The sinoatrial node in medication-resistant inappropriate sinus tachycardia: to modify or to ablate?

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Inappropriate sinus tachycardia (IST) is defined as a resting heart rate >100 beats per minute (with a mean heart rate >90 beats per minute over 24 hours) associated with highly symptomatic palpitations(1). The syndrome is associated neither with structural heart disease nor with any secondary cause of sinus tachycardia(2) and evidence suggests that enhanced intrinsic automaticity of the sinoatrial node, which can be due to anti-β-adrenergic antibodies, is behind its genesis(3). However, it is benign in terms of clinical outcomes and echocardiographic evidence of ventricular dysfunction(4), being rarely associated with tachycardia-induced cardiomyopathy(3).

Patients with IST are essentially treated with ß-blockers to alleviate their symptoms(5). Ivabradine, a drug that inhibits funny calcium channels, particularly abundant in the SA node, showed modest benefit, receiving class IIa recommendation in the treatment of IST(4). But, the duration of medical therapy might be indefinite, and, a considerable number of patients would respond inadequately, or have no response, even after prolonged therapy(5). Historically, such patients would have subtotal right atrial excision, atrioventricular junctional ablation with permanent pacemaker implantation, or chemical occlusion of the sinus node artery(6). These options are considered today unacceptable in this setting, and other therapeutic approaches should be unveiled when resistance to medical treatment appears.

Electrophysiological study was initially purely diagnostic, but recent advances in technology have allowed us to intervene(7); patients with ventricular and supraventricular tachyarrhythmias are successfully treated with percutaneous catheter procedures. Of these, SA node ablation/ modification has been proposed as alternative approaches in IST that is not responding to medical treatment; trials reported auspicious results, highlighted here.

Electrophysiologic mapping to the site of the earliest endocardial activation during either spontaneous sinus tachycardia or isoproterenol-induced sinus tachycardia has rendered these procedures feasible(8). Additionally, combination with intracardiac echocardiography permitted a more accurate electrophysiologic and anatomic localization of the sinoatrial node(9).

Sinus node modification is not a focal ablation, but requires complete abolition of the cranial portion of the SA node complex, the one that exhibits the most of the autonomic activity(9). It is defined as successful when the heart rate decreases by 30 beats per minute (bpm) during isoproterenol infusion(8). Short-term success was also defined by other investigators when there was a reduction of the baseline sinus rate to less than 90 bpm and the sinus rate during isoproterenol infusion by more than 20% or by 25%(8). The acute success rate for modification has been varying between 76 and 100 % across trials, while long-term clinical outcomes are modest at best, with reported freedom from IST ranging from 23 to 85%(10).

Complications specific to SA node modification include superior vena cava (SVC) syndrome, diaphragmatic paralysis, and sinus node dysfunction(10). And while modification with conventional methods has its setbacks, modification using laser energy can be considered in the setting of IST. This modality creates clear-cut homogenous transmural lesions of the myocardium that comprises the scattered "functional" SA node(11). The burnt myocardium will then heal into a dense fibrous scar, decreasing potential amplitudes. And when adapting laser energy settings to the thickness of the myocardial wall, collateral damages such as esophageal fistulae, lung burns, and phrenic nerve palsy will be avoided(11); thus, this technique may prove itself as a new intriguing alternative for the safe and effective treatment of IST.

SA node modification is apt in achieving acute reductions in postprocedural heart rate. However, and as aforementioned, success rates are suboptimal in terms of symptomatic control with a significant recurrence rate(12). Catheter ablation aiming at either total exclusion and obliteration of the SA node has been described and performed, success being defined as a slowing of >50% from the baseline rate of tachycardia along with a junctional escape rhythm(12). With radiofrequency (RF) applications, the earliest local atrial activation time would shift from a cranial location to a more caudal one, usually at the mid-lateral right atrium(5). Reviews have reported that acute success rates were consistently to be as high as 88.9%, with an overall frequency of recurrence of 19.6%, the latter occurring within a wide range of post-ablation intervals, anywhere from a few weeks to several months after the procedure(12). Additionally, Takemoto and colleagues documented a significant drop in B-type natriuretic peptide levels, 6 to 12 months after ablation, suggesting fewer stretching shears on cardiac muscle.

Two types of response of the sinus tachycardia to RFA were observed across studies, whether a step-wise reduction in sinus rate accompanying migration of the site of earliest atrial activation in a cranial-caudal direction along the lateral right atrial wall, or an abrupt drop in heart rate in response to RFA at a focal site of earliest atrial activation(13).

However, RFA of inappropriate sinus tachycardia requires a large number of applications of radiofrequency energy and is, as in SA node modification, associated with a high recurrence rate(13). Complete remission is achieved only in approximately 50% of patients in some studies(14); longer history of IST and those reporting near syncope/syncope having a higher probability of recurrence(15).

While other studies have shown that RF ablation of the SA node can achieve even longer-term reductions in the sinus rate and relief of symptoms in two-thirds of patients with drug-refractory, inappropriate sinus tachycardia(13), aiming specific sites related to the SA node should be elaborated, for better and optimal outcomes Killu and colleagues created a lesion in the arcuate ridge resulting in complete abolition of the tachycardia, since arrhythmias arising in this region may exhibit both electrocardiographic and clinical similarities to IST(16). This has led to consider ablation of the arcuate ridge as a treatment of refractory IST, necessitating larger trials to confirm its potential role.

Phrenic nerve injury is a severe and dreaded complication of SN ablation(12). Pericarditis, right diaphragmatic paralysis, and SVC syndrome are other undesirable side effects of the procedures, variously reported in studies. but a common complication was observed in them all, atrial tachyarrhythmias(12). It has been hypothesized that myocardial pathology, such as inflammation and fibrosis, considered iatrogenic due to the ablation procedures, may be promoting arrhythmias both in the region of the SA node, as well as in remote locations(12). Through multivariable analysis, higher resting heart rates post-ablation and smaller cranial-to-caudal shifts have been defined as predictors of atrial arrhythmias(15). In conclusion, catheter ablation

could be considered an effective treatment for highly symptomatic, drug-refractory patients, even for those who did not respond to SA node modification(5).

The sinus node is located close to the epicardial surface and catheter-based ablations do not always make full-thickness lesions across the atrial muscle, leading to failure of the ablation(17), besides the numerous trabeculae and the widely variable anatomy.

Surgical ablation is not a first-line or routine management strategy for IST, but it has been proposed when IST resists or recurs after SN modification/ endocardial ablation(17). Effectively, in several studies, epicardial lesions, through a single small incision in one of the intercostal spaces, successfully slowed heart rate and shifted activation to a more caudal location, and surprisingly, subsequent endocardial lesions led to an even greater drop in heart rate and more caudal site of earliest activation(18). These outcomes were again replicated when using minimally invasive thoracoscopic ablation of the epicardial site of the SA node, concluding of the promising efficacy and the safety of this approach, since it preserves the phrenic nerve(17), although continued follow-up after surgery is required.

Medication-resistant IST remains a medical challenge for physicians and cardiologists; and in the era of great advances in interventional cardiology, its treatment remains debatable. Sinus node modification/ ablation is not recommended as first-line therapy in IST, this procedure should be considered only in drug-refractory patients who have severe symptoms(13). Although the number of patients in the available studies is generally small, both procedures have documented an encouraging success rate in the short-term, while being less impressive in the long-term. It has been hypothesized that this discrepancy is due to the relatively large potential area of atrial pacemaker cells(18); modification or ablation may fail to ablate or isolate all the pathways that comprise the functional SA node because they often target the anatomic part and the area of earliest atrial activation(19). Others have explained that the long-term slowing in rhythm fails because these procedures inconsistently produce transmural lesions in the right atrium. Surgical treatment of IST has proposed a solution to the latter conflict when isolating the SA node with a wide cuff of surrounding atrial muscle(19). And with the advent of bipolar RF clamps and minimally invasive cardiac surgical techniques with thoracoscopic guidance, this approach appears more appealing than before, especially when combined with endocardial ablation(19). But again, current data specifies employing these techniques in highly selected cases.

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