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ELECTROPHYSIOLOGY

CASE REPORT: CLINICAL CASE

Cardioneuroablation for the Treatment of Hypervagotonic Sinus Node Dysfunction

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ABSTRACT

Hypervagotonic sinus node dysfunction (SND) is a form of SND with sinus bradycardia caused by enhanced vagal tone. Indirect proof of hypervagotonia as the mechanism can be inferred from resolution of bradycardia following atropine infusion. In symptomatic patients, pacemaker implantation is recommended. We describe cardioneuroablation as a treatment for hypervagotonic SND. (J Am Coll Cardiol Case Rep 2024;29:102185) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 43-year-old woman was transferred for symptomatic sinus bradycardia. She had been admitted 1 week before presentation with weakness and lightheadedness.

PAST MEDICAL HISTORY

The patient had a history of hypertension, pulmonary embolism, psoriatic arthritis, schizoaffective disorder (bipolar type), and prior intravenous drug use on chronic methadone.

LEARNING OBJECTIVES

- To understand the role of hypervagotonia in symptomatic sinus node dysfunction.
- To review the indications and procedural steps for performing cardioneuroablation.
- To understand a novel potential indication for cardioneuroablation to treat hypervagotonic sinus node dysfunction as an alternative to permanent pacing.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for her sinus bradycardia includes fibrosis, infiltrative disease, medications, metabolic abnormalities, hypothyroidism, and increased vagal tone.

INVESTIGATIONS

Electrocardiogram (ECG) demonstrated sinus bradycardia at 37 beats/min (**Figure 1A**). There was no structural heart disease on transthoracic echocardiography, and thyroid function was normal.

MANAGEMENT

Clonidine and quetiapine were discontinued, and methadone was down-titrated significantly. Methadone was not completely discontinued because of concern for withdrawal. Despite washout of these

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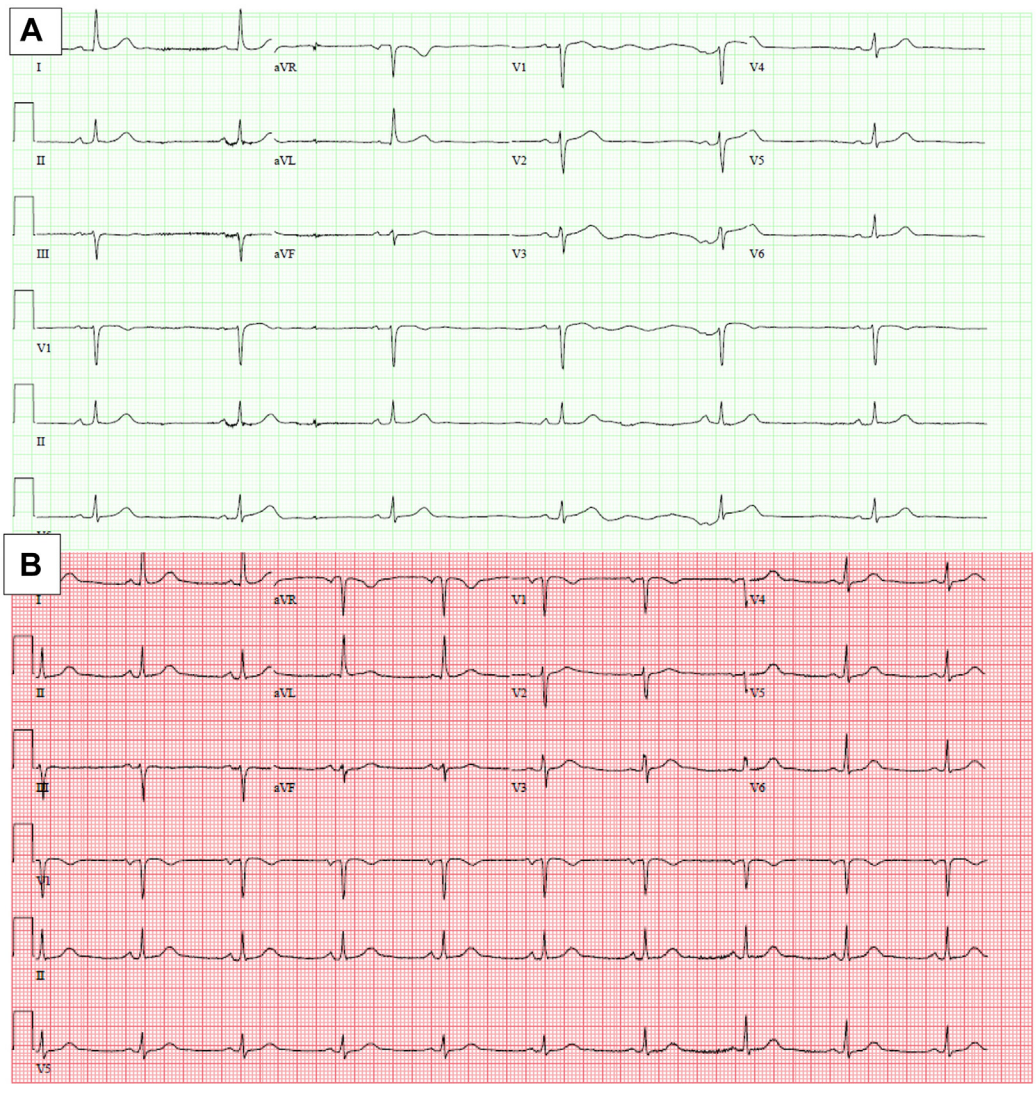
ABBREVIATIONS AND ACRONYMS

CNA = cardioneuroablation
ECG = electrocardiogram
GP = ganglionated plexus
HV = hypervagotonic
LA = left atrium
RA = right atrium
RAGP = right anterior ganglionated plexus
RSPV = right superior pulmonary vein
SND = sinus node dysfunction
SVC = superior vena cava

medications, the patient had lightheadedness and dizziness with persistent sinus bradycardia. A total of 2 mg of atropine was administered at the bedside with immediate resolution of sinus bradycardia and increase in heart rate to 65 beats/min. This type of response to atropine was consistent with hypervagotonic sinus node dysfunction (HV-SND).[1,2] A single-chamber atrial pacemaker was considered to treat her symptomatic HV-SND; however, given her age and history of intravenous drug misuse, this was not optimal because of increased infection risk. Cardioneuroablation (CNA) was attempted to effectively remove vagal efferent input to the sinus node.

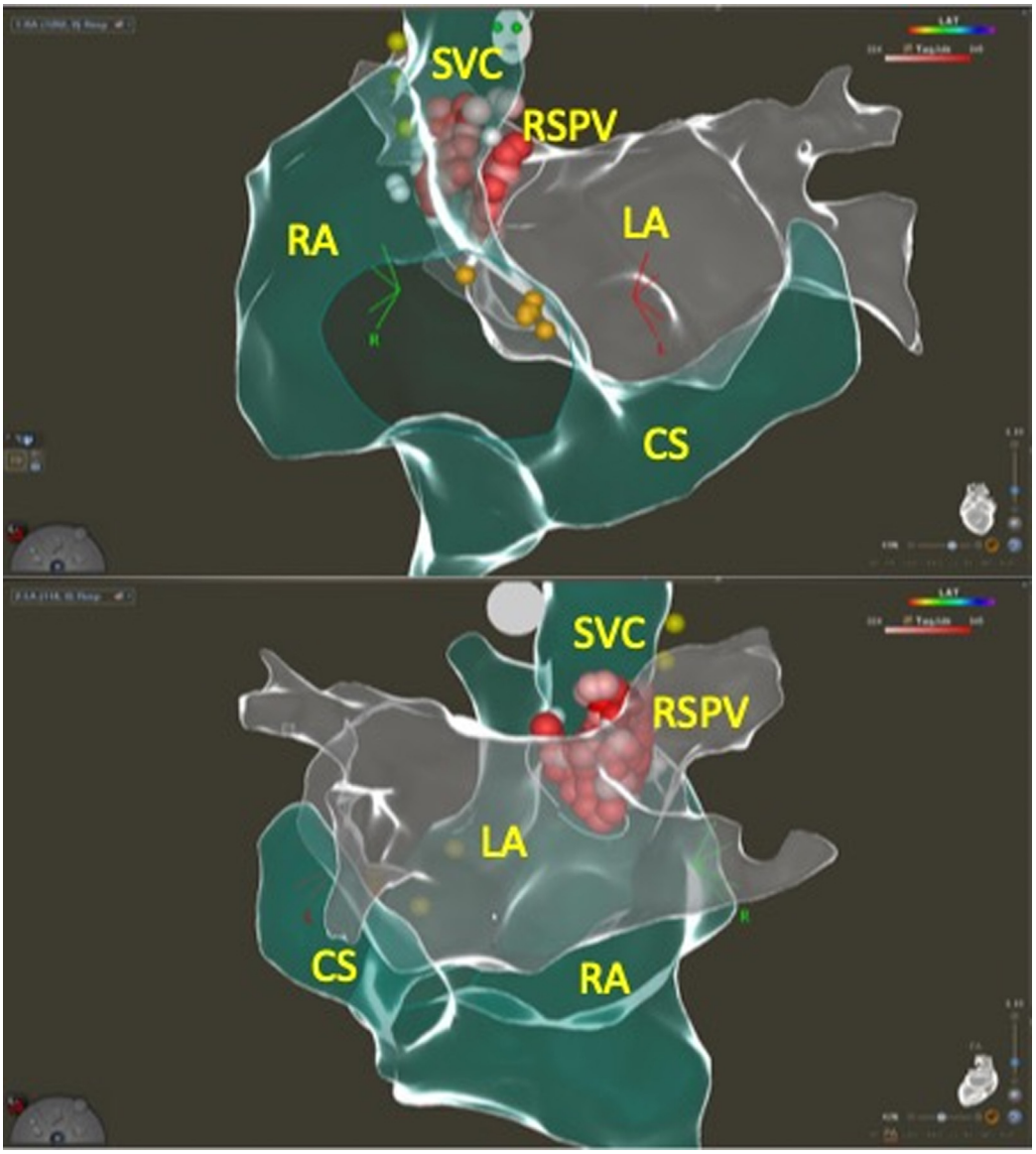
CNA was performed under general anesthesia. Baseline ECG showed sinus bradycardia at 40 beats/min. Anatomic reconstruction of the right atrium (RA) and left atrium (LA) was performed with a multipolar catheter (Pentaray, Biosense Webster, Inc) using the CARTO mapping system (Biosense Webster, Inc). Areas of electrogram fractionation anterior to the right superior pulmonary vein (RSPV) opposite to the septal aspect of the superior vena cava (SVC) were marked on the electroanatomic map.

FIGURE 1 Preprocedural and Postprocedural ECGs



(A) Baseline ECG. (B) Postprocedure ECG with a sinus rate of 57 beats/min. ECG = electrocardiogram.

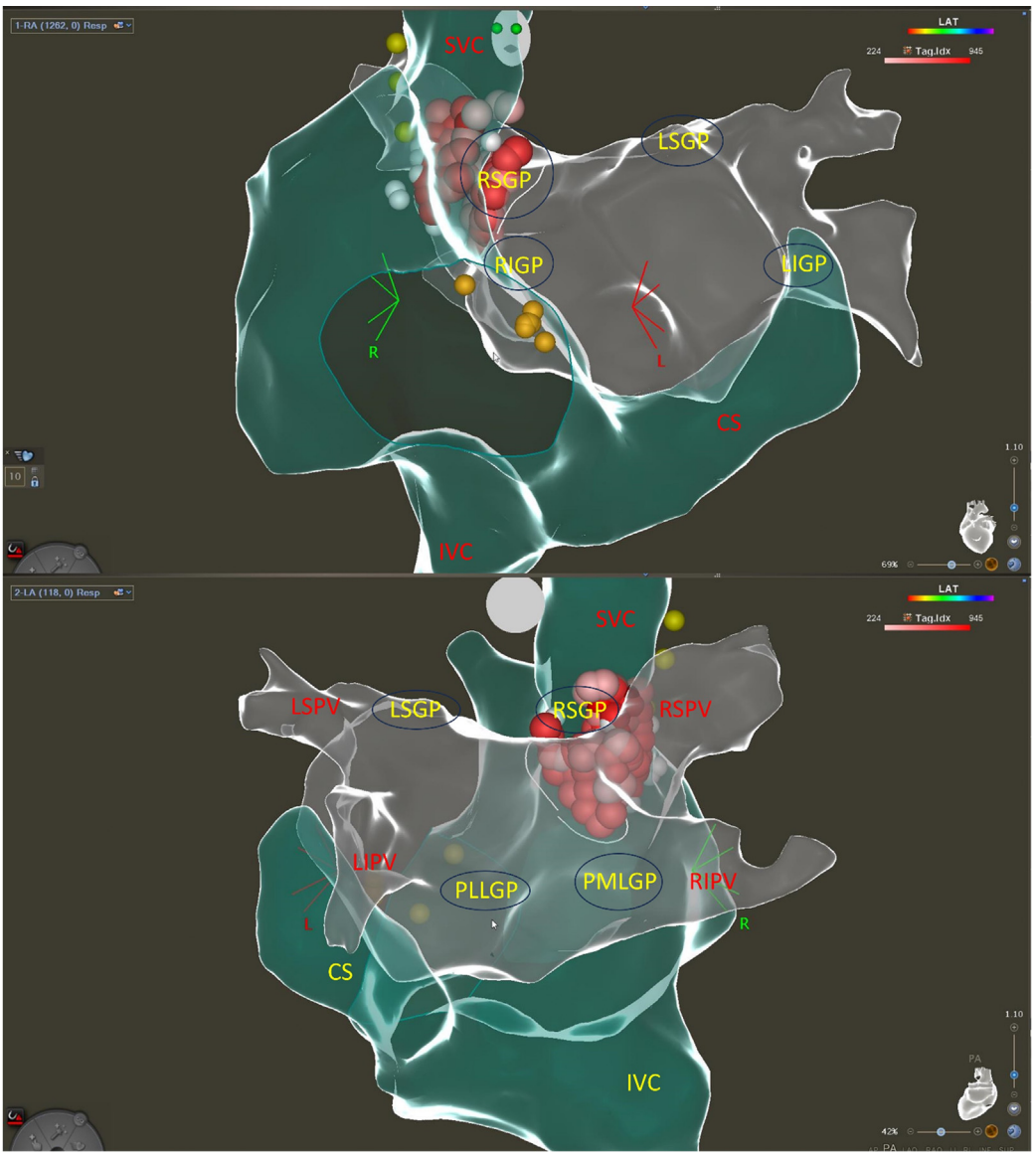
FIGURE 2 **Ablation Lesion Set**



A 3D electroanatomic map showing the CNA lesion set. Anteroposterior and posteroanterior view of the right atrium (RA), left atrium (LA), and superior vena cava (SVC) with ablation lesions in red at the RA ganglionic plexi. Yellow dots indicate the course of the right phrenic nerve. CS = coronary sinus; RSPV = right superior pulmonary vein.

Radiofrequency ablation was performed with point-by-point cluster lesions using an irrigated catheter (ThermoCool SmartTouch SF, Biosense Webster, Inc) with a power of 35 W for up to 60 seconds per lesion until complete elimination of the targeted LA and RA electrograms was observed (Figure 2). During ablation, resolution of the sinus bradycardia with an increase in sinus rates up to 68 beats/min was noted. At the end of the procedure, the sinus rate was 60 beats/min, and no change was observed following infusion of 2 mg of atropine, suggesting effective vagal denervation of the sinus node.

FIGURE 3 **Anatomic Locations and Targets for Ganglionated Plexi**

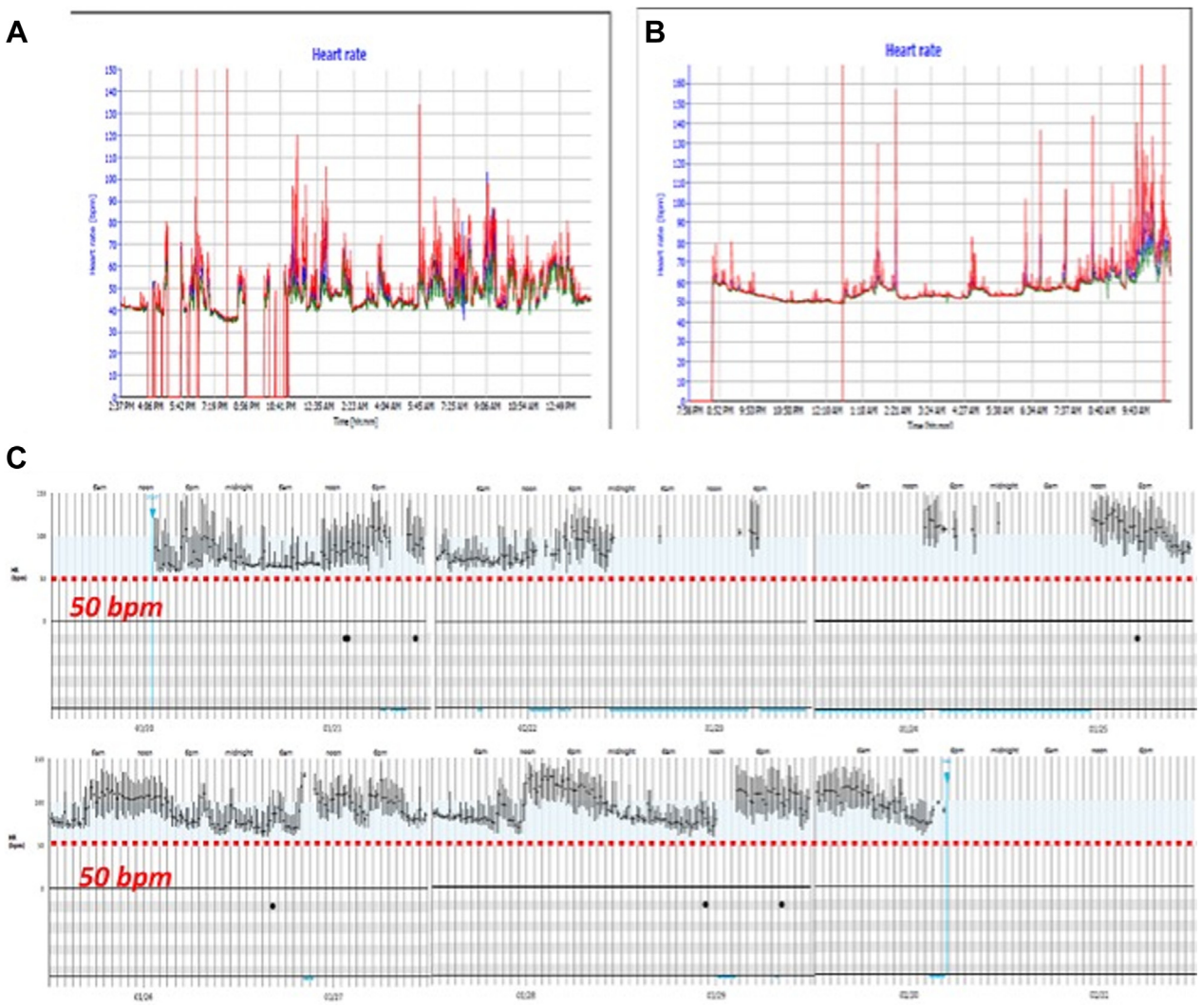


A 3D electroanatomic map with locations of major ganglionated plexi. The target of ablation for the plexus carrying parasympathetic input to the sinus node is the right superior ganglionated plexus (RSGP)/right anterior ganglionated plexus located between the right superior pulmonary vein (RSPV) and the superior vena cava (SVC). Others highlighted are the right inferior ganglionated plexus (RIGP), left superior ganglionated plexus (LSGP), left inferior ganglionated plexus (LIGP), posterolateral left atrial ganglionated plexus (PLLGP), and posteromedial left ganglionated plexus (PMLGP). IVC = Inferior vena cava.

DISCUSSION

HV-SND is a rare form of SND that manifests as symptomatic sinus bradycardia, particularly in young patients.[1,2] The diagnosis is based on clinical history and can be confirmed by evaluating the sinus rate response to atropine infusion. In the case of SND induced by an HV state (as opposed to SND caused by intrinsic disease of the sinus node), atropine infusion results in resolution of the bradycardia. We describe a case of CNA as an effective therapy for HV-SND. Through targeted ablation of the right anterior ganglionated plexus (RAGP) with sequential LA and RA radiofrequency ablation, pacemaker implantation

FIGURE 4 **Heart Rate Variability Preablation and Postablation**



(A) The 24-hour Holter of heart rate variability pre-CNA with the rate between 35 and 75 beats/min. (B) The 24-hour Holter postprocedure with the rate between 50 and 84 beats/min. (C) The 10-day extended Holter postdischarge with the heart rate consistently >55 beats/min.

in a young patient with high risk of downstream infection was avoided.

CNA targeting ganglionated plexi (GPs) was first described in 2005 by Pachon et al[3] in a series of 21 patients with neural-mediated syncope and symptomatic functional atrioventricular block. Since then, there has been growing interest in targeting GPs for vasovagal syncope with predominant cardioinhibitory response. However, few cases of CNA as a therapeutic option for HV-SND in the absence of syncope are described. The cardiac autonomic nervous system has 3 main components: an afferent sensory portion and 2 efferent branches (parasympathetic and sympathetic). The efferent fibers have preganglionic and postganglionic neurons. Central or extrinsic ganglia in the brain and along the spinal cord house the cell bodies for the sympathetic system, whereas the parasympathetic system consists of epicardial neural networks that converge in GPs located in specific anatomic areas (**Figure 3**). In particular, the RAGP receives and contains predominantly cholinergic input that is delivered to the sinus node muscarinic receptors and is responsible for the negative chronotropic effect. The RAGP consists of a

superior portion adjacent to SVC/RA junction near the posterosuperior surface and an inferior portion in the interatrial groove anterior to the RSPV (**Figure 3**).[4-6]

In contrast to the cranial posterolateral RA, which is targeted in sinus node modification, the RAGP lies in the interatrial groove between the posteroseptal RA and LA. Physiologically, with removal of efferent vagal input during CNA, inappropriate sinus tachycardia can be seen. Sinus slowing should raise suspicion of inadvertent sinus node ablation and unintentional sinus node modification.

We use a simple anatomic approach to locate and target the RAGP during CNA. This approach has been described by Rivarola et al., and is based on the reproducible location of the RAGP between the anterior aspect of the RSPV and the septal aspect of the SVC.[4,7,8] Fragmented multicomponent bipolar electrograms can be recorded here, which are thought to indicate proximity to the GP; however, this is nonspecific, as fractionated electrograms are also seen at other RA locations such as the crista and lateral SVC. High-frequency stimulation at the LA or RA sites adjacent to the RAGP has been used to confirm proximity to the GP.[8,9] However, there is no evidence that high-frequency stimulation is needed to effectively locate the RAGP, and prior studies using this strategy have targeted a similar anatomic area between the RSPV and the SVC. The simple anatomic approach to locating GPs can be applied to CNA for other populations, including those with dysautonomia. Nonetheless, further studies are needed to determine the optimal method to identify and target the vagal GPs.

Procedural endpoints for CNA are similarly heterogeneous. Most groups have focused on complete elimination of targeted electrograms and acute evidence of vagal denervation with an increase in the sinus rate. Atropine testing preablation and postablation is also helpful to determine the extent of vagal contribution to the baseline sinus rate and evaluate the sinus rate response following ablation. Ideally, once effective vagal denervation has been achieved, atropine infusion should not affect the sinus rates. In our case, the sinus rate obtained following CNA was comparable to that seen before the procedure after chemical vagal denervation with atropine. Additionally, repeat atropine infusion at the end of the procedure did not result in further increase in sinus rate, suggesting effective denervation. As a result, high-frequency stimulation was deferred.

CNA is being increasingly used as a therapeutic strategy for vasovagal syncope with predominant cardioinhibitory response and may have additional indications in cases of HV-SND like the one described in this report; however, more data are needed to establish the long-term efficacy and safety of this procedure. Similar to atrial fibrillation ablation, there remains a risk of perforation, tamponade, phrenic nerve palsy, and stroke if targeting the left-sided GPs in particular. Additional unique risks include injury to the sinus node artery as it crosses the aortocaval junction. Case series suggest that the risk of this is higher in elderly patients with acute aortic angulation for which a preprocedural computed tomography scan should be considered.[10] Continuous longitudinal follow up is crucial because there are reports suggesting vagal reinnervation within the first 6 months of a CNA in some patients.[11]

Finally, there is some evidence that medical therapy with theophylline can be beneficial in patients with hypervagotonia,[2] although in some cases, permanent pacing is still necessary to correct the bradycardia. In our case, we did not consider theophylline given the lack of conclusive data demonstrating safety and interaction with methadone use.

FOLLOW-UP

The patient was monitored for 24 hours following the procedure with no further episodes of sinus bradycardia and was subsequently discharged. A postprocedural 10-day ECG monitor showed sinus rate ranges of 58-147 beats/min and an average heart rate of 90 beats/min (**Figures 1B and 4**). The patient remained asymptomatic during a follow-up period of 10 months.

CONCLUSIONS

We report the successful use of CNA to treat symptomatic HV-SND. Additional large-scale studies are needed to determine the long-term efficacy and safety of this treatment modality.

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