients has been reported [12]. Three main HR patterns have been suggested as consistent with IST (Fig. 2). The HR may be normal at rest but respond excessively to physiologic demand. The resting HR may be moderately elevated with further inappropriately marked response to demand. Finally, the HR was persistently and markedly elevated, with graded HR response to activity.

Whether IST is a single entity with a homogeneous pathophysiology is unclear. IST could result from an intrinsic abnormality in the sinus node, an elevated intrinsic heart rate, or a disturbance of autonomic function, either excessive resting sympathetic nerve influences or deficient resting vagal nerve influences [1, 13–15]. Perhaps the conflicting data (which will be discussed in more detail in a later section), reflects the truly heterogeneous makeup of the affected population that has made defining and delineating this condition so challenging.

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