Cardioneuroablation: Don't underestimate the posteromedial left atrial ganglionated plexus

Ciro Ascione, MD, Léa Benabou, MD, Mélèze Hocini, MD, Pierre Jaïs, MD, Michel Haïssaguerre, MD, Josselin Duchateau, MD, PhD

From the Hôpital Cardiologique Haut-Lévêque, CHU de Bordeaux, L'Institut de RYthmologie et modélisation Cardiaque (LIRYC), Université de Bordeaux, Bordeaux, France.

Introduction

Cardioneuroablation (CNA) is a technique used to modulate cardiac parasympathetic tone in patients with sinoatrial (SA) and atrioventricular (AV) vagally mediated syncope. We describe the case of a patient who developed AV block after a first procedure of CNA, requiring a completion.

Case report

A 47-year-old man with a medical history of obstructive sleep apnea syndrome and gastric bypass surgery for obesity presented repetitive episodes of reflex syncope. These episodes first appeared in 2010 and were associated with vegetative symptoms. Tilt table testing in another institution was able to reproduce the reflex syncope and demonstrated a VASIS type 1 profile (mixed response with drop in blood pressure and bradycardia, no asystole). In 2018 episodes progressively increased in frequency, and additional neurological investigation with an electroencephalogram and brain magnetic resonance imaging were performed, without any abnormal findings. Syncopal episodes became extremely frequent and recurred on a daily basis by the end of 2021. In November 2021 the patient underwent a video electroencephalogram, during which vasovagal sinus arrest was shown to precede the syncopal event (Supplemental Figure 1). The patient was then referred to our institution.

Physical examination was completely normal, and blood pressure was 120/80 mm Hg. The electrocardiogram showed sinus rhythm at 67 beats per minute (bpm), and normal AV and intraventricular conduction without repolarization alterations. Blood tests were unremarkable. He was under budesonide/formoterol and salbutamol inhalation therapy for asthma. During the electrocardiogram monitoring, different episodes of sinus bradycardia and symptomatic sinus pauses were documented, lasting up to 17 seconds at night. Since all the episodes were concomitant to high-vagal-status conditions and associated with parasympathetic signs and symptoms, a CNA procedure under general anesthesia was scheduled. Preprocedural atropine test was decided to not be performed in this case.

The patient was brought to the electrophysiology (EP) laboratory on January 26, 2022. He was in sinus rhythm at 59 bpm. A preliminary EP study showed borderline SA nodal function (after 1 minute of atrial pacing at 600 ms sinus node recovery time [SNRT] was 1460 ms, corrected SNRT was 420 ms). AV and HV intervals were, respectively, 50 and 46 ms, and the AV Wenckebach point (WP) was 540 ms.

The vagal nerve stimulation was performed with a quadripolar catheter placed inside the internal right jugular vein at the level of the upper wisdom tooth, using a standard cardiac pacing system (EPS320; Micropace, Canterbury, NSW, Australia. Frequency: 30 Hz, pulse width: 0.5 ms, current intensity: 25 mA), in the absence of a dedicated neural stimulator. It elicited a moderate response with a heart rate drop of 17 bpm (from 63 bpm to 46 bpm).

A map of both right and left atria (Figure 1) was obtained using a multipolar catheter (PentaRay; Biosense Webster Inc, Diamond Bar, CA). Ablation of the right superior and

KEY TEACHING POINTS

- Different ganglionated plexi (GPs) have different effects on sinoatrial (SA) and atrioventricular (AV) conduction. While the superior right and posterior right GPs mostly affect the SA node, the predominant AV node influences come from the posteromedial left GP.
- It is important to consider ablation for ganglia that converge on both SA and AV node, since functional AV block could be masked by concomitant SA bradyarrhythmia.
- Acute success indicators of cardioneuroablation should not be overestimated.

KEYWORDS Cardioneuroablation; Catheter ablation; Syncope; Vagal denervation; Ganglionated plexi

(Heart Rhythm Case Reports 2023;9:67–69)

Funding Support: This work was supported by the Agence Nationale de la Recherche (grant no. IHU LIRYC ANR-10-IAHU-04). Disclosures: The authors declare that there are no conflict of interests. **Address reprint requests and correspondence:** Dr Ciro Ascione, Division of Cardiac Electrophysiology, CHU de Bordeaux, Av. Magellan, 33604 Pessac, France. E-mail address: ciroascione92@gmail.com.

https://doi.org/10.1016/j.hrcr.2022.10.012

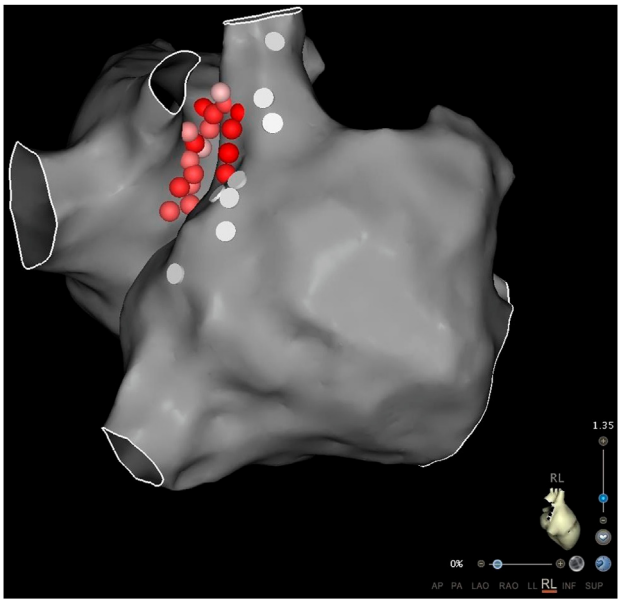

Figure 1 Three-dimensional mapping of the right and left atria at the time of the first procedure. White dots represent phrenic nerve capture at high output pacing, red dots represent ablation sites.

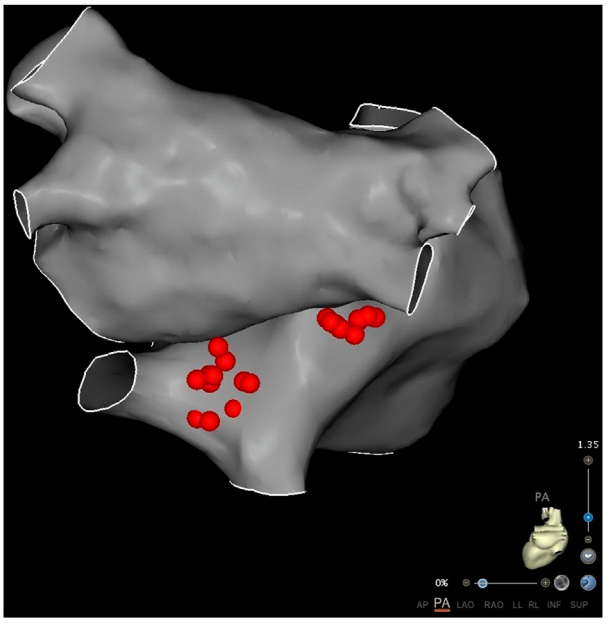

Figure 2 Three-dimensional mapping of the right and left atria at the time of the second procedure. Red dots represent ablation sites.

posterior ganglionated plexi (GP) was performed using a computed tomography–guided anatomical approach, both from left and right atria. The computed tomography segmentation was merged with the biatrial electroanatomical map.

After the ablation, the EP parameters were tested again, with an improvement of SNRT (1060 ms, pacing at 600 ms) and WP at 360 ms. Right vagal stimulation no longer elicited a significant heart rate drop.

During the first night after the procedure, the patient had a recurrent episode of syncope with high-grade AV block (Supplemental Figure 2). Sinus bradycardia or arrest was no longer recorded.

The patient was brought back to the EP laboratory the next day for a second procedure, this time under conscious sedation. Basal heart rate was 83 bpm. AH, HV, and PR intervals were, respectively, 50, 54, and 138 ms; the AV WP was 320 ms and AV effective refractory period was 250 ms for a baseline cycle length of 600 ms. Since general anesthesia was not available, vagal nerve stimulation was not performed. The posteromedial left atrial GP was targeted this time, at the level of the coronary sinus ostium, from the right and left atria (Figure 2). After the ablation there was no sensible change in basal HR, the PR interval was slightly reduced to 120 ms (AH 32 ms, HV 56 ms), the WP decreased to 290 ms, and AV nodal effective refractory period decreased to below 200 ms.

A loop recorder (Biotronik BIOMONITOR) was implanted before discharge. At 4 months of follow-up, no bradyarrhythmias or recurrent syncopal episode were documented, and the patient has had no recurrent syncope.

Discussion

CNA is a treatment for neurocardiogenic syncope, consisting of autonomic denervation via catheter ablation of GPs in both left and right atria.[1] It is a technique described to modulate both SA and AV bradyarrhythmia, with good long-term clinical outcomes.[2,3] GPs are embedded in epicardial fat pads[4] and there is no general consensus on nomenclature. The ones commonly targeted, according to the classification made by Armour and colleagues,[4] are the superior right atrial GP (SRGP) and the posterior right atrial GP (PRGP), respectively on the posterior superior surface of the right atrium adjacent to the superior vena cava and on the posterior surface of the right atrium adjacent to the interatrial groove, also referred to as a single element: the right atrial GP; the superior left GP on the posterior surface of the left atrium between the pulmonary veins; the inferior left GP, located in the inferoposterior area around the root of the left inferior pulmonary vein; the PRGP on the posterior surface of the right atrium adjacent to the interatrial groove; and the posteromedial left atrial GP (PMLGP), located between coronary sinus ostium and lower part of the left atrium.[4,5]

In canine models, there was a predominance of right vagal projections ending on SA nodal tissue.[6] The posterior and superior right GPs have been demonstrated to mediate vagal influences preferentially via the SA node,[6,7] and SRGP stimulation in some human studies has shown to affect the SA node activity without AH interval prolongation.[8,9] In animal models, the sole ablation of the SRGP has been shown to mitigate both the right and left vagal nerve stimulation–induced bradycardia, but to reduce only right vagal nerve–mediated AH interval prolongation, without significant effect on the left vagal nerve influence.[10] In humans, there were no statistical differences in heart rate modification after superior left GP, inferior left GP, and inferior right GP ablation, whereas heart rate increased significantly after SRGP (which was referred to as right anterior GP) ablation.[11] For this

reason, Right Superior and Right Posterior GPs are considered by some authors as the primary targets of CNA, even if other studies showed that in some cases there is a residual response to vagal nerve stimulation, which is eliminated through ablation of other GPs.[12]

On the other hand, stimulation of the left vagus nerve elicited a greater change in AV conduction time than did right vagal stimulation.[13] In addition, supramaximal left vagal stimulation is more likely to produce severe AV block than right vagal stimulation.[14] Based on different canine studies, this effect seems to be mediated through the PMLGP, located at the inferior vena cava–left atrial junction, in close proximity to the CS ostium.[6,7]

Our patient had repetitive episodes of SA bradycardia and SA block, which may have masked any AV conduction alterations. There is currently no consensus on how to perform can; hence our initial approach was conservative, and anatomically guided ablation[15] was restricted to the right superior and right posterior GPs, which innervate the SA node.

Given the unavailability of a dedicated system, the vagal nerve stimulation was performed only during the first procedure with a standard EP pacing system, with the possibility to achieve only submaximal activation. Also, left vagal pacing could have unmasked a functional AV block, but for the aforementioned physiological principles vagal stimulation was performed only from the right side. Another way to facilitate AV block exposure, not performed in this case, is to pace from the atrium during the vagal stimulation.

Vagal denervation owing to the ablation reduces heart rate variability and makes the heart unresponsive to atropine.[1,2] An atropine challenge test may be performed to evaluate the sinus node functionality and to assess the efficacy of the procedure. In our case, however, it should be noted that the sinus node appeared entirely denervated after the first procedure, and hence the result of atropine test would likely have been noncontributory.

Conclusion

This case report demonstrates that ablation restricted to the SRGP/PRGP may not be enough for neurocardiogenic syncope due to sinus arrest, even after what could be considered a good acute outcome. Functional AV block may be masked by the concomitant SA bradyarrhythmia. A more systematic approach, extending the ablation to the PMLGP, should be considered.

Appendix
Supplementary Data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2022.10.012.

References

1. Pachon JC, Pachon EI, Pachon JC, et al. 'Cardioneuroablation' - new treatment for neurocardiogenic syncope, functional AV block and sinus dysfunction using catheter RF-ablation. Europace 2005;7:1–13.
2. Pachon JC, Pachon EI, Cunha Pachon MZ, Lobo TJ, Pachon JC, Santillana TG. Catheter ablation of severe neurally meditated reflex (neurocardiogenic or vasovagal) syncope: cardioneuroablation long-term results. Europace 2011;13:1231–1242.
3. Pachon JC, Pachon EI, Lobo TJ, et al. Syncopal high-degree AV block treated with catheter RF ablation without pacemaker implantation. Pacing Clin Electrophysiol 2006;29:318–322.
4. Armour JA, Murphy DA, Yuan BX, Macdonald S, Hopkins DA. Gross and microscopic anatomy of the human intrinsic cardiac nervous system. Anat Rec 1997;247:289–298.
5. Pauza DH, Skripka V, Pauziene N, Stropus R. Morphology, distribution, and variability of the epicardiac neural ganglionated subplexuses in the human heart. Anat Rec 2000;259:353–382.
6. Ardell JL, Randall WC. Selective vagal innervation of sinoatrial and atrioventricular nodes in canine heart. Am J Physiol 1986;251:3–5.
7. Lazzara R, Scherlag BJ, Robinson MJ, Samet P. Selective in situ parasympathetic control of the canine sinoatrial and atrioventricular nodes. Circ Res 1973;32:393–401.
8. Carlson MD, Geha AS, Hsu J, et al. Selective stimulation of parasympathetic nerve fibers to the human sinoatrial node. Circulation 1992;85:1311–1317.
9. Quan KJ, Lee JH, Geha AS, et al. Characterization of sinoatrial parasympathetic innervation in humans. J Cardiovasc Electrophysiol 1999;10:1060–1065.
10. Hanna P, Dacey MJ, Brennan J, et al. Innervation and neuronal control of the mammalian sinoatrial node a comprehensive atlas. Circ Res 2021;128:1279–1296.
11. Hu F, Zheng L, Liang E, et al. Right anterior ganglionated plexus: the primary target of cardioneuroablation? Heart Rhythm 2019;16:1545–1551.
12. Pachon -MEI, Pachon MJC, Higuti C, et al. Relation of fractionated atrial potentials with the vagal innervation evaluated by extracardiac vagal stimulation during cardioneuroablation. Circ Arrhythm Electrophysiol 2020;13:e007900.
13. Irisawa H, Caldwell WM, Wilson MF. Neural regulation of atrioventricular conduction. Jpn J Physiol 1971;21:15–25.
14. Hamlin RL, Smith CR. Effects of vagal stimulation on S-A and A-V nodes. Am J Physiol 1968;215:560–568.
15. Piotrowski R, Baran J, Kułakowski P. Cardioneuroablation using an anatomical approach: a new and promising method for the treatment of cardioinhibitory neurocardiogenic syncope. Kardiol Pol 2018;76:1736–1738.