Changes in autonomic response during cardioneuroablation in an elderly patient with carotid sinus syndrome

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Introduction

Carotid sinus syndrome (CSS) is an underrecognized form of recurrent reflex syncope characterized by an exaggerated response to carotid sinus baroreceptor stimulation. It corresponds to almost 10% of all reflex syncopes and is more prevalent in elderly patients.[1] Current guidelines recommend dual-chamber pacing in patients with CSS and severe and recurrent syncope to reduce the number of episodes and to relieve symptoms. However, pacing does not completely reduce syncope recurrence, especially in patients with a predominant vasodepressor or mixed component, and it is associated with long-term complications such as lead dysfunction, venous occlusions, and device infections, particularly in young patients.

Endocardial ablation of a ganglionated plexus (GP), also called cardioneuroablation (CNA), is a relatively new technique for treatment of vasovagal syncope (VVS), sinus nodal dysfunction, and functional atrioventricular block.[2] Its main objective is elimination of the efferent pathway of the parasympathetic autonomic nervous system by endocardial catheter radiofrequency GP ablation, abolishing the vagal cardioinhibitory response. However, this therapeutic approach has been used mainly for VVS, particularly in young patients, and only anecdotal cases have been reported for CSS.[3,4] Furthermore, although the main cause of syncope in the elderly is a reflex mechanism, there is little evidence of CNA use in this population and the best approach (uniatrial or biatrial) for its use. In this case report, we present the successful use of CNA for treatment of CSS in an elderly woman.

KEY TEACHING POINTS

- Cardioneuroablation (CNA) could be a reasonable treatment option for elderly patients with carotid sinus syndrome (CSS) in whom atrioventricular conduction disorders have been ruled out.
- Carotid sinus massage represents a valuable tool for assessing appropriate denervation, thus avoiding the inconveniences of extracardiac stimulation.
- Biatrial denervation usually is necessary in patients with CSS in order to abolish the cardioinhibitory vagal response.

Case report

A 77-year-old woman (weight 33 kg) with a history of hypertension was admitted to our center because of loss of consciousness. She presented with several episodes of dizziness and 1 episode of syncope in the last 2 years. At admission, the electrocardiogram showed sinus bradycardia (52 bpm), PR interval of 200 ms, and bifascicular block (right bundle branch block and left posterior fascicular block). Transthoracic echocardiogram revealed no significant structural heart disease. Right carotid sinus massage (CSM) showed a ventricular pause due to sinus arrest of 7 seconds, with reproduction of the syncope and drop in systolic arterial pressure of only 20 mm Hg. After a monitoring period of 3 days without presentation of any bradyarrhythmia, an electrophysiological study was performed. Atropine test (0.04 mg/kg) revealed an increase in heart rate of >30%. In addition, an exercise test showed chronotropic incompetence (maximum heart rate of 58 bpm on treadmill test). Based on these results and the only documented bradyarrhythmia

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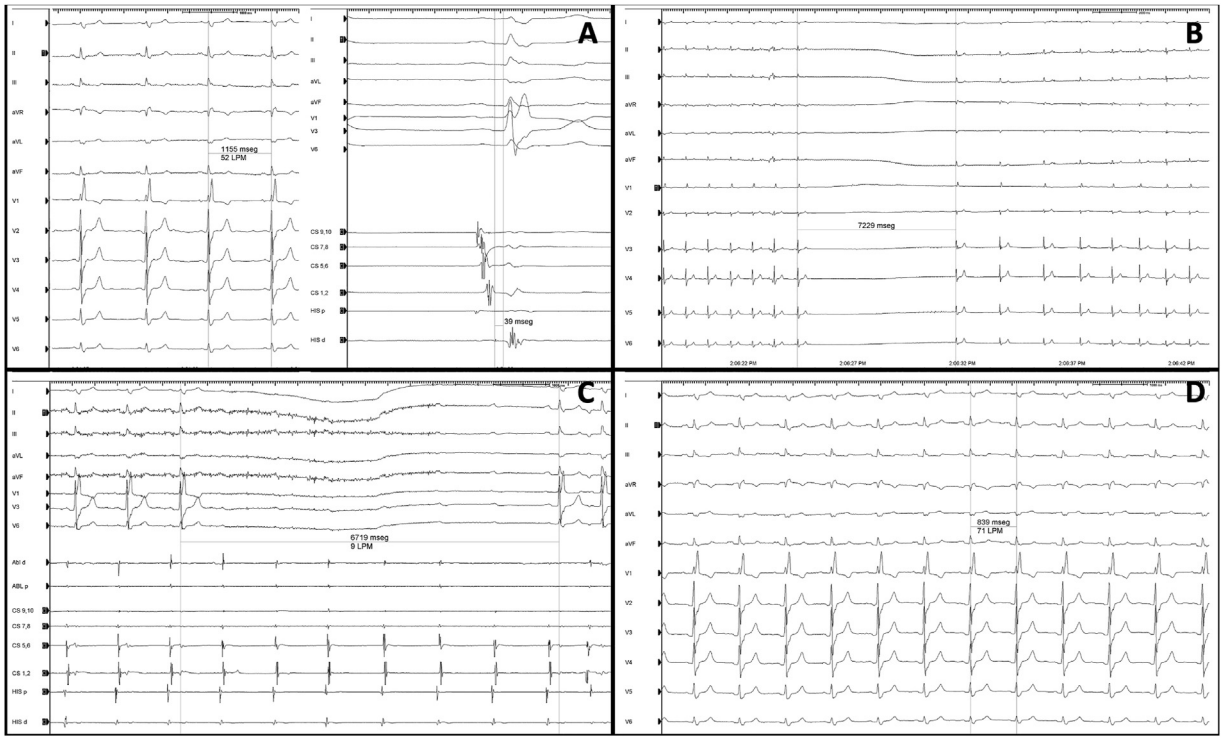

Figure 1 Electrophysiological study. **A:** Basal electrocardiogram and intervals at the beginning of the procedure. **B:** Carotid sinus massage (CSM) before cardioneuroablation (CNA) showing a ventricular pause of 7.2 seconds due to sinus arrest. **C:** CSM after ablation of the right superior ganglionate plexus showing a ventricular pause due to atrioventricular block but no decrease or variation of the PP interval. **D:** Final CSM showing no response.

being sinus pause with CSM, the patient was offered an attempt at CNA, and a pacemaker was offered if the procedure did not improve her symptoms or if an infrahisian conduction disturbance was observed during electrophysiological study. After being given an explanation of the risks, the patient provided informed consent.

The procedure was performed with the patient under conscious sedation. Electroanatomic and activation mapping of the right atrium was performed using the PentaRay catheter and the CARTO system (Biosense Webster, Diamond Bar, CA). Basal conduction intervals were registered at the beginning of the procedure (AH interval 91 ms; HV interval 39 ms; effective refractory period AV 600/390 ms; Wenckebach point 158 bpm; sinus node recovery time 1541 ms; corrected sinus node recovery time 381 ms) (Figure 1A). Location of the GP was performed based on an anatomic approach. Extracardiac vagal stimulation was not performed because of difficulty in advancing the catheter to the jugular foramen. Before ablation, CSM, which was performed in order to use it as an endpoint of appropriate denervation, showed sinus arrest of 7.2 seconds (Figure 1B). Because of the patient's low weight, a right atrial approach with unique ablation of the right superior GP from the superior vena cava initially was performed, aiming to avoid a transseptal puncture (Thermocool Smarttouch, Biosense Webster). An increase in heart rate from 52 to 71 bpm was noted. CSM then was repeated, which showed a ventricular pause due to atrioventricular block but no decrease or variation of sinus heart rate. This finding was interpreted as successful denervation of the sinus node but a shift of the parasympathetic response to the atrioventricular node (Figure 1C). Subsequently, transseptal puncture was performed to ablate the left superior GP and the left inferior GP, respectively. CSM was repeated after ablation of each GP; however, no response and no ventricular pauses were demonstrated when the left inferior GP ablation was performed. Finally, completion of the ablation of the right superior GP was conducted from the left atrial side (Figure 2). At the end of the procedure, heart rate remained stable at 70 bpm, no response to CSM or atropine was observed, and a new right atrial activation electroanatomic map showed a superior shift in the earliest atrial activation in sinus rhythm (Figure 3).[5] Basal conduction intervals were registered (AH interval 87 ms; HV interval 41 ms; effective refractory period AV 600/390 ms; Wenckebach point 150 bpm; sinus node recovery time 1315 ms; corrected sinus node recovery time 556 ms). The patient was discharged with an implantable loop recorder. After 6 months, she remained free of any symptoms, and no bradyarrhythmias have been registered to date.

Discussion

To the best of our knowledge, this is the first case reporting successful use of CNA for treatment of CSS in an elderly, frail patient. Although several studies have described its efficacy in reducing syncope burden in VVS, there is little evidence for its use in CSS, with only 2 cases of young patients reported in the literature.[3,4] In this regard, although the physiopathology of neuromediated syncope is complex, in CSS the abnormal efferent response is due to a disturbance of carotid sinus

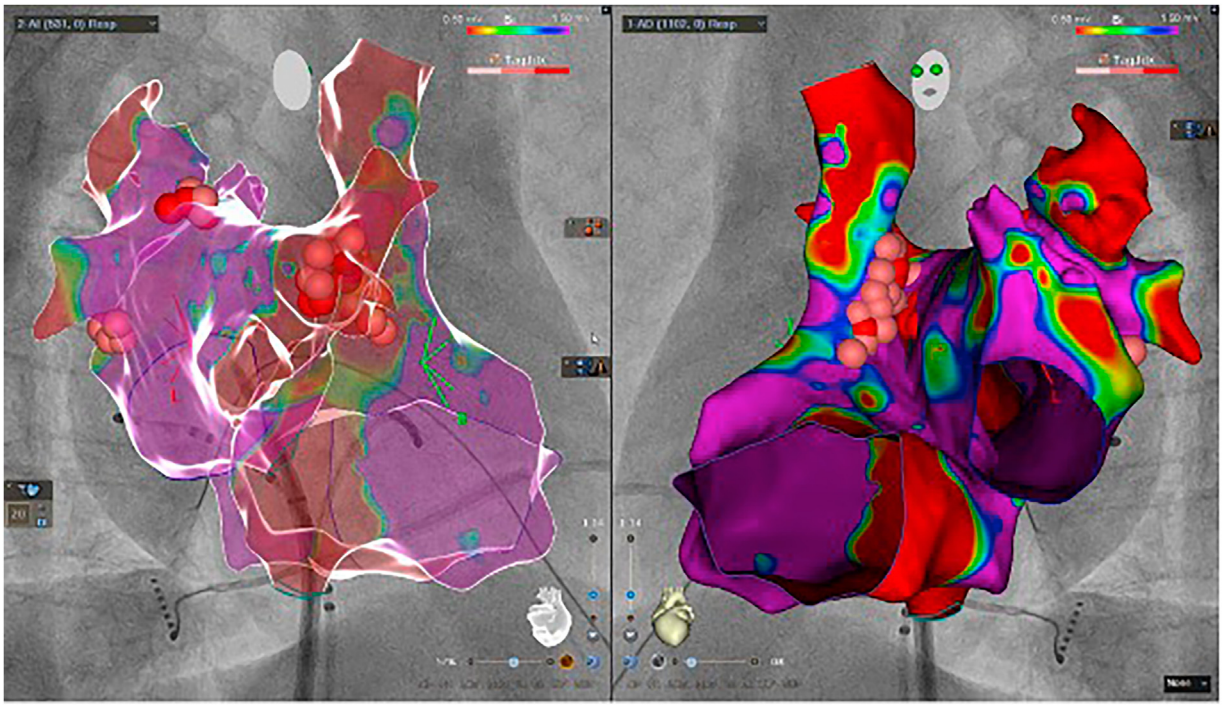

Figure 2 Electroanatomic map of the right and left atria with the ablation set at the right superior ganglionated plexus (GP), left superior GP, and left inferior GP.

baroreceptor function. Furthermore, it is important to distinguish between the dominant vasodepressor, the dominant cardioinhibitory, and the mixed forms because CNA potentially will be more effective in the latter 2 forms.

Even though the most common etiology of unexplained syncope in elderly patients is a reflex mechanism, there is no evidence of use of this technique in this population.[6] In the last decade, some studies have reported encouraging long-term results in reduction of syncope burden in VVS and functional sinus nodal dysfunction, with syncope-free survival rates >90% at 1 year.[7,8] However, most of these studies only included young patients, with the vast majority of the patients <50 years old. In a recent study, Quin et al compared the use of CNA in patients with symptomatic sinus bradycardia aged >50 years or <50 years.[9] In their study, although symptoms and quality of life improved in all patients, the magnitude of improvement was larger in young patients. However, in the case of VVS, we firmly believe that although the older the patient the greater the likelihood of an intrinsic cause of bradyarrhythmia, if an infrahisian conduction disorder can be ruled out and no advanced atrioventricular conduction disorder is documented, some patients may benefit from the procedure. In our patient, despite existing bifascicular block she presented an appropriate response to atropine, which points toward the presence of an extrinsic component. Moreover, regardless of the underlying mechanism, we considered that part of the cardioinhibitory response could be modulated with the procedure.

One of the main limitations of CNA is the lack of robust efficacy endpoints and the difficulty in assuring correct denervation. The absence of response to the atropine test, one of the most popular, has the main disadvantage that the test can only be used at the end of the procedure, and it cannot be used to assess for correct denervation for each GP. Extracardiac vagal stimulation, which can be attempted using high-frequency pacing of the vagus nerve through a catheter in the jugular foramen, could overcome this limitation. However, despite some encouraging reports using an ultrasound-guided approach,[10] it can be difficult to reach the jugular foramen, as in this case, and more importantly to achieve a vagal response using high-frequency stimulation. Moreover, it implies the need for utilization of radioscopy for catheter advancement. Because of these limitations, we hypothesize that, although never reported, CSM could be an excellent method for assessing appropriate denervation of each GP in patients with positive CSM, as illustrated in our patient. Interestingly, in this case, after ablation of the right superior GP using a right approach, the CSM could elucidate a complete denervation of the sinus node but a shift toward the atrioventricular node, which was abolished after ablation of the superior and inferior left GPs (Figure 2). For this reason, we did not consider ablation of the left posteromedial GP to be necessary. This is in line with the complexity of the intrinsic cardiac autonomic nervous system and the innervation of the sinus and atrioventricular nodes. According to studies in dogs, innervation of the sinus node seems to be mediated by the right superior GP, whereas innervation of the atrioventricular node seems to be mediated by the left GPs,[11] which could explain the response of our patient. This phenomenon could one reason for the finding reported by Piotrowski et al.[12] They observed that in some patients,

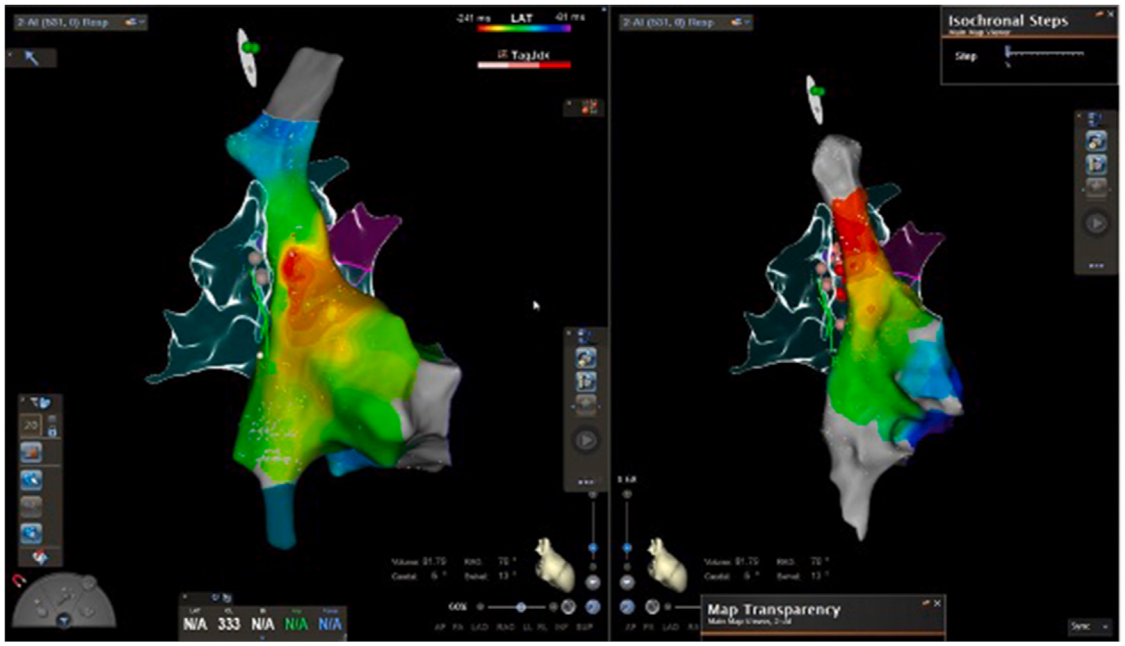

Figure 3 Activation map of the right atrium before **(left)** and after **(right)** cardioneuroablation showing a superior shift of the earliest site of atrial activation in sinus rhythm.

the response to tilting was normalized after CNA, whereas in other patients, cardiodepression with asystole was changed to vasodepression. Thus, although the most plausible explanation could be that CNA acts locally on cardiac GP and does not influence other aspects of VVS such as peripheral dilation, it can be speculated that the ablation strategy also plays a role.

Whether a unique right atrial approach in these patients is sufficient remains controversial, but recent studies have elucidated this question. Debruyne et al[13] reported 95% reduction in syncope burden in 20 patients with neurally mediated syncope and functional sinus nodal dysfunction using unifocal right-sided ablation. However, in their study, at 6 months only 80% of patients were free of syncope, and the only methods for assessing denervation were shortening of the P-P intervals and the atropine test. Furthermore, a recent meta-analysis of 465 patients reported that CNA limited to right atrial ablation was associated with a significant lower freedom from syncope (81.5%; 95% confidence interval [CI] 51.9%–94.7%; $P < .0001$) compared to left atrial GP ablation (94.0%; 95% CI 88.6%–96.9%) and biatrial ablation (92.7%; 95% CI 86.8%–96.1%).[8] In our experience and according to other investigators, a biatrial approach usually is needed, especially when targeting the right superior and left posteromedial GPs. In addition, it is crucial to assess denervation for each GP using extracardiac vagal stimulation, if feasible. In those patients in whom extracardiac stimulation is not possible, CSM may be an alternative for step-by-step assessment of the efficacy of the procedure.

Conclusion

CNA could be a reasonable option for treatment of dominant cardioinhibitory CSS in elderly patients in whom atrioventricular conduction disorders have been ruled out. During the procedure, CSM represents a valuable tool for assessing appropriate denervation, thus avoiding the inconveniences of extracardiac stimulation. Importantly, a shift from predominant "right" to "left vagus" response can be observed, highlighting the importance of biatrial denervation or, at least, thorough consideration in those patients in whom a right atrial approach is contemplated. Specific prospective studies in elderly patients with cardioinhibitory VVS should be performed to support these conclusions.

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