

Reviews

Deciphering the Sinus Tachycardias

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Summary: Sinus tachycardia is the most common rhythm disturbance encountered in clinical practice. Primary sinus tachycardia without an underlying secondary cause, despite often being associated with troublesome symptoms, is often neglected leading to multiple consultations and frustration on part of both the practitioner and the patient. The fact that primary sinus tachycardias are a heterogeneous group of disorders is seldom appreciated; hence, a firm diagnosis is rarely reached and management is haphazard. Furthermore, there may be prognostic implications for prolonged or recurrent sinus tachycardia, making it imperative that this group of arrhythmias receive adequate and appropriate attention. Normal sinus tachycardia (i.e., secondary), inappropriate sinus tachycardia, postural orthostatic tachycardia syndrome (POTS) and sinus node reentry tachycardia make up this group of arrhythmias. Their definitions, clinical features, diagnostic criteria, pathophysiologic mechanisms, and optimum management are discussed in this review.

Key words: sinus tachycardia, inappropriate sinus tachycardia, postural orthostatic tachycardia syndrome, postural orthostatic tachycardia syndrome, sinus node reentry tachycardia

Introduction

The primary sinus tachycardias are arguably the most neglected rhythm disturbance encountered in clinical practice.

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The main reason for this is that although considerable time and effort are expended in investigating and eliminating secondary causes, the primary entity remains clinically perplexing. In the animal kingdom, a fascinating inverse relationship exists between heart rate and life expectancy.¹ In humans, a substantial and indisputable body of epidemiologic data after adjustment for other risk factors, associates higher heart rates with increased mortality, not just in patients with underlying cardiovascular disease but also in the population at large.² Thus, sinus tachycardia merits appropriate identification and management.

The sinus tachycardias form a heterogeneous group of disorders (Fig. 1) ranging from normal sinus tachycardia (NST), which can be a response to physiologic or pathologic circumstances, to inappropriate sinus tachycardia, where there is a breakdown in the mechanisms that regulate the tachycardia response; sinus tachycardia associated predominantly with upright posture, called the postural orthostatic tachycardia syndrome (POTS), forms one end of the spectrum of the inappropriate sinus tachycardias (IST), and that arising from reentry circuits close to or within the sinus node is known as sinus node reentry tachycardia. These arrhythmias differ in their clinical manifestations, pathophysiologic basis, and management and require appropriate identification.

Definitions

Normal sinus tachycardia (NST) is an appropriate increase in sinus rate to > 100 beats/min^{3,4} in response to a variety of physiologic, pathologic, and/or pharmacologic stimuli. An underlying cause is present and should be identified.

Inappropriate sinus tachycardia (IST) is defined as a persistent increase in resting heart rate to > 100 beats/min, which is out of keeping with the level of physiologic, pharmacologic, and/or pathologic stress.^{5,6} Characteristically, there is nocturnal normalization of the heart rate, and in its absence other reasons for the tachycardia should be sought. Exclusion of a primary underlying cause is a prerequisite for this diagnosis.

Postural orthostatic tachycardia syndrome (POTS) is an abnormal sinus tachycardia which is triggered by orthostasis and relieved by recumbency.⁷ There is no significant hypotension during upright posture and neither an underlying cause nor clinical signs of autonomic neuropathy should be present.^{7,8}

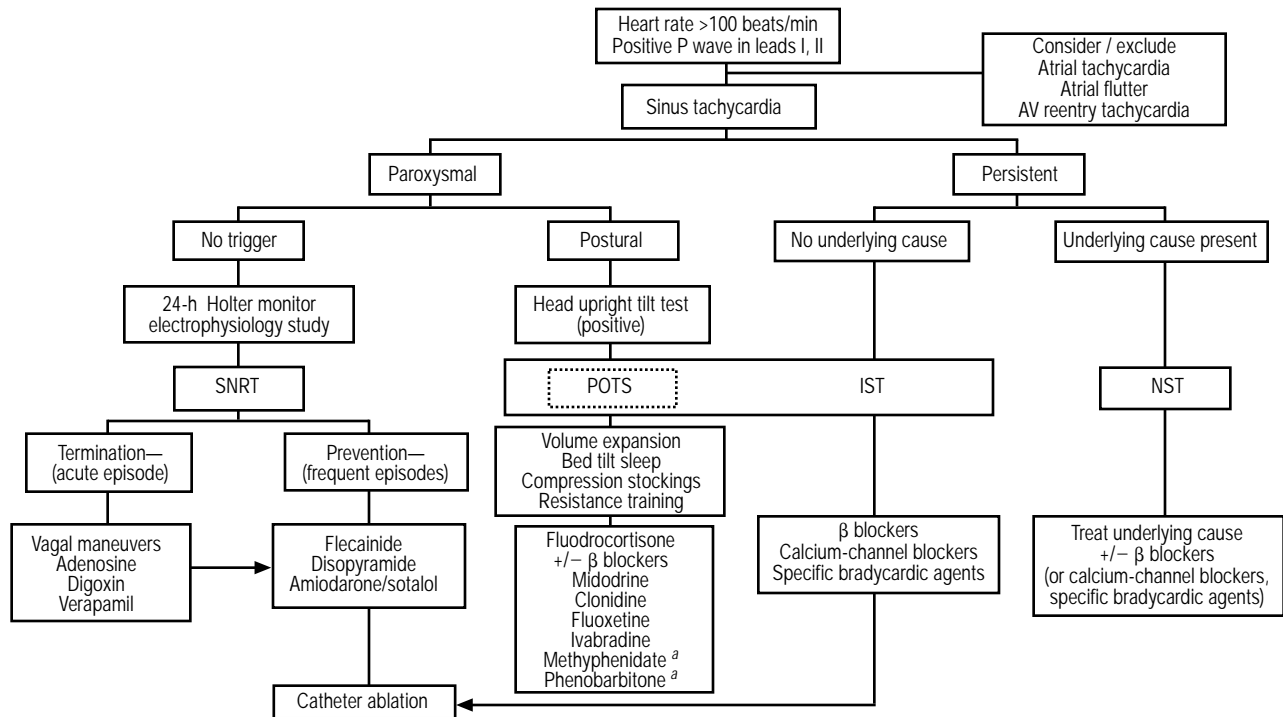


FIG. 1 The differential diagnosis, investigation, and management of sinus tachycardia. SNRT = sinus node reentry tachycardia, POTS = postural orthostatic tachycardia syndrome, IST = inappropriate sinus tachycardia, NST = normal sinus tachycardia, AV = atrioventricular, ^a = risk of dependence.

Sinus node reentry tachycardia (SNRT) is sudden, paroxysmal, and usually nonsustained. The heart rate is usually 100 to 150 beats/min but may be as low as 80 beats/min. The arrhythmia is commonly triggered and terminated by an atrial premature beat.⁶

Although this group of four arrhythmias comprises the sinus tachycardias, it is sometimes difficult to differentiate between them (especially between IST and POTS, as patients with POTS frequently have persistent elevation of heart rate and patients with IST frequently have fluctuation of heart rate during orthostatic challenge) and from other rhythm disturbances, especially atrial tachycardia originating close to the sinus node and right upper pulmonary vein tachycardia. Occasionally, atrial flutter and nodal tachycardias may also need to be considered as part of the differential diagnosis. The distinction between the several forms of sinus tachycardia and other "atrial tachycardias" is crucial, since each type of sinus tachycardia requires specific treatment and practically all other forms of regular atrial tachyarrhythmia can be eradicated by appropriate therapy.

Etiology and Basic Underlying Mechanisms

The sinus node is a versatile and complex structure. Anatomically, it is spindle shaped and lies in the lateral and epicardial aspects of the junction between the superior vena cava and the right atrium, with its base set against the prominent termi-

nal crest (or crista terminalis), which marks the internal site of the cavoatrial junction.⁹ The node cells are arranged as interweaving fascicles embedded in a dense fibrous matrix. There is no insulation of the node from the surrounding atrial cells, but rather a small zone of transitional cells is interposed. This inhomogeneous arrangement allows islands of fibrous tissue to lie between the pacemaker cells in and around the sinus node providing a substrate for sinus node reentry.¹⁰

Physiologically, the sinus node pacemaker cells depolarize spontaneously and regularly in order to generate cardiac impulses automatically. The rate of depolarization is modulated by autonomic tone (i.e., sympathetic and parasympathetic input), stretch, temperature, hypoxia, blood pH, and in response to other hormonal influences (e.g., tri-iodothyronine and serotonin). Sinus node pacemaker cells, unlike atrial and ventricular myocytes, do not exhibit a conventional stable resting membrane potential (Fig. 2). This is primarily due to the lack of a particular class of potassium channel (the inward rectifier channel) in sino atrial nodal cells. These cells do, however, possess other types of potassium channels that play an important role in the generation of action potentials. The unstable membrane potential, "the pacemaker potential," of the sinoatrial nodal cells decays faster than that of any other cardiac cell and, in physiologic circumstances, generates an action potential roughly once every second.¹¹ The spontaneous decay of this potential is due to at least three factors. First, a small current of sodium ions flows into the cell. This small sodium current has two components—the background inward current (I_b)

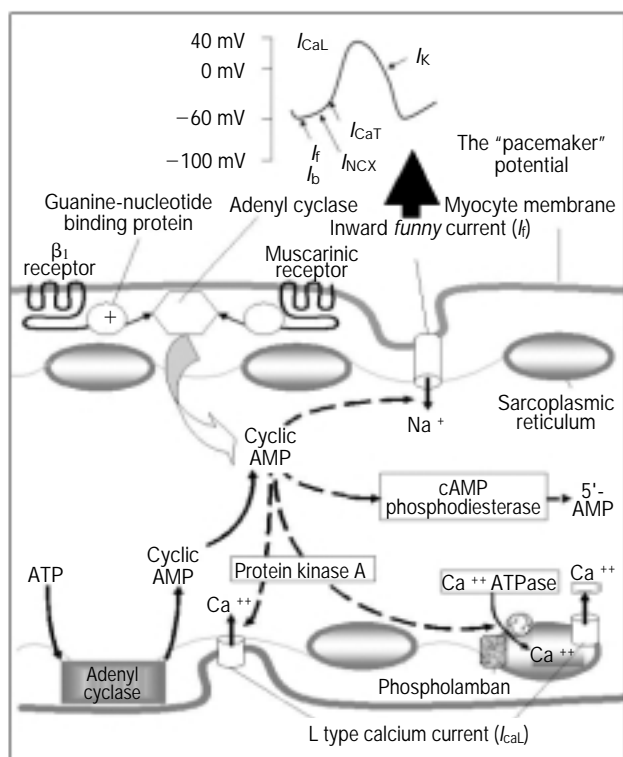


FIG. 2 The molecular basis for normal sinus tachycardia. Catecholamines stimulate Gs proteins in pacemaker cells by binding to β_1 receptors. This eventually results in the opening of the inward funny (I_f) channels leading to sodium influx. This increases the gradient of the slope of the "pacemaker current" resulting in earlier depolarization and tachycardia. Accompanying catecholamine stimulation of β_1 receptors is synergistic vagal withdrawal, which prevents inhibition of adenylyl cyclase. I_f = inward "funny" current, I_b = background current, I_K = outward potassium current, I_{Ca} = inward calcium current (T = transient current, L = long acting current), I_{NCX} = inward sodium calcium exchanger, cAMP = cyclic adenosine monophosphate, ATPase = adenosine triphosphate.

and the "funny" (I_f) current. The term "funny" current denotes ionic flow through channels activated in polarized cells (≥ -60 mV) unlike other time and voltage-dependent channels which are activated by depolarization.¹² Second, the depolarization in the membrane potential caused by this sodium current inactivates the voltage-dependent "delayed rectifier" potassium channels, resulting in a decrease in the permeability of the membrane to potassium. Finally, when the membrane potential reaches -55 mV, two distinct Ca^{++} channels come into play. Transient or "T-type" calcium channels ($I_{Ca,T}$) open first before long-lasting or "L-type" calcium channels ($I_{Ca,L}$) and these tip the "pacemaker potential" beyond the threshold of -40 mV triggering an action potential.

Physiologic NST is predominantly catecholamine driven, but there is synergistic vagal inhibition. Norepinephrine and epinephrine released from sympathetic nerve endings or into the circulation from the adrenal medulla, act upon myocardial beta 1 (β_1) adrenergic receptors linked to stimulatory guanine-

nucleotide-regulatory-proteins (Gs proteins), which are in turn positively coupled to adenylyl cyclase. Activation of these receptors leads to an increase in cyclic adenosine monophosphate (cAMP) which directly triggers the opening of the inward sodium channels responsible for the "funny" current and indirectly stimulates opening of "L-type" calcium channels. The net effect of the former is an increase in sodium influx into the cell, causing faster depolarization of the pacemaker potential and hence a faster heart rate. Most pathologic and pharmacologic causes of NST effect this response either directly or indirectly via β_1 adrenergic receptor stimulation, but other mechanisms are also likely to be involved—for example, inhibition of cAMP by methylxanthines.

Several mechanisms have been postulated for IST and POTS, and there is a considerable overlap between these for the two entities. Enhanced automaticity of the sinus node¹³ and abnormal autonomic regulation with excess sympathetic and reduced parasympathetic tone¹⁴ are two principal mechanisms proposed for IST. It is unclear whether these mechanisms are a direct result of impaired neural input into the sinus node or whether they represent an inherent abnormality within the sinus node itself.⁶ However, the causative mechanisms may overlap, which perhaps explains the variable responses to beta blockers and calcium-channel blockers in many patients.⁶

In POTS, a large part of its heterogeneous nature results from an abnormality in any one or more of the many components that make up the complex physiologic baroreceptor reflex that is essential for maintaining hemodynamic stability during orthostatic stress (Fig. 3). The less common central beta hypersensitivity form, which exhibits an exaggerated tachycardia response to orthostatic stress despite an appropriate increase in peripheral vascular resistance,¹⁵ has pathophysiologic features similar to IST, but the exact reasons why the baroreflex fails to suppress the tachycardia are unknown. In one family with inherited POTS, the basic abnormality is a defective norepinephrine-transporter mechanism.¹⁶ This leads to failure of synaptic clearance of norepinephrine, leading to an exaggerated sympathetic response to physiologic stimuli and hence the orthostatic tachycardia. In a proportion of other cases, intrinsic sinus node abnormalities have also been reported.¹⁷

In the majority of patients with POTS, the abnormality involves failure of peripheral vasoconstriction—the so-called "partial dysautonomia" form, and again the pathophysiologic mechanisms involved are only partly known. There is some evidence that this entity may be due to partial sympathetic denervation, especially in the legs,¹⁸ with arteries more likely to be affected than veins.¹⁹ Patients with orthostatic intolerance have reduced venous compliance in the lower extremities, which may limit the dynamic response to orthostatic change and thereby contribute to symptoms of orthostatic intolerance in this population group.²⁰ The exact trigger for this partial selective denervation is unknown although a significant proportion of patients with POTS report a preceding viral illness, and these individuals tend to have a better long-term prognosis.^{21–23}

Other possible mechanisms for POTS include "idiopathic hypovolemia"²⁴ and reduced circulating blood volume,²⁵ for

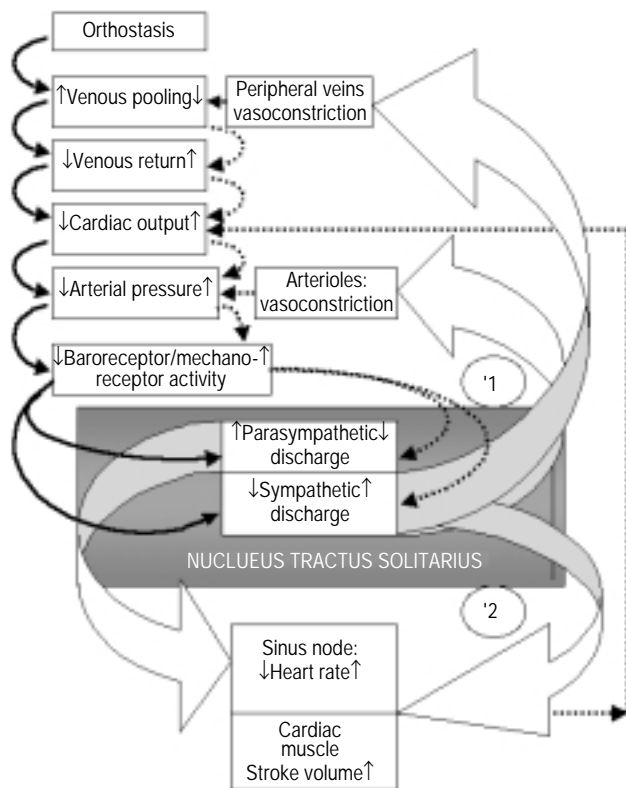


FIG. 3 Orthostatic stress and its baroreceptor reflex response. The bold arrows demonstrate the physiologic consequence of orthostasis, the large arrows the autonomic response mediated via the baroreceptor reflex, and the dotted arrows denote the appropriate corrective measures instigated to prevent cardiovascular collapse. Postural orthostatic tachycardia syndrome (POTS) results either from (1) a failure of the peripheral vasculature to vasoconstrict appropriately to orthostatic stress (partial dysautonomia form), or (2) due to a failure of central mechanisms to terminate the tachycardia response (central beta hypersensitivity form).

example, due to splanchnic bed blood pooling,^{26, 27} and reduced red cell mass resulting from an impaired erythropoietin response.²⁸ It is interesting that there is also increased microvascular filtration with increased arterial blood flow in patients with POTS.²⁹ Sometimes there is evidence of autoantibodies to ganglionic nicotinic acetylcholine receptors in certain cases.³⁰

Clinical Features

Demographics

Normal sinus tachycardia is by far the most common of the sinus tachycardias. Symptomatic physiologic NST may be more prevalent in females, but this is unlikely to be the case for the pathologic and pharmacologic varieties where a more equal distribution between the two genders is more likely. The vast majority (90%) of patients with IST are female with an av-

erage age of approximately 30 years.^{5, 13, 31, 32} It is interesting that these individuals are often health-care workers, probably because this cohort is involved in regular medical self-assessment.⁵ Postural orthostatic tachycardia syndrome also appears to be far more prevalent in females, but some studies have shown an equal gender distribution.^{7, 24, 33, 34} Sinus node reentry tachycardia shows no age or gender predilection, but it accounts for < 5% of all regular supraventricular tachycardias.³⁵

Clinical Presentation

Many patients with sinus tachycardia have no specific symptoms, especially when the arrhythmia is appropriate. Often, however, such as in patients with IST, palpitations that are fast and regular, chest pain, dyspnea, dizziness, lightheadedness, and presyncope may be reported. Patients with POTS may additionally complain of other autonomically mediated symptoms including tremor, constipation, and bladder-related problems. Many patients with POTS also complain that they feel cold and are unable to tolerate extreme heat.³⁶ They may also suffer from marked fatigue and exercise intolerance and be misdiagnosed with chronic fatigue syndrome.³⁷ Paroxysmal, regular, and usually self-terminating palpitations are a clue to the diagnosis of reentry tachycardias; SNRT presents in this way. The degree of disability in patients with various sinus tachyarrhythmias varies from none to total incapacitation.

Clinical examination may allow the identification of signs that point to an underlying primary cause in NST but is otherwise unhelpful in establishing the diagnosis. A persistent sinus tachycardia in the absence of any particular clinical reason or signs of an underlying cause should trigger suspicion of IST. Simple clinical maneuvers, such as getting gently up from bed, in POTS may reproduce the tachycardia and the patient symptoms, raising suspicion of the diagnosis. Although in SNRT the arrhythmia is unlikely to be present during clinical consultation, a thorough examination is essential because this cohort exhibits a higher incidence of underlying organic heart disease.³⁸

Investigations

The investigations for NST are guided by the suspected underlying cause. A 12-lead electrocardiogram (ECG) usually confirms the presence of sinus tachycardia and may add more information if the underlying cause is cardiac. The ECG is also useful in identifying atrial flutter, atrial tachycardia, and nodal tachycardias. The only absolute ECG criterion for sinus rhythm is an upright P-wave vector in leads I and II. During sinus tachycardia, the morphology of the P wave may change with its axis becoming more vertical, but the P-wave vector remains similar or identical to that in normal sinus rhythm (i.e., positive in leads I and II). This effect is due to a superior shift in the site of origin of depolarization within the sinus node during sinus tachycardia.³¹ In atrial and pulmonary vein tachycardias, not only is there a different site of origin for the arrhythmia, but the pattern of conduction through the atria is also different. Therefore, atrioventricular reentry tachycardia (AVRT), atri-

oventricular nodal reentry tachycardia (AVNRT) atrial flutter, and most focal and reentrant atrial tachycardias have characteristic P-wave morphologies distinct from sinus rhythm. Occasionally, atrial and pulmonary vein tachycardias have initial P-wave vectors in the frontal plane similar to those of sinus tachycardia. However, a more complete assessment of the P-wave morphology on the 12-lead ECG, for example, negative P waves in lead aVL or entirely positive P waves in lead V₁, and the onset pattern of the tachycardia usually distinguishes these arrhythmias from sinus tachycardia. Except for their paroxysmal nature and usually a faster heart rate (> 150 beats/min), it is clinically difficult to distinguish right upper pulmonary vein tachycardias and atrial tachycardias originating in the region of the crista terminalis/sino atrial node from sinus tachycardias. These arrhythmias can only be distinguished realistically during electrophysiology studies.

A 24-h Holter recording is a useful investigation tool for differentiating between sinus tachycardias. It is the investigation

of choice for IST, which classically demonstrates a persistent increase in sinus rate to > 100 beats/min during waking hours and usually normalization in this rate during sleep. Patients with POTS report symptoms during upright posture which correlate with a sinus tachycardia, or a sudden increase in heart rate. For these patients, a head upright tilt test also usually triggers symptoms associated with sinus tachycardia, or an increase in heart rate to > 30 beats/min from baseline, within a few minutes of upright posture but without a significant drop in blood pressure (Fig. 4). The sensitivity and specificity of the tilt test in POTS are unknown; however, there is no reason to believe it should be any different from those in vaso-vagal syncope (i.e., sensitivity ~ 65% and specificity ~ 94%) as there is a considerable degree of overlap in the underlying mechanisms between the two conditions. Once a positive tilt test result has confirmed the diagnosis, the task is to differentiate between the various subtypes of POTS so that treatment can be targeted appropriately (Fig. 5). Patients with the central

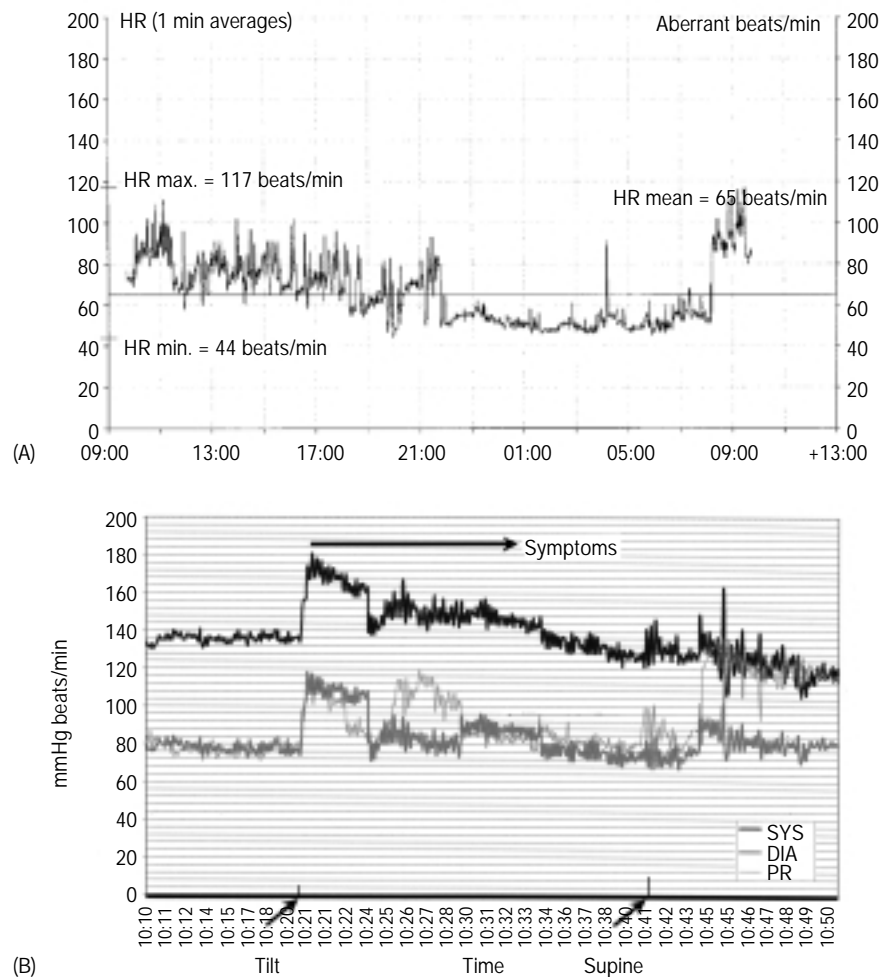


FIG. 4 A tachocardiogram (A) and tilt test recording (B) from a patient with postural orthostatic tachycardia syndrome (POTS). The tachocardiogram, with a 50 beats/min increase in heart rate (HR) during orthostatic stress associated with symptoms, raised suspicion of the diagnosis. A head upright tilt test to 60° reproduced the tachycardia and symptoms without a significant drop in blood pressure. SYS, DIA = systolic, diastolic blood pressure; PR = pulse rate.

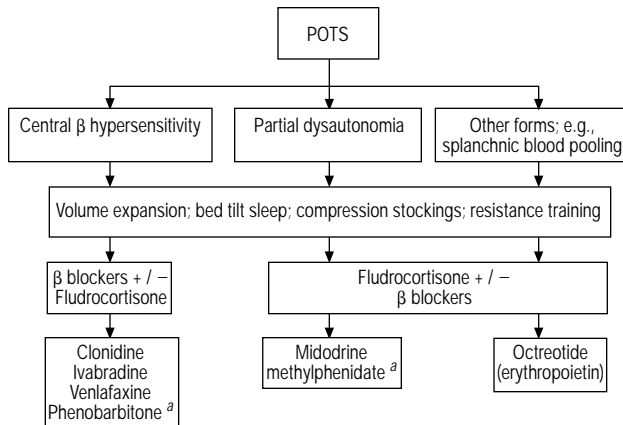


FIG. 5 The classification and management of postural orthostatic tachycardia syndrome (POTS). Nonpharmacologic measures, especially fluid replacement, form the bed rock in the management of all forms of POTS. Following this, in the central beta hypersensitivity form the addition of beta blockers is most appropriate and then, if necessary, fludrocortisone; in the partial dysautonomia form fludrocortisone followed by beta blockers is most appropriate. In the more resistant forms of POTS, the other agents listed above may be tried. There is only evidence for the use of phenobarbitone in the central hypersensitivity form and octreotide in the splanchnic vascular bed pooling form. ^a = risk of dependence.

beta hypersensitivity form usually have concomitant high serum catecholamine levels (norepinephrine > 600 ng/ml) and may exhibit an excessive increase in supine heart rate response to low-dose isoprenaline infusion (heart rate increase > 30 beats/min with 1 µg/min infusion).³⁶ In certain patients with the more common mild idiopathic partial dysautonomia form, there is excessive pooling of blood in the legs while standing;³⁹ others may exhibit sympathetic denervation of the skin by galvanic skin testing or quantitative testing of the sudomotor axon reflex.^{21, 33, 40, 41} However, this subtype of POTS is usually a diagnosis of exclusion. The other forms of POTS ("idiopathic hypovolaemia,"²⁴ splanchnic bed blood pooling,^{26,27} reduced red cell mass,²⁸ etc.) are rare and seldom require identification clinically as their management is similar to that of the partial dysautonomia form.

A 24- or 48-h Holter ECG recording may also occasionally capture short sudden bursts of sinus tachycardia triggered

and/or terminated by atrial premature beats characteristic of SNRT, exposing its paroxysmal nature (Fig. 6). In patients with very occasional palpitations, cardiac event recorders or even implantable monitors may be necessary to catch the underlying rhythm disturbance. In the vast majority of patients, however, electrophysiology studies are usually required to confirm the diagnosis beyond doubt.

Management (Table I)

Conservative and Nonpharmacologic Therapy

The majority of patients with transient short episodes of physiologic NST associated with emotion or physical exertion respond to simple reassurance and do not require treatment. For the other NSTs, the identification and elimination of the underlying cause is the mainstay of management.

Nonpharmacologic strategies, in particular intravascular volume expansion, form the bedrock in the management of POTS (Fig. 5). Many patients need 5–8 × 250 ml glasses of fluids daily and a high salt diet (10–15 g daily).²² Sleeping with the head of the bed elevated 4 inches^{42, 43} increases vasopressin secretion and expands plasma volume. Resistance training (e.g., water-based or weight-lifting exercises) combined with the use of physical countermeasures such as squatting have also been recommended.⁴⁴ The use of compression stockings, preferably thigh length, with an ankle pressure of at least 30 mmHg may also be useful.³⁶ The overlap in the pathogenesis of IST and POTS may imply that such conservative measures should also be considered for patients with IST, but there is a lack of firm clinical data to advocate their use.

Simple clinical vagal maneuvers such as carotid sinus massage and the Valsalva will usually terminate SNRT. Such measures may also be used as self-administered therapy in patients in whom drug therapy is contraindicated or intolerable.

Pharmacologic Therapy

Beta blockers are generally effective in the management of symptomatic and prolonged episodes of NST related to emotional stress and other anxiety-related disorders,^{1, 45–52} following acute myocardial infarction,^{53, 54} and in the acute management of symptomatic thyrotoxicosis in combination with carbimazole or propylthiouracyl while these curative treatments

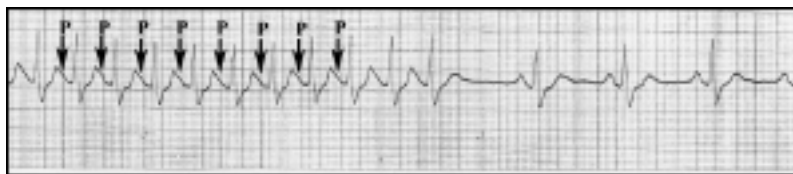


FIG. 6 A rhythm strip from a patient with narrow complex tachycardia illustrating a prolonged episode that responded to vagal maneuvers (carotid sinus massage). The differential diagnosis is sinus node reentry or atrial reentry tachycardia. Although the tachycardia P wave is almost hidden by the T wave of the previous beat, it was apparent from the 12-lead electrocardiogram that the tachycardia P-wave polarity was identical to that of sinus rhythm. The diagnosis of sinus node reentry was subsequently proven at electrophysiology study.

TABLE I A summary of the management of sinus tachycardia

Sinus arrhythmia	Management	Classification ^b of recommendation	Level ^a of evidence	
NST	Nonpharmacologic:	Treat / eliminate cause	I	C
	Pharmacologic:	i) β -blockers		
		a) Anxiety	I	B
		b) Acute myocardial infarction	I	A
		c) CCF	I	A
	ii) Ca^{++} channel blockers	IIa	C	
IST	Pharmacologic:	i) β -blockers	I	B
		ii) Ca^{++} channel blockers	IIa	C
	Invasive therapy:	Catheter modification/ablation sinus node	I	B
POTS	Nonpharmacologic:	i) Volume expansion ($\uparrow NaCl$ /fluid intake)	IIa	B
		ii) Head up tilt sleep	IIa	B
		iii) Physical manoeuvres/resistance exercises	IIa	B
		iv) Compression stockings	IIa	B
	Pharmacologic:	i) β -blockers	IIa	B
		ii) Mineralocorticoids (fludrocortisone)	IIa	B
		iii) β -blockers+fludrocortisone	IIa	B
		iv) Central sympatholytic agents (clonidine)	IIb	B
		iv) α receptor agonists:		
		a) centrally acting, e.g., methyphenidate	IIb	C
		b) peripherally acting, e.g., midodrine	IIb	C
		v) Serotonin specific reuptake inhibitors	IIb	C
		vi) Others:		
		a) Erythropoietin /octreotide /ergotamine	IIb	C
b) Phenylbarbitone	IIb	C		
Invasive therapy:	Catheter modification / ablation of sinus node	III	B	
SNRT	Pharmacologic:	i) β -blockers	I	C
		ii) Ca^{++} channel blockers	IIa	C
		iii) Class I(a) /I(c) /III agents	IIa	C
	Invasive therapy:	Catheter ablation	I	B

^a The level of evidence was ranked as follows. Level A (highest): data are derived from multiple randomized clinical trials; level B (intermediate): data are based on a limited number of randomized trials, nonrandomized studies, or observational registries; level C (lowest): the primary basis for the recommendation is expert consensus.

^b Classifying indications have been categorized as follows: Class I: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective. Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Class IIa: The weight of evidence or opinion is in favor of the procedure or treatment. Class IIb: Usefulness/efficacy is less well established by evidence or opinion. Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

Abbreviations: NST = normal sinus tachycardia, IST = inappropriate sinus tachycardia, POTS = postural orthostatic tachycardia syndrome, SNRT = sinus node reentry tachycardia, CCF = congestive cardiac failure.

take effect^{55,56} In addition, when NST becomes hemodynamically disadvantageous, for example, in congestive cardiac failure, it becomes a target for therapy in itself. Beta blockers are very appropriate in such settings; their use in congestive cardiac failure is strongly advocated, and this has been shown to have favorable prognostic implications.^{54,57-59} However, to avoid decompensation, extreme caution must be exercised in terms of both the initial dosages used and dosing intervals.

Beta blockers are the core management of IST and should be used first line in the majority of patients. Long-acting preparations are more appropriate in this setting, but the dose needs to be up-titrated slowly to prevent excessive bradycar-

dia during sleep. In POTS, beta blockers can also be used and may be the most effective monotherapy in the central beta hypersensitivity form. With the other forms of POTS they may be combined with fludrocortisone if necessary,^{60,61} but only after nonpharmacologic measures have been implemented. Unfortunately, the association of POTS with fatigue, exercise intolerance, and cold peripheries makes the use of beta blockers difficult in many patients. Beta blockers are ineffective for the prevention of sinus node reentry whereas other antiarrhythmic drugs may be helpful.³⁸

Calcium-channel blockers: The nondihydropyridine calcium-channel blockers such as verapamil and diltiazem are use-

ful alternatives to beta blockers in the management of sinus tachyarrhythmias, especially in patients intolerant of beta blockers or for those in whom beta blockers are contraindicated. There is evidence for their effectiveness in patients with NST secondary to acute myocardial infarction,⁶² symptomatic thyrotoxicosis,⁶³ and in patients with IST.⁶⁴ Verapamil has also been shown to be effective in terminating and preventing the reinduction of sinus node reentry.^{38,65}

Mineralocorticoids: Fludrocortisone, with or without bisoprolol (and probably other beta blockers), has been shown to be effective in POTS, particularly where partial dysautonomia and idiopathic hypovolemia are a feature, but this again requires a high salt/fluid intake and regular monitoring of plasma potassium levels.^{60,61} Fludrocortisone has also been combined effectively with sleeping in the head-up tilt position.⁴²

Specific bradycardic agents (e.g., ivabradine): This novel group of drugs, none of which have yet been approved for clinical use, is very likely to play a major role in the management of sinus tachyarrhythmias in the future.⁶⁶ These agents block the “funny” (I_f) current that is responsible for spontaneous depolarization in the sinus node pacemaker cells in order to achieve their bradycardic effects.⁶⁷ As such, they are free of the negative inotropic and hypotensive effects associated with beta blockers and calcium-channel blockers: fatigue, cold peripheries, or impotence. However, I_f channels are not confined to the sinus node and are also found in the retinal rod cells, liver, and testes. Visual phenomena including flashing lights and flickering vision have been reported with this class of drugs. Specific bradycardic agents have been shown to reduce effectively the physiologic NST induced by hydralazine administration in humans⁶⁸ and by emotional mental stress⁶⁹ and are likely to be particularly useful for patients with IST and POTS; however, there are no data to support this at present. They have also been shown to suppress effectively pathologic NSTs in acute myocardial infarction and cardiogenic shock settings.⁷⁰ Specific bradycardic agents, however, are likely to be of limited value in the pharmacologic management of SNRT.

Other useful agents: A variety of other agents have been used for the management of POTS with variable degrees of success. These include alpha (α) receptor agonists (e.g., centrally acting methylphenidate;⁷¹ or peripherally acting agents such as midodrine^{72,73}); central sympatholytic agents (e.g., clonidine^{31,72,74}); serotonin specific re-uptake inhibitors (e.g., venlafaxine⁷⁵); barbiturates (e.g., phenobarbitone³⁶); ergotamine; and the predominantly splanchnic vasoconstrictor octreotide.⁷³ Erythropoietin which increases red cell mass and has vasoconstrictor properties may benefit certain patients. However, evidence tends to suggest that patients most likely to respond to this therapy include those with orthostatic hypotension and not orthostatic tachycardia.^{28,76}

Adenosine, digoxin, or verapamil may be effective if vagal maneuvers fail to terminate an acute episode of SNRT.^{38,65} Vaughan Williams class Ia (e.g., disopyramide) / Ic (e.g., flecainide), class III (e.g., amiodarone), and class IV (verapamil) antiarrhythmic agents may help reduce the frequency of recurrent paroxysms.^{38,65}

Invasive Therapy (Catheter Modification/Ablation of the Sinus Node)

Invasive therapy plays no role in the management of NST or POTS. In fact, sinus node modification and/or ablation may worsen symptoms in individuals with POTS, with a large proportion requiring permanent pacing.⁷⁷ Catheter modification of the sinus node is potentially an important therapeutic option in the management of refractory cases of IST.³² This intervention involves destruction of the cephalic and most rapidly discharging portion of the sinus node. Although success rates of approximately 75% have been reported in the short term and 66% in the medium to long term, this intervention runs a risk of bradycardia which may need permanent pacing.^{78,79} Catheter modification of the sinus node is very effective treatment for SNRT with success rates close to 100%,⁸⁰⁻⁸⁴ but is considered only in patients with frequent episodes of tachycardia not responding adequately to drug therapy.⁸⁵

Conclusion

The benefits of treating sinus tachycardia in myocardial ischemia and cardiomyopathy are well established. The association between higher sinus rates and lower life expectancy, however, has led to an interesting debate about the value of treating “normal” heart rates in the general population. It has been postulated that lowering the heart rate in humans from 70 to 60 beats/min would increase life expectancy from 80 to 93.3 years.¹ However, before contemplating this unproven “pre-emptive” medical approach on a global scale, targeted accurate diagnosis and appropriate management of sinus tachycardias is essential not only for alleviating patient symptoms but also for the delivery of any potential long-term prognostic benefits to affected individuals.

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