Endocardial autonomic denervation of the left atrium to treat recurrent micturition syncope

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Introduction

Micturition syncope (MS) is one type of neurally mediated syncope.[1] MS has been reported as classically occurring in the healthy men after sleep or recumbency, and alcohol intake may be a predisposing factor.[2,3] MS is a clinical disease affecting quality of life and increasing the risk of physical trauma in patients. Left atrial (LA) vagal denervation via the radiofrequency (RF) catheter ablation targeting the left ganglionated plexi (GP) were showed to be effective in patients with refractory vasovagal syncope.[4,5] In this case report, we aim to assess the feasibility of LA vagal denervation to treat a patient with recurrent MS.

Case report

A 33-year-old man was referred with a history of repetitious episodes of syncope averaging 1 per month over the past 4 years. His syncope often occurred during or at the termination of urination in the afternoon or midnight, and alcohol intake was found to be a predisposing factor. Nausea, vomiting, and lethargy symptoms typically accompanied the syncopal episodes and patient usually recovered within 1 minute in a supine position. The patient had failed a series of pharmacologic and nonpharmacologic treatments, including urinating in a squatting or sitting position, isometric exercises, avoiding alcohol before sleep, 10 mg daily of midodrine, and 80 mg daily of propranolol. Syncope attacks remained frequent, and the latest syncope after micturition resulted in a significant maxillofacial trauma. The results of a physical examination were unremarkable. The carotid ultrasound, electroencephalogram, and computed tomography brain scan were found to be normal. No abnormality was detected from the urine analysis and the renal ultrasound. An electrocardiogram, echocardiogram, and magnetic resonance image scan of the heart demonstrated no evidence of structural heart disease. A head-up tilt test (HUTT) at baseline and with nitroglycerin provocation was performed with negative result. By collecting the Holter data, deceleration capacity (DC) and heart rate variability evaluation were generated automatically with the use of specific software (MIC-12H Analysis Platform, Jinke Instruments, Beijing, China).

An alcohol ingestion test was performed to confirm the diagnosis given that the alcohol intake was an established triggering factor. The patient ingested 550 mL of beer containing 3% alcohol (16.5 mL ethanol) and then remained in supine position until micturition. Lightheadedness and nausea occurred during urination, and the patient fainted. His telemetry revealed sinus bradycardia with heart rate decreasing from 80 beats/min to 41 beats/min and blood pressure dropping from 120/80 mmHg to 60/40 mmHg. The heart rate and blood pressure resumed back to normal quickly after

KEY TEACHING POINTS

- Micturition syncope (MS) is regarded as a form of neurally mediated syncope. MS and vasovagal syncope have different neural afferent pathways but may share similar efferent pathways.
- Given the poor sensitivity of the head-up tilt test in patients with MS, the deceleration capacity of the heart rate can serve as an effective tool for evaluating the autonomic nervous function in these patients.
- Cardioneuroablation, an emerging treatment for vasovagal syncope, shows potential as a therapeutic option for patients with refractory MS. However, larger studies are needed to confirm its effectiveness.

KEYWORDS Autonomic modification; Catheter ablation; Ganglionated plexi; Micturition syncope; Deceleration capacity
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lying down, and his symptoms resolved quickly. After obtaining the written informed consent, LA vagal denervation using anatomically guided GP ablation was performed.

Left atrium ganglionated plexus ablation

The ablation procedure was performed using conscious sedation. Two femoral venous accesses were obtained, and a 6F decapolar steerable electrode catheter (St. Jude Medical, Sao Paulo, MN) was placed in the coronary sinus and a 6F quadripolar electrode catheter (St. Jude Medical) was placed in the right ventricular apex. After a single transseptal puncture, intravenous heparin was administered to maintain an activated clotting time of 200–300 seconds. The 3-dimensional geometry of the LA was reconstructed with an EnSite NavX mapping system (St. Jude Medical).

An anatomically guided GP ablation approach has been described previously in detail.[4] In brief, 5 presumptive GP sites were anatomically located, and a positive vagal response (VR) induced by ablation was defined as an increase in R-R interval of $\geq$50%. A 4-mm-tip deflectable catheter (St. Jude Medical) was used to deliver RF energy at the targeted GP sites with a positive VR. The temperature and power limits were 60°C and 40 W, respectively. At each GP site, if tentative RF energy delivery induced any VR within 10 seconds, additional RF energy was delivered for at least 30 seconds until VR inhibition. Otherwise, the tentative ablation was terminated. Additional ablation was then delivered adjacent to the initial lesion to create a cloudlike lesion cluster. The endpoint of the ablation procedure was the elimination of all VRs at each identified GP target.

The X-ray exposure time was 3 minutes, and the total procedure time was 46 minutes. The endpoint of inhibition of vagal response was achieved in all 5 approached GP sites, including LSGP, LIGP, LLGP, RAGP, and RIGP (Figure 1). The RF delivery times for the 5 GP sites were 140, 130, 130, 130, and 130 seconds. Intriguingly, during RF energy delivery at LSGP, a long R-R interval pause with 3 seconds was induced, and additional ablation abolished the VR (Figure 2). There were no complications related to the procedures and during the follow-up.

Follow-up

All medications were ceased after the ablation, and follow-up occurred at 3, 12, and 26 months at the clinic. The patient remained syncope free during the 26-month period of follow-up. The results of a HUTT performed at 26 months was negative, and the alcohol ingestion test at 26 months failed to induce syncope or prodrome symptoms. Holter monitoring was performed at baseline, 1 day, 3 months, and 12 months after the procedure, and the chronologic changes are displayed in Table 1. Minimum, mean, and maximum heart rate increased from the preoperative period. The time- and frequency-domain

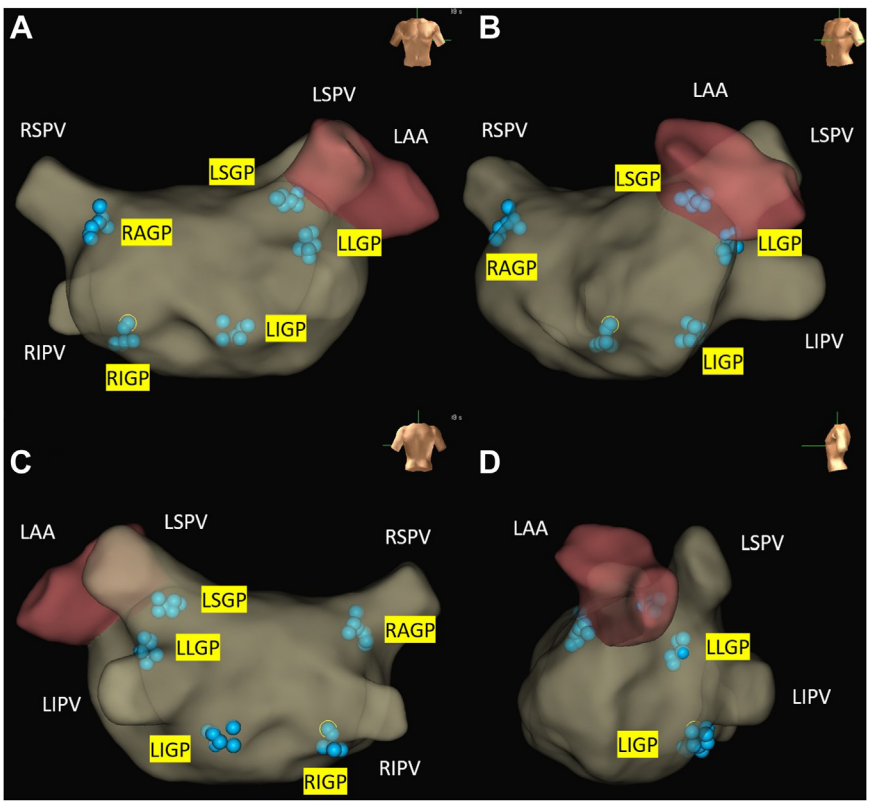

Figure 1 A 3-dimensional diagram of the left atrial endocardial surface showing the locations of the GPs (*blue points*). **A:** Anterior-posterior view. **B:** Left anterior oblique view. **C:** Posterior-anterior view. **D:** Left Lateral View. GP = ganglionated plexi; LAA = left auricular appendage; LIGP = left inferior ganglionated plexus; LIPV = left inferior pulmonary vein; LLGP = left lateral ganglionated plexus; LSGP = left superior ganglionated plexus; LSPV = left superior pulmonary vein; RAGP = right anterior ganglionated plexus; RIGP = right inferior ganglionated plexus; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

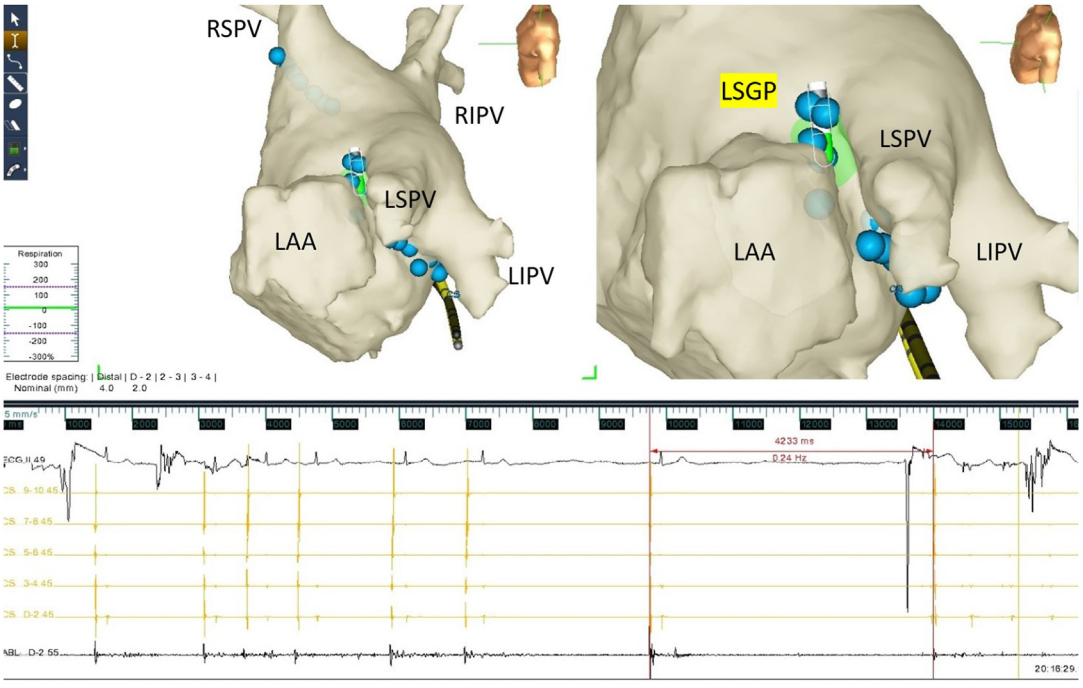

Figure 2 Left atrial ganglionated plexus catheter ablation. Radiofrequency catheter ablation in LSGP triggered a long R-R interval of 4233 ms. LAA, left auricular appendage; LSGP: LSGP, left superior ganglionated plexus; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

heart rate variability declined at 3 months after the procedure but returned to baseline levels at 12 months. The DC was persistently reduced at 1-day, 3-month, and 12-month follow-up compared with baseline.

Discussion

In this study, we accurately quantified vagal tone in a patient with MS before and after GP ablation by DC, which clarifies the pathogenesis of MS.

Etiologic mechanism of MS

Initially, certain postures and maneuvers during micturition are thought to be associated with the onset of syncope, such as the upright position, the Valsalva maneuver, the breath hold, and the lordotic posture, which might interfere with venous return and result in hypotension.[2] Gradually, it has become clear that there is a rich neuroreflex association between the bladder and the cardiovascular system. Anatomic and clinical studies have demonstrated that bladder distension causes an increase in blood pressure and heart rate, and this effect is reversed after micturition, which is thought to be related to the autonomic nervous system.[6,7]

Consequently, imbalances in the autonomic nervous system, particularly enhanced vagal activity, play an important role in the pathophysiology of MS. It is considered to have a different afferent pathway but the same efferent pathway as vasovagal syncope (VVS).[7] As for VVS, the most typical mechanism is thought to be involve central hypovolemia because of the upright posture, with subsequent induces activation of left ventricular baroreceptors. The afferent pathway has been shown to be vagal C-fibers, and the efferent results in vagally mediated bradycardia and sympathetic withdrawal from the vascular tone.[8] While in MS, the trigger has been

Table 1 Twelve-channel, 24-hour Holter ECG data before and after the procedure

Variables	Before ablation	1 day after ablation	3 months after ablation	12 months after ablation
DC, ms	13.7	3.5	6.1	7.3
SDNN, ms	140.6	106.3	128.1	143.3
rMSSD, ms	22.9	24.3	19.6	23.8
ln(LF), ms^2	5.77	4.90	5.62	5.89
ln(HF), ms^2	4.96	4.32	4.07	5.03
Minimum HR, bpm	44	64	57	52
Maximum HR, bpm	121	136	128	117
Mean HR, bpm	62	72	68	65

DC, Deceleration capacity; ECG, electrocardiogram HF, high frequency; HR, heart rate; LF, low frequency; ln, natural logarithm; rMSSD, root mean square of successive differences; SDNN, standard deviation of all N-N intervals.

attributed to the activation of bladder mechanoreceptor during micturition. Next, afferent activity is transmitted via sympathetic, parasympathetic, and somatic nerves and efferents through the vagus nerve.[9]

In the present study, recurrent syncope in a middle-aged male patient was consistently associated with micturition and accompanied by transient reductions in blood pressure and heart rate, suggesting that the vagus nerve plays a major role in the pathogenesis of MS.

Assessment of autonomic function in MS

Unlike VVS, patients with MS were found to have poor positive responses to the HUTT, even during the provocation phase, with approximately 50% and generally classified as vasodepressor or mixed.[3,10] This finding might be related to the different neural afferent pathways in patients with MS and VVS, with prolonged standing simulated by the HUTT usually triggering VVS.[10]

Previous studies have shown that in VVS, in addition to syncopal episodes, increased cardiac parasympathetic tension is also present during asymptomatic period, which can be quantitatively assessed by DC. We demonstrated that DC in patients with VVS was significantly increased at baseline and significantly decreased after GP ablation, which could be maintained during long-term follow-up.[11,12]

Despite different afferent pathways, considering that MS may share the same efferent pathway as VVS, the heart, and blood vessels, DC was further used to assess cardiac parasympathetic tension in this case. This patient had an apparently higher baseline DC of >13 ms and a lower DC at the 12-month follow-up. The consistent reduction DC after GP ablation and syncope burden in the patient suggest that increased parasympathetic tension is present in MS and, similar to VVS, is modulated by the GP. In addition, this study preliminary demonstrated that DC can be used for the assessment of vagal function in patients with MS.

GP ablation in MS

In this case, 5 GPs with positive vagal response were successfully identified and eliminated. GP, as the main intrinsic cardiac autonomic nervous system, is often clustered within the epicardial fat pads of the atria.[5,13] GP ablation has a satisfactory effect on long-term symptom improvement in VVS, suggesting that parasympathetic activity plays important roles in these patients.[12,14,15] Similarly, the patient in this study remained symptom free after the procedure and showed a reduction in parasympathetic tone. This once again indicates that in patients with MS, GP might also act as the effector in syncope events, functioning through increased vagal tone.

Conclusion

Atrial denervation using catheter GP ablation could serve as a potential treatment option in a refractory patient with MS. However, larger studies are required to further assess the efficacy and safety of this technique. DC as a new indicator of vagal tone can help to guide the selection of patients who are suitable for denervation in the future.

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