JACC: CASE REPORTS VOL. 4, NO. 15, 2022

MINI-FOCUS ISSUE: ELECTROPHYSIOLOGY

ADVANCED

CASE REPORT: CLINICAL CASE

Treatment of Symptomatic Functional Atrioventricular Block by Cardioneuroablation as an Alternative to Pacemaker Implantation

Jose Carlos Pachon-M, MD, PhD,[a,b,c] Felipe Augusto Ortencio, MD,[a] Enrique Indalecio Pachon-M, MD, PhD,[a,b,c] Tasso Lobo, MD,[a] Tomas Guilhermo Santillana-P, MD,[a] Carlos Thiene Pachon, MD,[a] Maria Zelia Cunha-P, MD,[b] Juan Carlos M. Pachon-M, MD, PhD,[a,b,c] Juan Carlos Zerpa-A, MD,[a] Ricardo Carneiro Amarante, MD, PhD[a,b,c]

ABSTRACT

A woman with recurrent presyncope caused by a functional atrioventricular (AV) block after meals, with limiting symptoms, underwent cardioneuroablation and AV node vagal denervation without pacemaker implantation. Normal AV conduction was recovered with complete abolishment of symptoms. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:990-995) © 2022 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/).

PRESENTATION

The patient was a 57-year-old woman who had begun to have recurrent episodes of presyncope after meals approximately 6 months earlier. She reported significant deterioration in her quality of life because of the constant need to control her diet and fear of unpredictable symptoms in public or in an unsupportive environment. The patient's history included a thyroidectomy 3 years earlier, 2 cesarean sections, and an appendectomy. She also had a normal electrophysiological study (EPS) 3 years earlier because of asymptomatic sinus pause.

LEARNING OBJECTIVES

- To understand that functional AV block by autonomic reflex is a common entity with challenging clinical management and that cases with limiting symptoms are typically treated with pacemaker implantation.
- To realize that—rather than pacemaker implantation—AV block may instead be treated with cardioneuroablation, which uses endocardial ablation to achieve vagal denervation, eliminating the functional inhibition of the AV node without pacemaker implantation.

INVESTIGATION

Results of the patient's resting electrocardiogram, echocardiogram, carotid Doppler, blood tests, and thyroid function were all normal. The 24-hour Holter monitoring showed a mean-minimum heart rate of 77/39 beats/min with periodic pauses of up to 2.6 seconds caused by a Mobitz II second-degree

From the [a]Sao Paulo University, São Paulo, Brazil; [b]São Paulo Heart Hospital, São Paulo, Brazil; and the [c]Dante Pazzanese Cardiology Institute, São Paulo, Brazil.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received January 25, 2022; revised manuscript received March 28, 2022, accepted April 27, 2022.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.04.029

atrioventricular block (AVB), 2:1 conduction, and high-degree AVB after meals. In stress testing, the patient's maximum heart rate was 141 beats/min with normal atrioventricular (AV) conduction. A 7-day loop recording showed several pauses in the heartbeat after meals caused by second-degree degree Mobitz II AVB, 2:1 conduction, and high-degree AVB without sinus depression, followed by presyncope (Figure 1). Invasive EPS was performed with pharmacologic testing. Basal EPS parameters were normal. The ajmaline challenge (1 mg/kg per 5 minutes intravenously [IV]) was negative for Brugada syndrome and showed normal His-Purkinje conduction. As expected, adenosine induced a 13-second AVB. Atropine (2 mg IV) showed a good response (heart rate from 55 to 75 beats/min and Wenckebach from 140 to 165 beats/min). Ventricular stability was normal. Thus, functional AVB was considered because organic AVB was ruled out. Therefore, cardioneuroablation (CNA) was indicated with the aims of AV node denervation and avoiding pacemaker implantation. The patient was informed of the risks and benefits of all therapeutic possibilities and agreed to the procedure.

MANAGEMENT

The CNA was performed under general anesthesia controlled by bispectral index monitoring. The procedure focused on AV node vagal denervation by anatomic landmarks with 3-dimensional (3D) electroanatomic fractionation mapping (Ensite Velocity, Abbott) to tag atrial fibrillation (AF) nests, mainly related to the third and fourth ganglionated plexus areas. Progressive denervation was controlled and confirmed by extracardiac vagus nerve stimulation (ECVS) (10 to 50 Hz/50 μs/70 V) (Figure 2) through the right and left internal jugular veins near the jugular foramen. Basal ECVS reproduced the AVB without and with atrial stimulation (Figure 3A). At the conclusion of the procedure, the ECVS was repeated, showing a reduction in the vagal response of the sinus node and the absence of an AV node response, completely eliminating the induced AVB and confirming the vagal denervation (Figures 3B and 3C). No further denervation of the sinus node was necessary. The final ablated points are shown in the 3D model in Figure 4.

ABBREVIATIONS AND ACRONYMS

3D = 3-dimensional
AF = atrial fibrillation
AV = atrioventricular
AVB = atrioventricular block
CNA = cardioneuroablation
ECVS = extracardiac vagus nerve stimulation
EPS = electrophysiological study

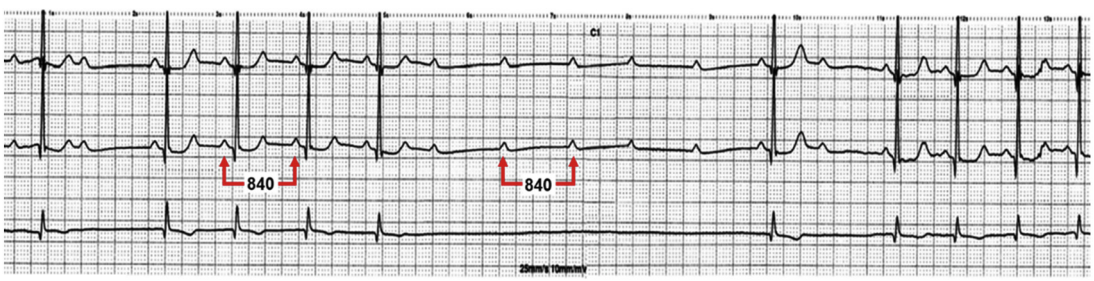
FOLLOW-UP

At 24 months after the procedure, the patient remained totally asymptomatic, with normal sinus rhythm and absence of AVB on both the electrocardiogram and in serial 24-hour Holter monitoring, even after copious meals. No further AVB has occurred (Figure 5).

DISCUSSION

Symptomatic AVB is a severe entity, which may be progressive and can confer a significant risk of falls, accidents, and sudden death.[1] It has organic and functional causes. The latter presents the greatest clinical challenge because, despite its better prognosis, reversibility is not always achieved, and its intermittent and erratic presentation often makes treatment difficult, causing morbidity and lower quality of life. CNA was first proposed in the 1990s and published in 2004,[2,3] with the aim of treating functional bradyarrhythmias without pacemaker implantation. The goal was to achieve long-term partial vagal denervation through endocardial ablation of

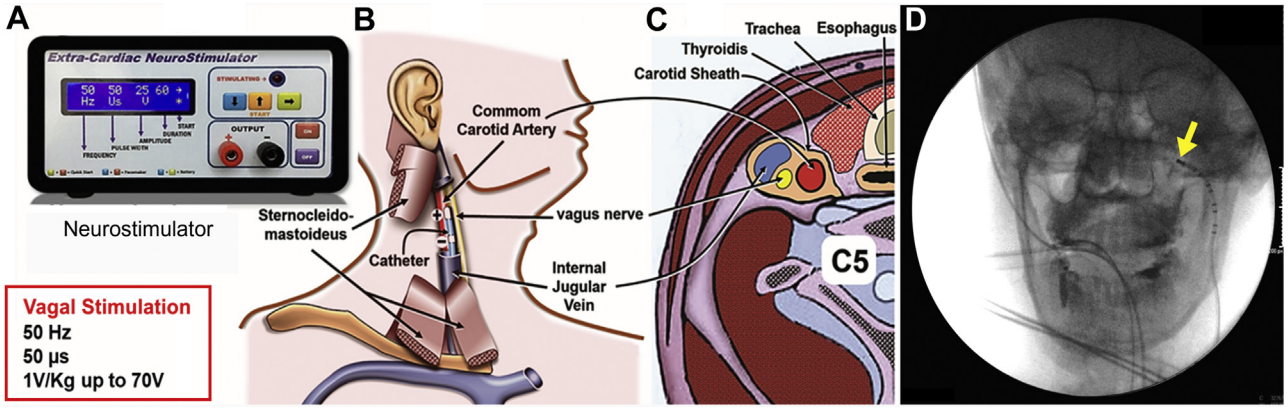
FIGURE 1 7-Day Loop Recording Showing Symptomatic Paroxysmal High-Degree Atrioventricular Block After Meals



There is no PP interval modification.

JACC: CASE REPORTS, VOL. 4, NO. 15, 2022
AUGUST 3, 2022:990–995

FIGURE 2 Extracardiac Vagal Stimulation

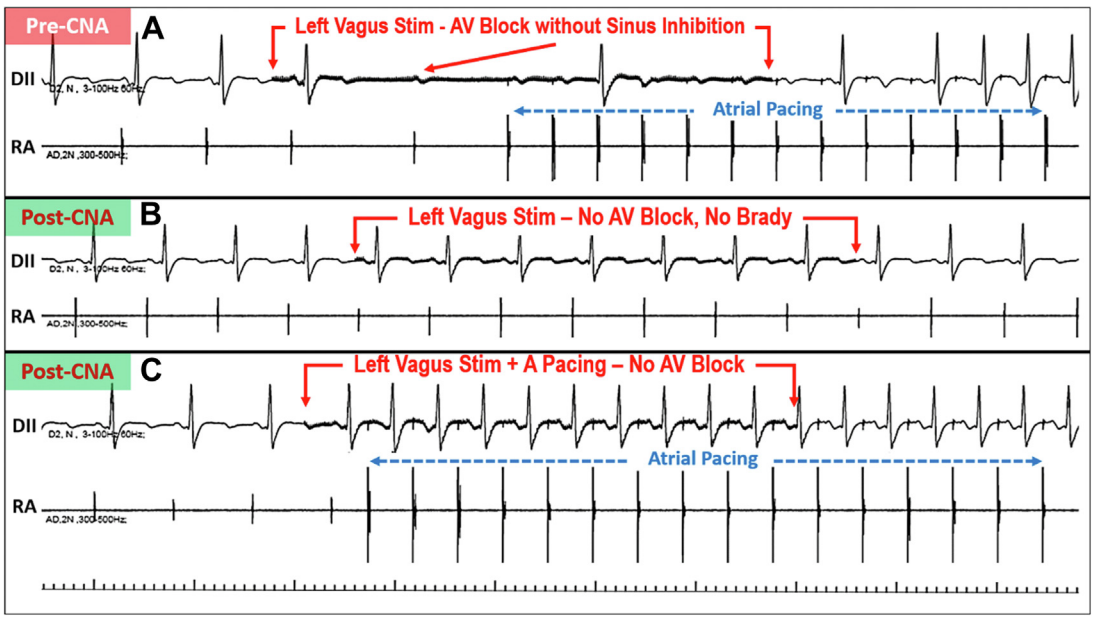


(A) Neurostimulator. **(B)** Catheter progression within the internal jugular vein. **(C)** Close relationship of the vagus with the vein. **(D)** X-ray with the catheter placed at the left jugular foramen **(yellow arrow)**.

the postganglionic vagal neurons in atrial walls and in the epicardial ganglionic plexuses.[3,4]

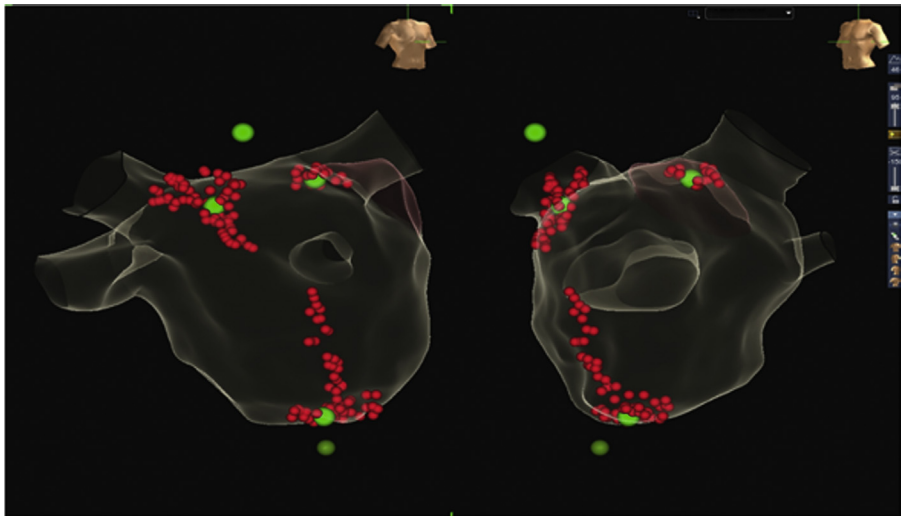
Three fundamental steps of CNA are mapping of the neuromyocardial interface, demonstration of the vagal effect, and confirmation of vagal denervation. At the beginning, the neuromyocardial interface was accessed by online spectral mapping of AF nests,[2,5] giving rise to anatomic maps, which currently allow purely anatomic CNA to be performed by presuming the positions of the main ganglionic plexuses.

FIGURE 3 Left Vagus Stimulation Pre- and Post-CNA



(A) Left vagus stimulation pre-cardioneuroablation (CNA), showing vagal atrioventricular block (AVB) without sinus node depression. **(B)** Left vagus stimulation post-CNA, showing no bradycardia and no AVB. **(C)** Left vagus stimulation post-CNA showing no AVB, even with high-frequency atrial pacing. A Pacing = atrial pacing; AV = atrioventricular; Brady = bradycardia; Stim = stimulation.

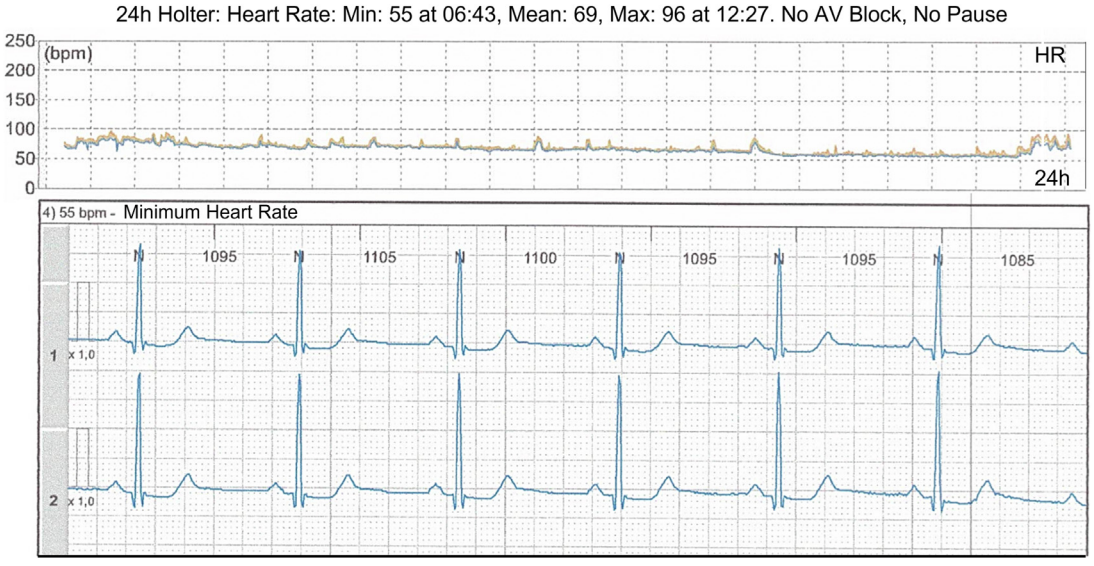
FIGURE 4 **Atrial Fibrillation Nest Mapping of Sites of Cardioneuroablation Radiofrequency Application and Presumed Location of Ganglionated Plexuses**



Red dots indicate sites of cardioneuroablation radiofrequency application and **green dots** indicate the presumed location of ganglionated plexuses in a 3-dimensional navigation system (Ensite Velocity, Abbott) obtained by atrial fibrillation nest mapping using fractionation software.

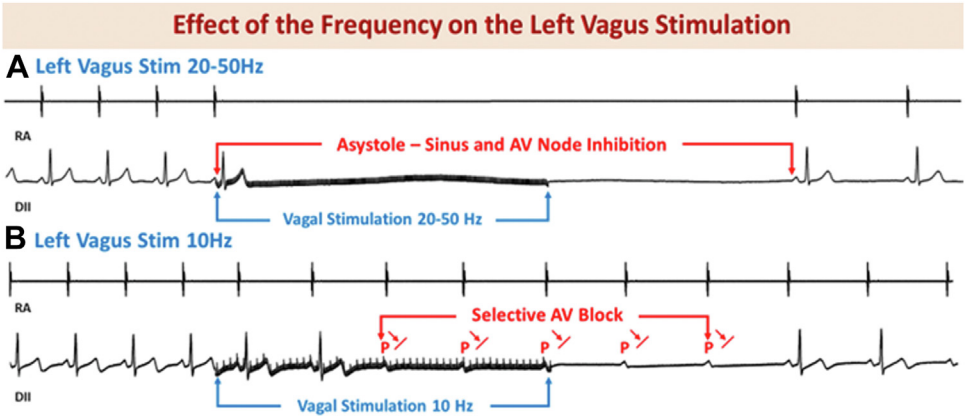
However, owing to high interindividual variability, it is recommended that it be complemented by AF nest ablation.[5] In a normal heart, these structures are directly related to innervation.[2,6] They may be found by spectral mapping, conventional filtered recordings, or—more simply—by using the fractionation mapping software we developed in 2005,[7,8] which can tag potential innervation areas in a 3D electroanatomic model. The other fundamental steps of CNA, demonstration of the vagal effect pre-CNA (**Figure 3A**) and complete elimination of vagal action post-CNA, are easily achieved with ECVS by placing

FIGURE 5 **Holter Monitoring 24 Months Post-Cardioneuroablation Showing Normal Atrioventricular Conduction**



AV = atrioventricular; HR = heart rate.

FIGURE 6 Selective AV Block Induced by Extracardiac Vagus Nerve Stimulation



Different responses to the extracardiac vagus nerve stimulation depending on the frequency. Left vagus stimulation at 10 Hz may reproduce the selective atrioventricular (AV) nodal inhibition without sinus depression.

an EP catheter inside of the left internal jugular vein (Figure 2). The latter is the best endpoint for CNA (Figures 3B and 3C).

Thus, with CNA directed to the innervation of the AV node,[3] it was possible to abolish reflex AV cardioinhibition[2,8,9] and recover physiological nodal AV conduction, even long term.[4] The patient's symptoms were completely abolished without pacemaker implantation or any other additional treatment.

An intriguing aspect of this case is the selective functional AV block without any modification of the preceding sinus cycle (Figure 1). Some investigators have shown this AV block related to an increase in endogenous adenosine.[1] However, in this case, it was possible to reproduce the same phenomenon by vagal action only through ECVS of the left vagus at a lower frequency (10 Hz) (Figure 6B). Typically, ECVS at a higher frequency causes sinus arrest (Figure 6A). These findings suggest that, in this specific case, the selective AVB is probably of cholinergic origin.

CONCLUSIONS

CNA may be an effective treatment in patients with a symptomatic functional AV block, even with a proven positive adenosine hypersensitivity test. Further studies should be carried out to deepen the knowledge and further the development of this innovative therapy.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Jose Carlos Pachon-M, Sao Paulo Heart Hospital and Sao Paulo Cardiology Institute, 204 Juquis Street, 61A, Sao Paulo 04081-010, Brazil. E-mail: pachon@usp.br.

REFERENCES

1. Brignole M, Moya A, de Lange FJ, et al, ESC Scientific Document Group. 2018 ESC guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39:1883–1948.

2. Pachon JC, Pachon EI, Pachon JC, et al. D. "Cardioneuroablation": new treatment for neurocardiogenic syncope, functional AV block and sinus dysfunction using catheter RF-ablation. *Europace*. 2005;7(1):1–13.

3. Pachon MJC, Pachon MEI, Lobo TJ, et al. Syncopal high-degree AV block treated with catheter RF ablation without pacemaker implantation. *Pacing Clin Electrophysiol*. 2006;29(3):318–322.

4. 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(9):1231–1242.

5. Pachon MJC, Pachon MEI, Pachon MJC, et al. A new treatment for atrial fibrillation based on spectral analysis to guide the catheter RF-ablation. *Europace*. 2004;6:590–601.

6. Pachon -MEI, Pachon-Mateos JC, 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(4):e007900.

7. Pachón-M JC, Pachón-M EI. Response by J.C. Pachón-M and E.I. Pachón-M to letter regarding article, "Relation of fractionated atrial potentials with the vagal innervation evaluated by extracardiac vagal stimulation during cardioneuroablation. *Circ Arrhythm Electrophysiol*. 2020;13(8):e008948.

8. Aksu T, Guler TE, Mutluer FO, Bozyel S, Golcuk SE, Yalin K. Electroanatomic-mapping-guided cardioneuroablation versus combined approach for vasovagal syncope: a cross-sectional observational study. *J Interv Card Electrophysiol*. 2019;54(2):177–188.

9. Bulava A, Osório TG, Hanis J, Pachón CTC, Pachón JC, de Asmundis C. Cardioneuroablation instead of pacemaker implantation in a young patient suffering from permanent 2:1 atrioventricular block after a slow pathway ablation. *HeartRhythm Case Rep*. 2020;6(5):261–264.

KEY WORDS ablation, atrial fibrillation, bradycardia, cardiac pacemaker, electrophysiology, palpitations, seizures, supraventricular arrhythmias