Cardioneuroablation for the treatment of severe syncopal high-grade atrioventricular block following abdominal tumor surgery

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Introduction

Frantz tumor, described in 1959 by Dr Virginia Frantz, is a solid pseudopapillary tumor of the pancreas. Although it may have malignant behavior, it is commonly a benign condition, more frequent in women under 30 years of age.[1] The definitive treatment is surgical resection.

Cardioneuroablation (CNA) is a catheter radiofrequency endocardial ablation aiming at vagal denervation for treating functional bradyarrhythmias and atrial fibrillation developed in the 1990s.[2]

KEY TEACHING POINTS

- Functional atrioventricular (AV) block of reflex origin can lead to severe outcomes, including recurrent syncope.
- The reflex functional origin is characterized by normal electrogram and appropriate response to atropine and ajmaline tests.
- Selective AV block without sinus node depression can be reproduced through extracardiac vagal stimulation of the left vagus nerve.
- Cardioneuroablation can be an effective ablative therapeutic alternative without the need for pacemaker implantation.

Case report

A 16-year-old woman underwent Whipple surgery for the resection of Frantz tumor on October 19, 2017. On September 22, 2018, she underwent a new surgery for correction of the pancreatic drainage. During this procedure there was related a "cardiac arrest" successfully treated with temporary pacemaker. Despite good recovery, she evolved with sporadic bradycardia and on February 12, 2021, there was syncope with seizures, owing to an intermittent high-grade atrioventricular (AV) block. The Holter showed minimum, mean, and maximum heart rates equal to 43, 90, and 167 beats per minute (bpm), respectively, in addition to 37 AV block pauses, the longest one lasting 5.7 seconds (Figure 1A). No other electrocardiogram (ECG) abnormalities were detected. ECG recordings from the intensive care unit showed repetitive AV block episodes, followed by syncope, without any electrolyte, inflammatory, ischemic, or metabolic abnormalities (Figure 1B).

The patient underwent an invasive electrophysiological (EP) study with atropine and ajmaline tests, revealing normal EP parameters, normal conduction safety margin in AV nodal and His-Purkinje system, and no carotid sinus hypersensitivity. Furthermore, the patient exhibited a good response to atropine in the sinus and the AV node, indicating preserved autonomic regulation (Figure 1C). These findings ruled out organic conduction system disease and reinforced the suspicion of a pure functional disorder.

Considering the absence of organic lesions and the positive response to atropine in both the sinus and AV nodes, CNA was recommended as a treatment option.[3] The patient was provided with a detailed explanation of all therapeutic possibilities, including their risks and benefits, and chose CNA.

Procedure

The procedure consisted of biatrial CNA controlled by extracardiac vagal stimulation (ECVS) (Figure 2A–2D). Parasympatholytic drugs were proscribed for the last 2 days. A conventional recorder and NAVX-EnSite® Velocity/Precision St Jude electroanatomic mapping system (NAVX-Ensite

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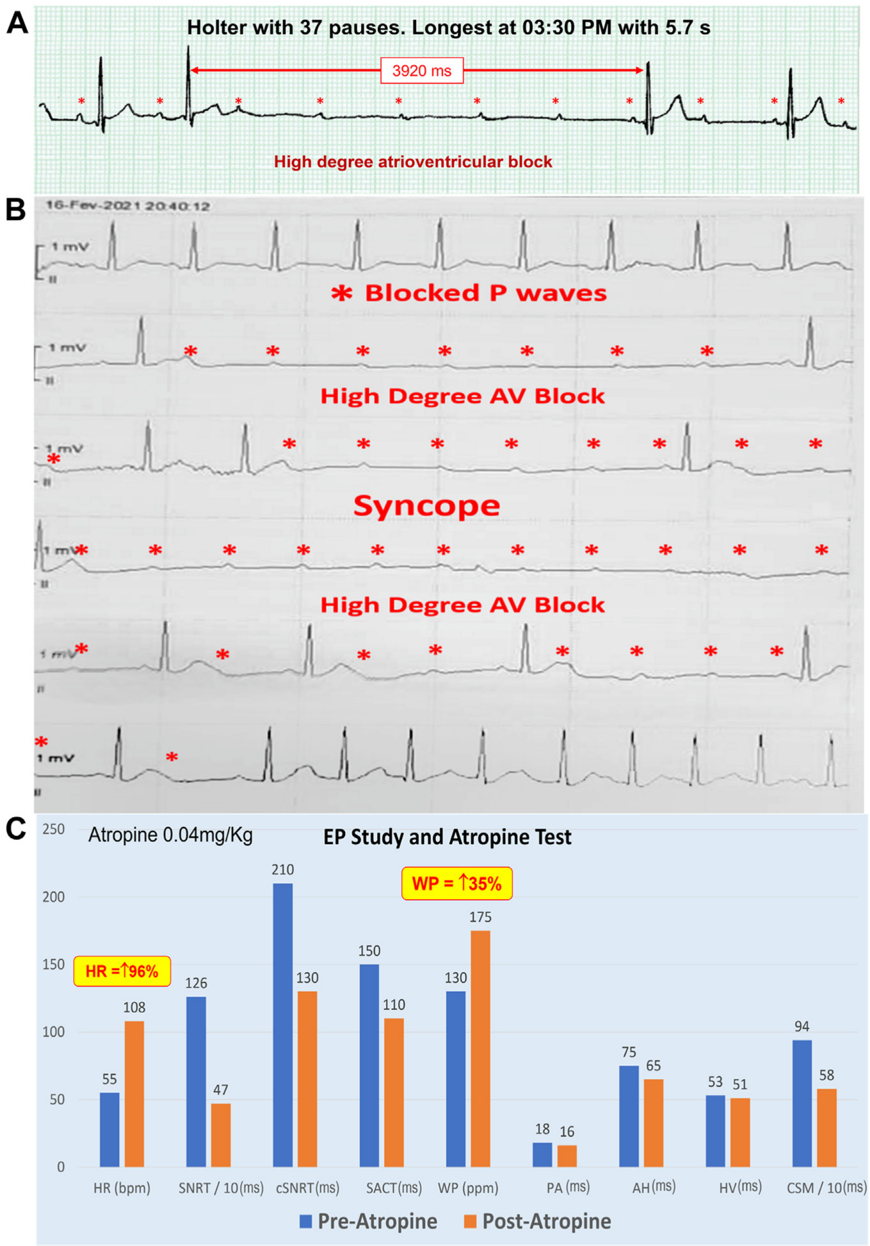

Figure 1 **A:** Holter showing 37 pauses caused by intermittent atrioventricular (AV) block, the longest being 5.7 seconds. **B:** Recordings during intensive care unit monitoring showing episodes of syncope caused by intermittent high degree of AV block. **C:** Results of the electrophysiological study and atropine test. Baseline parameters were normal. The atropine test showed a good response with an increase in sinus rate >50% and in the Wenckebach point >30%, showing good functional reserve of the conduction system and absence of organic disease. CSM = carotid sinus massage; cSNRT = corrected sinus node recovery time; HR = heart rate; SACT = sinoatrial conduction time; SNRT = sinus node recovery time; WP = Wenckebach point.

Velocity Precision Abbott, Minneapolis, MN) were installed. The catheters were deployed by femoral vein using the Seldinger technique. A duodecapolar catheter was positioned in the coronary sinus. The left atrium was accessed by transseptal puncture. A decapolar circular catheter was used to get the 3D anatomical model, simultaneously achieving AF nest[4] mapping by fractionation software. Coagulation activated time between 300 and 400 seconds was maintained by intravenous heparin infusion. Areas of high innervation probability, guided by high density of AF nests[4,5] tagged by the fractionation software, were ablated by using an irrigated Abbott FlexAbility catheter with 30 W / 40°C. Additional prolonged ablations of 1–2 minutes were performed in the anatomical areas of the 4 main ganglionated plexi (GP), to obtain deep epicardial effect (Figure 3C).

Control of vagal denervation

To assess the effectiveness and degree of vagal denervation, ECVS[6] was employed to monitor the progression of the procedure (Figure 2E and 2F, Figure 3A and 3B). Conventional ECVS at 50 Hz induced asystole owing to intense sinus node

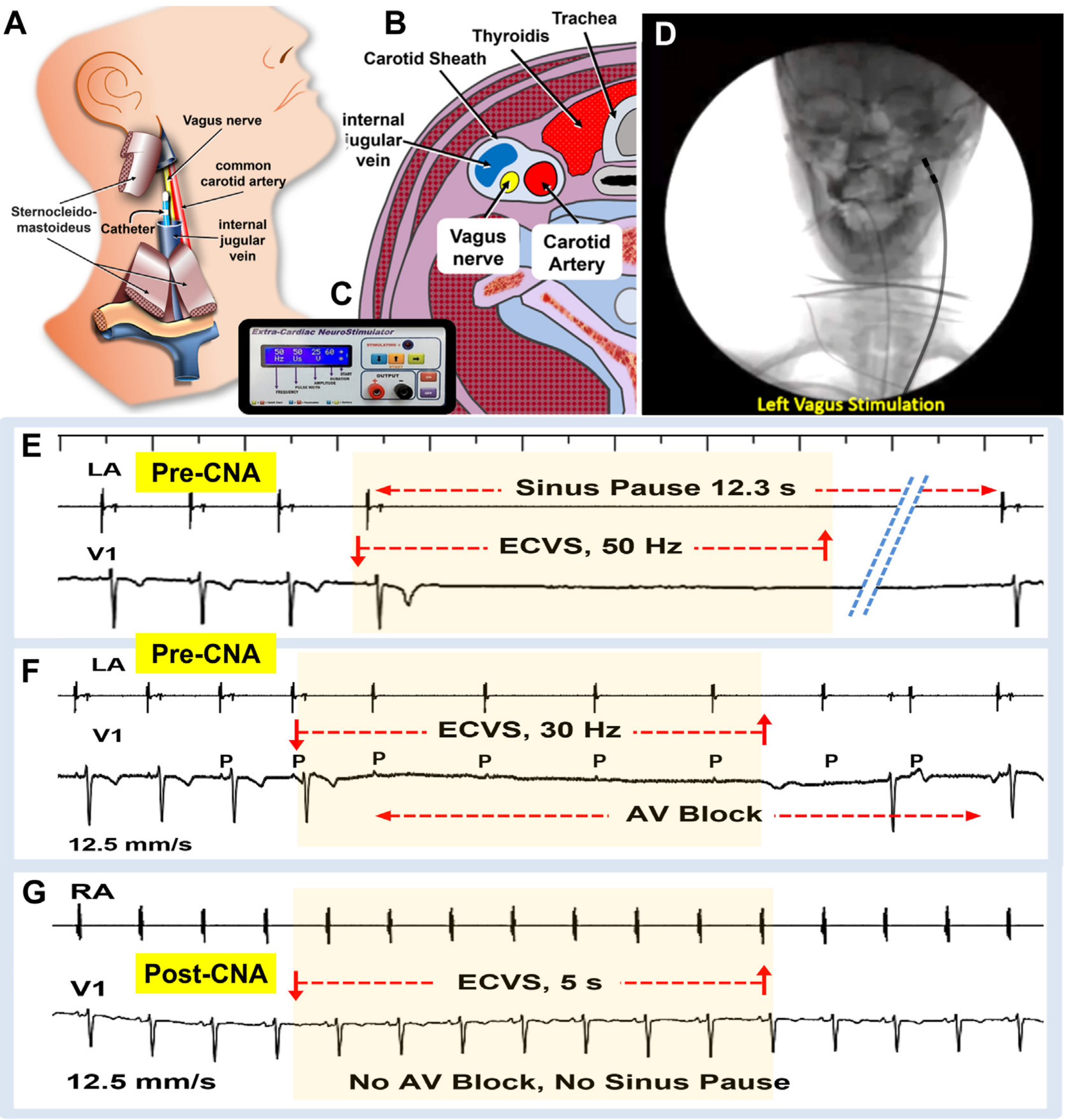

Figure 2 **A:** Scheme of extracardiac vagal stimulation (ECVS). This method aims to test the vagal innervation and to control the denervation progression during cardioneuroablation (CNA) by placing 1 catheter in the internal jugular vein. ECVS may be obtained along the internal jugular vein, but the point of the greatest response is close to the jugular foramen (**D**). In this case the ECVS on the left vagus was selected because of the predominance of the innervation in the atrioventricular (AV) node. **B:** The closeness between the jugular vein and the vagus allows stimulation without direct contact, with the use of a neurostimulator with appropriate setup (**C**). **E:** Basal condition with ECVS pre-CNA / 5 s / 50 Hz /50 µs/ 50 V showing immediate sinus arrest with temporary asystole. **F:** ECVS pre-CNA / 5 s / 30 Hz / 50 µs / 50 V. This step was crucial because of the reproduction of the spontaneous AV block by left vagus stimulation. **G:** Final ECVS post-CNA / 5 s / 50 Hz / 50 µs / 50 V after complete and successful CNA showing total elimination of the vagal effect in sinus and AV nodes, ending the CNA.

inhibition preventing the visualization of the AV block that was the main clinical finding (Figure 2E).

Reproduction of spontaneous AV block

To reproduce the clinical condition, by stimulating the left vagus with reduced frequency of 30 Hz, it was possible to get the advanced AV block without significant sinus depression.[7] This finding, indicating the vagal origin of the block, allowed for rationalization of the endpoint (Figure 2F).

Innervation mapping

Innervation mapping was performed using fractionation mapping on an electroanatomical model to detect AF nests.4 In this case, the EP map was consistent with the usual anatomical sites of the main GP.[8] The purple areas represent low probability of innervation (compact myocardium), while gray areas show AF nests with high innervation probability (Figure 3C).

Ablation of interatrial septum and GP2 areas

Interatrial septal ablation (region described in the original study as “Resting Rate Control”[2] or as either “Right Anterior GP”[9] or “P Point”[5]) is the most important to ablate for sinus node denervation.[2,6,9] It is in the interatrial septum, between the insertion of the right pulmonary veins, the roof of the left atrium, and the foramen ovale. It is ablated by transseptal

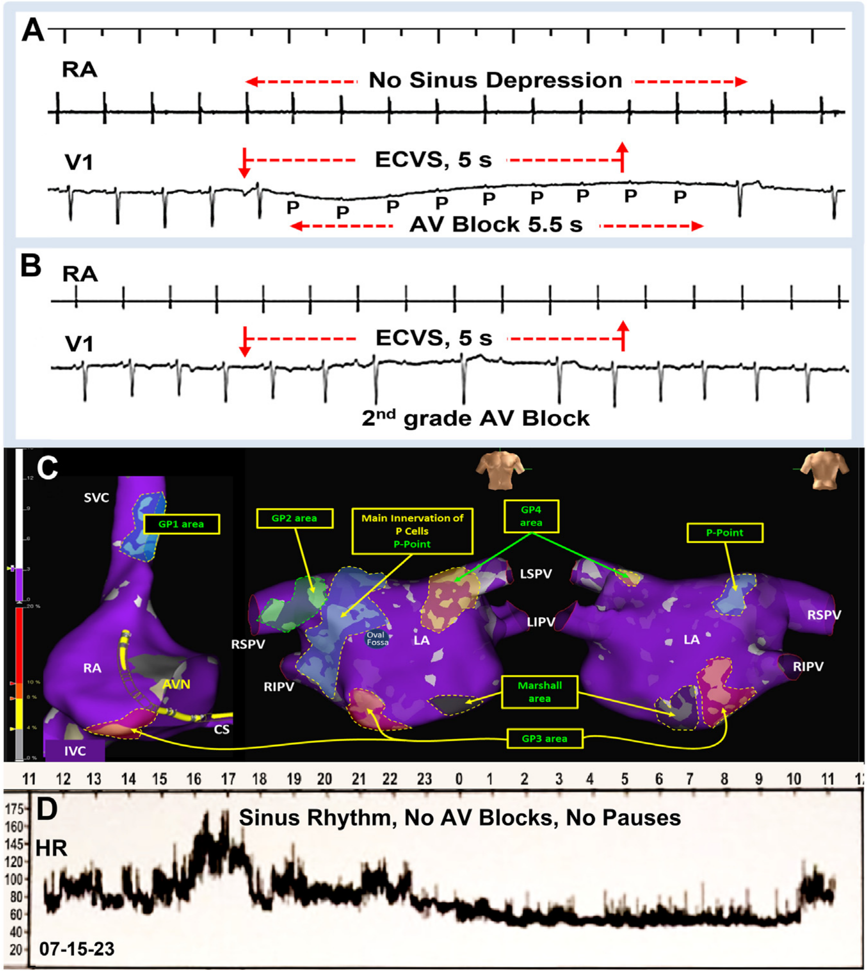

Figure 3 Sequential extracardiac vagal stimulation (ECVS) during cardioneuroablation (CNA). **A:** After interatrial septum (P point or right anterior ganglionated plexus) and GP2 area ablation, ECVS shows sinus node denervation with preserved atrioventricular (AV) node innervation. The result is the disclosure of high-grade AV block. **B:** After additional ablation of areas GP3 and Marshall vein, there is marked improvement in AV conduction, but there is still second-degree AV block. **C:** Final map of ablations with identification of AF nests, areas with a high probability of innervation, through fractionation mapping. After additional ablation of GP4 and GP1 areas, complete vagal denervation occurred with the elimination of sinus pauses and AV blocks. At this point no more ablation is necessary, and the CNA could be finished. AVN = AV node; CS = coronary sinus; GP = ganglionated plexi; IVC = inferior vena cava; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RA = right atrium; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; SVC = superior vena cava. **D:** Holter after 23.7 months. The patient is asymptomatic and no more AV block, sinus pause, or bradycardia occurred. The heart rate (HR) plot shows no sinus rate less than 45 beats/min.

puncture and may be also complemented by ablation from the right atrium. The GP2 area is usually located in the upper right pulmonary vein, near the insertion (Figure 3C). Following these ablations, a new ECVS was performed at 50 Hz, confirming the complete denervation of the sinus node but with the appearance of a high-grade AV block, since most of the innervation of the AV node was preserved even after the ablation of the interatrial septum and the GP2 area (Figure 3C).

Ablation of GP3 and Marshall vein areas

These ablations typically result in AV node denervation, which is the primary objective in this case. They were performed through the left atrium in the posterior septal space (Marshall vein area) and at the ostium of the coronary sinus from the right atrium. ECVS was repeated, revealing a significant reduction in AV block from high-grade to second-degree Mobitz I AV block (Figure 3B). As a second-degree AV block persisted, ablation was extended to the GP4 and GP1 areas (Figure 3C).

Ablation of GP4 and GP1 areas

These ablations were performed at the insertion of the left pulmonary veins and medially above the insertion of the superior vena cava, respectively (Figure 3C).

Following this step, a new ECVS was conducted, resulting in the complete disappearance of vagal-induced AV block. At this point, it was determined that further expansion of CNA was unnecessary, and the procedure was concluded (Figure 2G). No pacemaker implantation was required. The final ablation map is shown in Figure 3C.

Long-term outcome and post-CNA follow-up

The final ECG was normal, with Wenckebach point of 148 bpm. The patient remained completely asymptomatic up to the current follow-up of 29 months. All follow-up ECGs were normal. The last Holter (on July 15, 2023) was normal, with no AV block and no pause, the minimum, mean, and maximum heart rates being 45, 76, and 122 bpm, respectively (Figure 3D). No bradycardia, pauses, AV block, or abnormal sinus tachycardia occurred.

Discussion

Indication for CNA

The CNA should only be indicated in the absence of organic pathology or when there is still a significant possibility of improvement in vagal parameters, in the case of a nonprogressive disorder. Ruling out degenerative and progressive pathologies is crucial. The best alternative for a reliable evaluation is an EP study with pharmacological testing. The atropine test is essential for assessing the conduction without vagal effect. Typically, the sinus rate increases by more than 50%, and the Wenckebach point increases by more than 30% after 0.04 mg/kg up to 2 mg of intravenous atropine. Additionally, the measurement of the HV interval is decisive in cases of AV block. If there is doubt about the His-Purkinje conduction reserve, the ajmaline test is essential to ensure the functional integrity of infranodal conduction. In this patient, all data indicated that the AV block was functional. Sinus parameters were normal, and the atropine test showed a 35% increase in the Wenckebach point and a 96% increase in sinus rate. Thus, the atropine test predicted good response for CNA.

Functional high-grade AV block

We have observed this type of block in patients with a normal conduction system and a history of abdominal surgeries or abdominal visceral pathologies.[3] Probably they are caused by a viscero-visceral reflex mediated by the left vagus, as this nerve is highly involved with abdominal viscera and AV node. In this case, the syncopal AV block occurred after extensive abdominal surgeries. The first case of syncopal functional AV block after abdominal surgery treated with CNA was published in 2005.[2]

Reproduction of AV block

In CNA for the treatment of paroxysmal AV block, ECVS of the left vagus nerve is crucial. It is more specific to study the AV node than the right. In this patient, ECVS of the left vagus with lower frequency of 30 Hz was able to reproduce the total AV block observed clinically without significant sinus node depression (Figure 2F). It was important to support the vagal origin of the AV block. In any situation when there is sinus arrest during ECVS by stimulating the right or the left vagus, it is necessary to repeat the vagal stimulation during atrial pacing to reproduce the AV block and to confirm its disappearance after CNA. In this patient, after eliminating the AV block induced by ECVS, the procedure was concluded without the need to ablate additional areas shown by fractionation mapping.

Escalated denervation

Stepwise ECVS during CNA demonstrated a rational progression of the denervation. This tool is fundamental to rationalize and to finish the procedure with elimination of the vagal response, as typically there is a recovery of 30%–50% of innervation. Additionally, ECVS is extremely important for the treatment of functional AV blocks, as denervation of the AV node is much more challenging than denervation of the sinus node (Figure 3C). The AV nodal innervation receives contributions from virtually all GP, although GP3 and the Marshall area usually provide the largest contingent. However, in many cases, it is only possible to eliminate the AV block after ablating the GP4, the Waterston groove, the GP1 area, and other AF nests revealed by the fractionation software.

CNA endpoint

For treating functional AV block the endpoint is to achieve complete elimination of the vagal effect over the AV node. Therefore, after the ablation of the main targets the ECVS was repeated and no more bradycardia, asystole, or AV block was observed, allowing to have the best endpoint of acute success and the best rationale to finish the procedure (Figure 2G).

Conclusion

This case demonstrates that functional high-grade AV block with recurrent syncope can be successfully treated with CNA without pacemaker implantation, provided that the functional origin is rigorously proven and organic pathologies of the conduction system are ruled out. Controlled reproduction of the AV block through ECVS and its disappearance after CNA is essential. ECVS with lower frequency may reproduce selective AV block without sinus depression.

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