Targeted Treatment of Inappropriate Sinoatrial Node Tachycardia Based on Electrophysiological and Structural Mechanisms

de Asmundis C. et al. (2022). American Journal of Cardiology, 183:24-32. https://doi.org/10.1016/j.amjcard.2022.07.041

Introduction

The current paper by C. de Asmundis[1] and colleagues reviews the causal mechanisms and treatment of Inappropriate Sinoatrial Tachycardia (IST). IST is a non-physiological elevation in resting heart rate such that resting daytime sinus rate is >100bpm and average 24-hr heart rate is >90bpm. Symptoms may include palpitations, exercise intolerance, dyspnea, fatigue, syncope, chest pain, anxiety, and depression. The typical patient comprises of young women around 30 years of age.

Causal Mechanisms of IST

There are electrophysiological mechanisms that are heterogenous in which all of these may coexist in a single patient. These include: dysfunctional intrinsic sinoatrial node (SAN) pacemaker automaticity (the SAN paces and drives the atrium); abnormal function of the cardiac autonomic nervous; and/or various forms of macro or micro-reentry. There is dysfunctional intrinsic SAN pacemaker automaticity in which it increases due to the complex interplay between iconic currents and autonomic modulation.

Familial Form of IST

Familial IST is rare and is a result of a pathogenic mutation in the HCN4 gene which leads to increased sensitivity to cAMP dependent activation and thus a faster than normal pacemaker rate.

Autonomic Dysfunction

Based on a canine model, the autonomic ganglia (AG) that innervate the SAN and the interganglionic nerve along the SVC may play a role in IST. In humans, autonomic dysfunction is associated with reduced sleep quality, higher proportion of shallow Phase 2 sleep, and inability to reach rapid eye movement (REM) phase. The IST high heart rate presenting even at night indicates the mechanism resides primarily in the SAN and autonomic dysfunction is a modulator rather than primary cause.

Role of Inflammation

Inflammation from viral illnesses and other non-infectious inflammatory diseases can increase HR without change in blood pressure and increase sympathetic nerve activity, altering sympathovagal balance.

Role of Anti β-adrenergic receptor antibodies

Anti β-adrenergic receptor antibodies stimulate the corresponding membrane receptors and increase cAMP. The pathogenesis is unclear, and these antibodies may be just a marker of inflammation.

Re-entry and Fibrosis

Re-entrant arrhythmias are a result of an anatomical or functional block as well as an excitable gap throughout the circuit. This can result from cardiomyopathy/inflammation-induced fibrosis of SAN and resulting conduction block. It has been observed that structural fibrotic remodeling always presents in SAN re-entry. Histologic findings indicated intranodal fibrotic strands are found in arrhythmic hearts and not healthy hearts.

Embryology Hypothesis of enhanced automaticity or re-entry

Embryological origins of pacemaker cells in areas around the SVC and SAN-SACP borders need more study to determine if they are present and contribute to the structural and functional mechanisms of IST.

Targeted Treatment of IST Based on Electrophysiological and Structural Mechanisms

Pharmacological treatment

Pharmacological treatment aims to reduce HR and symptoms; however, it has low success. First line treatment is long-acting β blockers. Alternative treatments are calcium-channel blockers and ivabradine. Ivabradine is not effective in up to 30% of patients.

Hybrid SAN sparing IST ablation

Hybrid SAN sparing IST ablation is a novel treatment using a right side thoracoscopic approach, 3-line epicardial lesion set with endocardial mapping and endocardial ablation if a gap is found; high acute success rate (100%) with 4% pacemaker implantation and 12-month recurrence rate of 8%. Longer term follow-up will be necessary to determine if symptom improvement is sustained after ablation.

Key Takeaways

- Electrophysiologic mechanisms of IST are not fully understood but data point toward an intrinsic abnormality of sinus node automaticity and concomitant autonomic dysfunction that might be primary or secondary (more likely) to IST.
- Pharmacologic and conventional ablation approaches to treatment are currently used but none are fully effective and thus further study of additional interventions, such as hybrid SAN-sparing ablation, are needed.

Reference:

1. *de Asmundis, C. et al. (2022). Targeted Treatment of Inappropriate Sinoatrial Node Tachycardia Based on Electrophysiological and Structural Mechanisms. Am J Cardiol. 183:24-32. https://doi.org/10.1016/j.amjcard.2022.07.041*

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