

Cardioneuroablation in patients with vagally-mediated bradyarrhythmia

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ABSTRACT

Aim: To assess the clinical efficacy and safety of cardioneuroablation (CNA) in patients with vagally-mediated dysfunction of sinus and atrioventricular (AV) nodes.

Methods: Between August 2023 and March 2025, 21 CNA procedures were performed in patients with autonomic dysfunction of the sinus node and functional second- and third-degree AV block. Clinical follow-up assessments were conducted at 3, 6, 12, and 24 months post-procedure, including 24-hour Holter monitoring and validated quality-of-life questionnaires.

Results: A total of 21 patients (mean age 37.4 ± 10.2 years) were included. CNA resulted in a significant increase in mean heart rate (HR) from 53.2 ± 9.6 beats per minute (bpm) to 70.4 ± 7.8 bpm (mean difference $+17.1$ bpm; 95% confidence interval [CI]: 13.5-20.8; $p < 0.001$; Cohen's $d = 2.13$). Significant improvement in antegrade AV conduction (Wenckebach point: 541.9 ± 139.9 to 393.8 ± 63.7 ms; $p < 0.001$; $d = 1.34$) and corrected sinus node recovery time (cSNRT: 524.5 ± 273.1 to 320.5 ± 76.9 ms; $p = 0.030$) was observed. PR, AH, and HV intervals showed no significant changes (all $p > 0.05$). All six patients with prior syncope remained syncope-free throughout follow-up. Statistically significant improvement was observed in all five EQ-5D domains ($p \leq 0.025$).

Conclusion: In selected patients with confirmed vagally mediated bradyarrhythmias, CNA is a feasible catheter-based procedure that may reduce the need for permanent pacemaker implantation. These preliminary results from a single-center pilot cohort study demonstrate significant improvement in HR, electrophysiological parameters, and health-related quality of life. Confirmation in larger multicenter controlled studies is required before broader clinical implementation.

Keywords: cardioneuroablation, atrioventricular block, sick sinus syndrome, vasovagal syncope, autonomic nervous system, catheter ablation

INTRODUCTION

Functional cardiac rhythm dysfunctions associated with increased vagal activity represent a crucial clinical challenge. Among them, sinus node dysfunction (SND) and second-degree and third-degree atrioventricular (AV) blocks occurring in the setting of parasympathetic hypertonia occupy a special role [1]. These conditions are frequently accompanied by syncopal episodes, pronounced bradycardia, and in some cases necessitate permanent pacemaker (PPM) implantation [2]. Despite its established efficacy, PPM therapy has several important limitations, especially in young and physically active patients. These complications include discomfort related to the pacemaker pocket, functional restrictions of shoulder joint

and upper limbs, lead-related complications, risk of infections, long-term pacemaker dependency, the need for recurrent generator replacement, as well as esthetic and mechanical concerns [3]. These limitations highlight the need to explore alternative strategies of treatment that are more physiologic and less invasive.

Cardioneuroablation (CNA) is a relatively novel catheter-based therapeutic approach aimed at modifying cardiac parasympathetic innervation through radiofrequency ablation (RFA) of atrial ganglionated plexi [4, 5]. In recent years, CNA demonstrated efficacy in the treatment of vagal-induced bradyarrhythmias, decreasing the incidence of syncopal episodes and reducing the need for PPM [6]. Despite the promising nature of the method, the issues of patient selection, procedural methodology, and long-term outcomes remain

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subjects of scientific debate [7, 8]. Given the rising detection of cardiac rhythm disturbances associated with increased parasympathetic nervous system activity in young people, in-depth research of CNA remains essential.

METHODS

Study Design and Ethical Considerations

This study was designed as a prospective, single-center, single-arm pilot cohort study evaluating the feasibility and preliminary efficacy of CNA in patients with vagally mediated bradyarrhythmias, with assessment of clinical and instrumental parameters before and after the procedure, followed by longitudinal patient monitoring. Given the exploratory nature and small sample size ($n = 21$), findings should be interpreted as hypothesis-generating and require validation in larger controlled studies. Enrollment commenced in August 2023 and the present analysis includes patients enrolled through March 2025. The clinical phase of the study was conducted after the approval of the protocol by the Local Ethics Committee of the The Medical Centre Hospital of the President's Affairs Administration of the Republic of Kazakhstan (protocol no. 1, dated February 9, 2024). Written informed consent was obtained from all participants prior to enrolment.

Inclusion Criteria

Patients were eligible for inclusion if they met the following criteria:

1. Age ≥ 18 years;
2. Symptomatic sinus bradycardia, during daytime, including transient episodes;
3. Symptomatic bradycardia due to AV block during daytime, including transient episodes;
4. Severe asymptomatic sinus bradycardia with a heart rate (HR) < 45 beats per minute (bpm) during daytime;
5. Transient second- to third-degree AV block or persistent second-degree AV block;
6. Recurrent syncope or presyncope episodes with a documented association with bradycardia (without trauma);
7. Reflex pauses > 6 seconds.

In addition to the aforementioned criteria, the patients were required to meet the following criteria:

1. Positive response to the atropine test defined as:
 - a. Increase in sinus HR $> 50\%$ or achievement of HR > 90 bpm;
 - b. Conversion of second- or third-degree AV block to first degree AV block or complete normalization of AV conduction on sinus rhythm.
2. Presence of sinus rhythm at the time of enrolment;
3. Absence of structural or organic cardiac disorders.

The inclusion criteria were selected to ensure enrolment of adults with clinically relevant bradyarrhythmias and objectively documented conduction abnormalities associated with symptoms or increased clinical risk. Additional criteria, including a positive atropine test, sinus rhythm at enrolment, and absence of structural heart disease, were applied to

confirm preserved conduction responsiveness, ensure reliable rhythm assessment, and minimize confounding from underlying cardiac pathology.

Exclusion Criteria

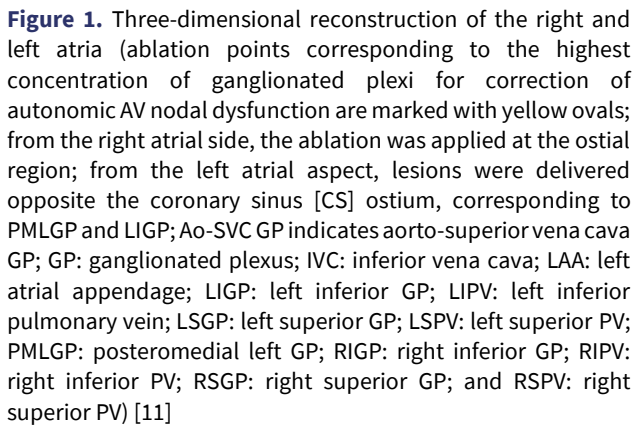
The patients were excluded if any of the following criteria were present:

1. **Confounding pharmacotherapy:** Chronic use of anti-arrhythmic drugs for tachyarrhythmias or presence of drug-induced sinus bradycardia and/or AV block;
2. **Cardiac devices:** Presence of implanted PPM, cardiac contractility modulation device or implantable cardioverter-defibrillator;
3. **Reversible causes:** Bradycardia secondary to electrolyte imbalance (e.g., hyperkalemia), hypothyroidism, or other reversible conditions, or obstructive sleep apnea syndrome (documented association between bradyarrhythmia and episodes of apnea/hypopnea);
4. **Negative atropine test:** Absence of response to atropine administration (up to a maximum dose of 0.02 mg/kg);
5. **Structural or ischemic heart disease:** Clinically significant coronary artery disease, post-infarction cardiosclerosis, hemodynamically significant congenital heart diseases, including surgically corrected defects;
6. **Medical history:** Open-heart surgeries, stroke or transient ischemic attack within the previous 3 months;
7. **Recent interventions:** Percutaneous coronary intervention within the previous 3 months or any catheter-based coronary or electrophysiological interventions within the previous 3 days.

The exclusion criteria were applied to minimize confounding and ensure a clinically homogeneous study population by excluding patients with pharmacologically induced or reversible causes of bradycardia, implanted cardiac devices, significant structural or ischemic heart disease, recent major cardiovascular or neurological events, and recent cardiac interventions that could influence cardiac conduction or study outcomes. Patients with a negative atropine test were also excluded to avoid inclusion of individuals without demonstrable conduction responsiveness.

Atropine Response Test

The patients who met the inclusion criteria underwent atropine test. A solution of atropine 1.0 mg/1.0 ml is diluted in 10 ml normal saline. Baseline HR, AV conduction, and PR interval were assessed prior to the test. Then, atropine was administered as an intravenous bolus via a peripheral catheter at a dose of 0.01 mg per kg body weight. Cardiac rhythm, HR dynamics, AV conduction, and PR interval were monitored for 15 minutes following the administration. Patients demonstrating the increase in HR for 50% or more compared with baseline values, improvement of second- and third-degree AV block to first-degree AV block or complete normalization of AV conduction were selected for subsequent catheter-based intervention. In all patients enrolled for the procedure, organic and structural heart diseases were excluded prior to intervention.



All CNA procedures were performed by using EnSiteX (Abbott), 3D electroanatomical navigation, via right femoral venous access under local anesthesia. Intravenous heparin (5,000 IU) was introduced during femoral venous puncture. During transeptal puncture, additional heparin was administered according to body weight. The targeted activated clotting time was maintained for more than 300 seconds in the left atrium during the procedure. A 10-pole catheter was positioned in the coronary sinus for pacing maneuvers and anatomical guidance all along the transeptal puncture. Transeptal access was achieved using Brockenbrough needle (Abbott) and a long Swartz introducer (Abbott).

The endpoint of RF sustained increase of HR by 50% or more compared to the baseline values recorded before the procedure. An additional efficacy criterion was absence of chronotropic response (HR slowing), following intravenous administration of phenylephrine, demonstrating adequate autonomic denervation of the targeted ganglionated plexi. CNA was done in the right atrium in nine patients, in the left atrium in six patients, and in both atria in six patients. In the

Study Outcomes

- (1) clinical history consistent with reflex or autonomic dysfunction (predominance of bradycardia during daytime activity or in emotionally stressful situations, absence of nocturnal predominance);
- (2) Holter monitoring demonstrating transient bradycardia or conduction abnormalities without evidence of intrinsic sinus node disease;
- (3) a positive atropine test, defined as $\geq 50\%$ increase in sinus HR or complete normalization of AV block following intravenous atropine (0.01 mg/kg), which confirmed vagal rather than intrinsic conduction system disease; and
- (4) absence of structural heart disease on echocardiography and coronary artery disease on non-invasive workup.

- (1) change in mean 24-hour HR on Holter monitoring;
- (2) improvement in health-related quality of life (EQ-5D, Wayne questionnaire, and syncope functional status questionnaire [SFSQ]);
- (3) change in electrophysiological parameters (Wenckebach point, AV ERP, and cSNRT); and
- (4) freedom from PPM implantation at 12 months.

Statistical analysis was performed to evaluate changes in parameters studied before and after the procedure. Continuous variables are presented as mean $\pm$ standard deviation (SD). Prior to selecting the inferential test, pairwise differences (post minus pre) were assessed for normality using the Shapiro-Wilk test, which is preferred for small samples ($n < 50$). Where differences were normally distributed (Shapiro-Wilk $p > 0.05$), paired student's t-test was used as the primary test; where differences were non-normally distributed, the Wilcoxon signed-rank test was used as the primary test and the t-test is reported as supplementary. Results are presented with 95% confidence intervals (CIs) of the mean difference and Cohen's d as an effect size measure ($d = 0.2$ small, $= 0.5$ medium, $= 0.8$ large). For ordinal data (EQ-5D domains), the Wilcoxon signed-rank test was used throughout. The significance level was set at a two-sided $p < 0.05$. Statistical analyses were performed using Python 3.x (SciPy v1.15, NumPy v1.26).

Table 1. Patient characteristics

Patient information		Patients (n = 21)
Age (mean)		37.4 ± 10.2
Gender	Male, n (%)	11 (52.3%)
	Female, n (%)	10 (47.6%)
Patients with syncope, n (%)		6 (28.5%)
Autonomic dysfunction of the sinus node, n (%)		17 (80.9%)
Isolated transient autonomic AV conduction disturbances, n (%)		2 (9.5%)
Combined autonomic dysfunction of sinus node and AV node, n (%)		2 (9.5%)

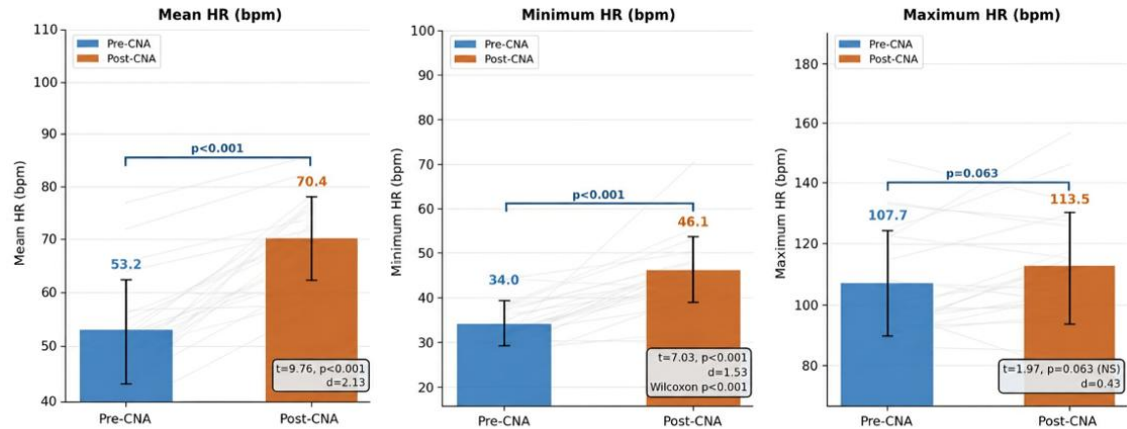


Figure 2. Comparison of HR parameters before and after CAN (left: M HR; center: minimum HR; & right: maximum HR; Bars: M ± SD; & individual patient lines shown in grey (created by the authors)

RESULTS

Between August 2023 and March 2025, a total of 21 CNA procedures were performed. Following the procedure, patients were prospectively followed by protocol at 3, 6, 12, and 24 months. Actual follow-up duration ranged from 4 to 25 months (mean: 14.5 months). No patients were lost to follow-up. The age of the patients ranged from 20 to 54 years (mean age 37.4 ± 10.2 years). At each follow-up visit, Holter monitoring was conducted, and the patients completed standardized quality-of-life questionnaires, including the EQ-5D, Wayne questionnaire, and the SFSQ for the patients with syncope. The full versions of these questionnaires are available in [Appendix A](#).

The primary clinical presentations were distributed as follows:

- **Autonomic SND:** 17 patients (80.9%) were diagnosed with autonomic SND. Among them, three patients (17.6%) experienced episodes of sinus arrest with pauses ranging from 3.2 to 5.7 s.
- **Isolated AV conduction disturbances:** Two patients (9.5%) were hospitalized with isolated transient autonomic AV conduction disturbances, including second-degree AV block (Mobitz type I and type II) and episodes of 2:1 conduction. One patient presented with persistent first-degree AV block, with a mean PR interval of 275 ms on 24-hour Holter monitoring.
- **Combined autonomic dysfunction:** Two patients (9.5%) had combined autonomic dysfunction involving both the sinus node and the AV node, characterized by sinus bradycardia and sinoatrial (SA) block in combination with transient second-degree AV block.

Clinically, the patients reported discomfort in chest, frequent episodes of dizziness, and six patients experienced syncope ([Table 1](#)).

Analysis of mean HR via Holter monitoring illustrated a statistically significant increase after the procedure ([Figure 2](#)). The mean HR increased from 53.2 ± 9.6 bpm pre-procedure to 70.4 ± 7.8 bpm post-procedure (mean difference: +17.1 bpm; 95% CI: 13.5-20.8 bpm; paired t-test: t (20) = 9.76, p < 0.001; Cohen's d = 2.13; Shapiro-Wilk test on differences: W = 0.986, p = 0.983; Wilcoxon signed-rank: W = 0, p < 0.001). Minimum HR also increased significantly from 34.0 ± 4.9 to 46.1 ± 7.4 bpm (difference: +12.2 bpm; 95% CI: 8.6-15.8; p < 0.001; d = 1.53; differences non-normally distributed [Shapiro-Wilk p = 0.003], Wilcoxon W = 1, p < 0.001). Maximum HR showed no statistically significant change (107.7 ± 17.0 vs. 113.5 ± 18.7 bpm; difference: +5.8 bpm; 95% CI: -0.4 to 12.0; p = 0.063; d = 0.43).

Note on instruments: The EQ-5D is a validated generic measure of health-related quality of life comprising five domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each scored 1-3 (1 = no problem, 3 = extreme problems). The SFSQ yields a composite syncope dysfunction score (SDS) from 0-100, with higher scores indicating greater impairment. The Wayne questionnaire is a 36-item self-reported instrument for autonomic nervous system status (score ≥ 15 indicates autonomic dystonia).

As previously noted, 6 out of 21 patients included in the study had a history of syncope. Following CNA, no episodes of syncope were reported in these patients throughout the follow-up period. According to the SFSQ, all of the patients remained syncope-free after the intervention. The SDS decreased significantly from 51 at baseline to 17.12 post-procedure. Moreover, CNA was associated with a meaningful improvement in EQ-5D scores across most domains, indicating its positive effect on patients' overall quality of life ([Figure 3](#)).

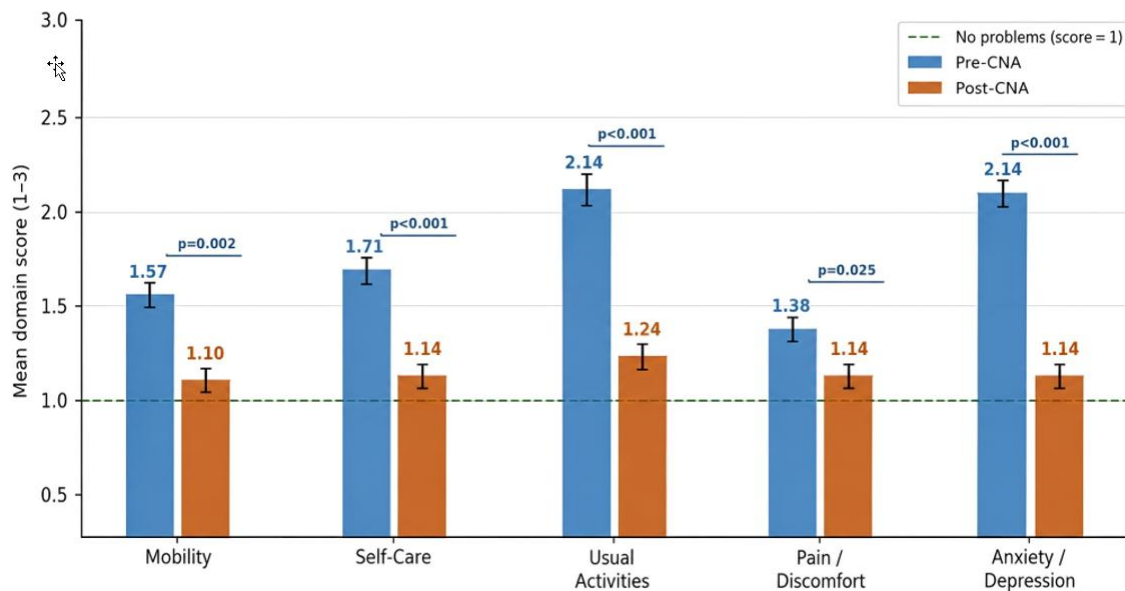


Figure 3. Changes in EQ-5D scores before and after CAN (created by the authors)

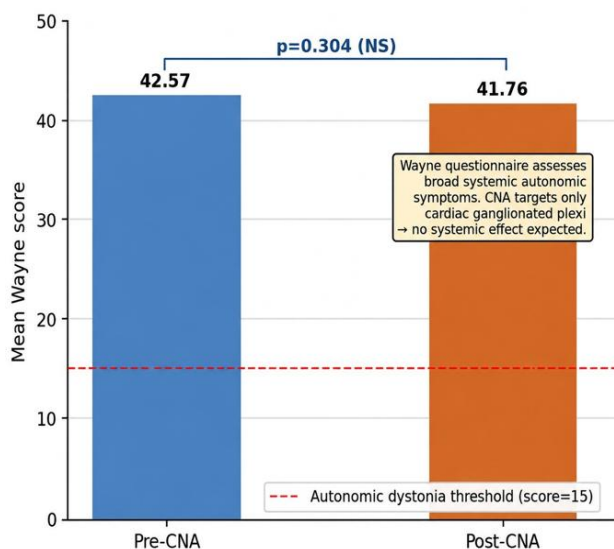


Figure 4. Comparison of Wayne autonomic scores before and after CNA (created by the authors)

In contrast, results from the Wayne questionnaire showed only a marginal reduction in mean autonomic scores (from 42.57 to 41.76; $p = 0.304$). These data suggest that CNA effectively modulates cardiac parasympathetic tone but has limited impact on non-cardiac systemic autonomic tone (Figure 4).

A summary of mean intraoperative measurements is presented in Table 2.

Electrophysiological Outcomes

Changes in key electrophysiological measurements, including indices of sinus node function, AV conduction, and refractory properties, were assessed before and after the intervention (Figure 5).

CNA resulted in significant improvement in multiple electrophysiological measurements (Figure 5). Antegrade conduction (Wenckebach point) decreased significantly from 541.9 ± 139.9 ms to 393.8 ± 63.7 ms (mean difference: -148.1 ms; 95% CI: -207.1 to -89.1; $t(15) = -5.35$, $p < 0.001$; Cohen's $d = 1.34$ [large]; Wilcoxon $W = 2$, $p = 0.001$; $n = 16$). The effective refractory period (ERP) of the AV node decreased from 438.0 ± 133.6 ms to 350.0 ± 98.0 ms (difference: -88.0 ms; 95% CI: -138.0 to -38.0; $t(9) = -3.98$, $p = 0.003$; $d = 1.26$ [large]; Wilcoxon $W = 0$, $p = 0.008$; $n = 10$). The corrected sinus node recovery time (cSNRT) decreased from 524.5 ± 273.1 ms to 320.5 ± 76.9 ms (difference: -204.1 ms; 95% CI: -384.1 to -24.0; $t(12) = -2.47$, $p = 0.030$; differences non-normally distributed [Shapiro-Wilk $p = 0.001$]; Wilcoxon $W = 4$, $p = 0.001$; $n = 13$). In contrast, PR interval (179.1 ± 42.8 vs. 179.0 ± 29.4 ms; $p = 0.995$), AH interval (95.4 ± 41.2 vs. 89.4 ± 23.6 ms; $p = 0.519$), and HV interval (50.1 ± 6.3 vs. 50.8 ± 6.1 ms; $p = 0.590$) showed no statistically significant changes, confirming that CNA does not affect supra-Hisian or infra-Hisian conduction.

Follow-Up Observations

The primary clinical endpoint was freedom from syncope or presyncope attributable to vagally mediated bradycardia throughout the follow-up period and absence of clinically significant bradycardia (HR < 40 bpm during daytime or pauses > 3 seconds). Secondary endpoints included: increase in mean

Table 2. M intraoperative parameters

Parameter	Pre-CNA (mean $\pm$ SD)	Post-CNA (mean $\pm$ SD)	Difference (95% CI)	p/Cohen's d
Wenckebach point (ms)	541.9 $\pm$ 139.9	393.8 $\pm$ 63.7	-148.1 (-207 to -89)	$p < 0.001/d = 1.34$
ERP AV node (ms)	438.0 $\pm$ 133.6	350.0 $\pm$ 98.0	-88.0 (-138 to -38)	$p = 0.003/d = 1.26$
cSNRT (ms)	524.5 $\pm$ 273.1	320.5 $\pm$ 76.9	-204.1 (-384 to -24)	$p = 0.030/d = 0.69^\dagger$
PR interval (ms)	179.1 $\pm$ 42.8	179.0 $\pm$ 29.4	-0.1 (-22.5 to 22.4)	$p = 0.995/d \approx 0$ (NS)
AH interval (ms)	95.4 $\pm$ 41.2	89.4 $\pm$ 23.6	-6.0 (-25.4 to 13.4)	$p = 0.519/d = 0.16$ (NS)
HV interval (ms)	50.1 $\pm$ 6.3	50.8 $\pm$ 6.1	+0.7 (-2.0 to 3.3)	$p = 0.590/d = 0.14$ (NS)

Note. † Non-normally distributed differences (SW $p < 0.05$); WSR test used as primary; t-test reported as supplementary; & NS: Not significant

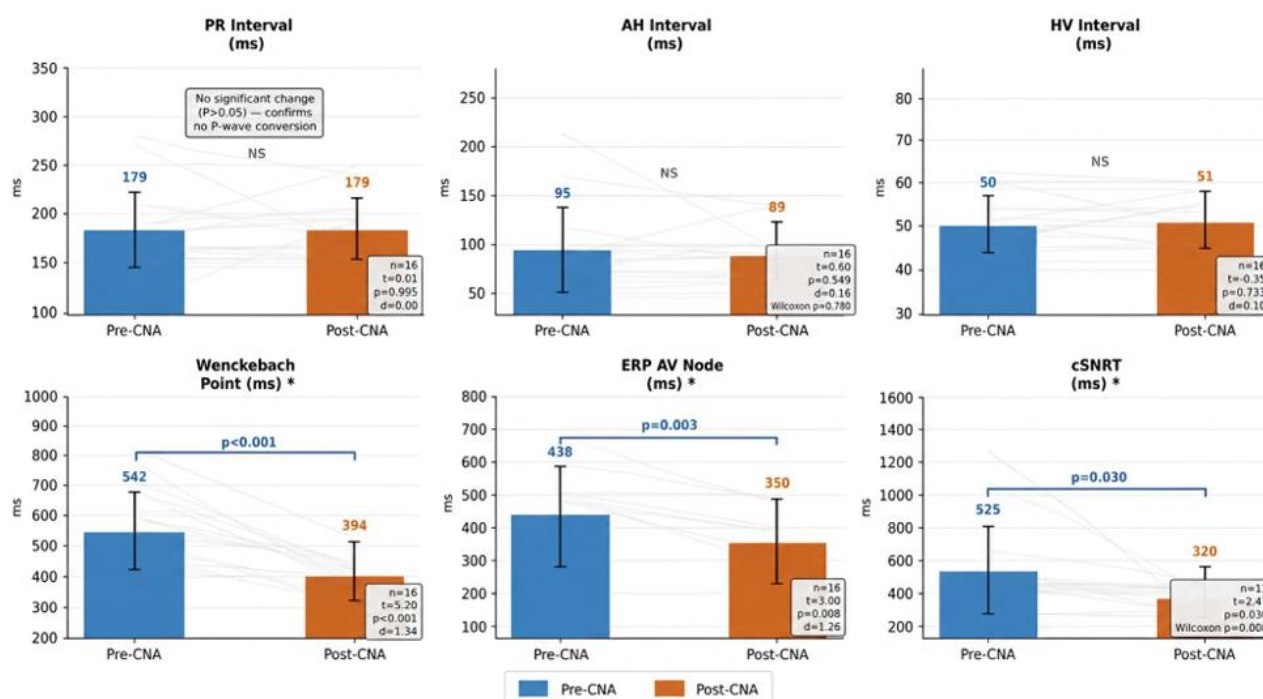


Figure 5. Electrophysiological parameters before (blue) and after (orange) CNA (top row: PR interval, AH interval, HV interval [all NS, confirming no infra-Hisian effect]; bottom row: Wenckebach point [$p < 0.001$, $d = 1.34$], AV node ERP [$p = 0.003$, $d = 1.26$], and cSNRT [$p = 0.030$, Wilcoxon $p = 0.001$]; & statistics shown in inset boxes (created by the authors)

24-hour HR on Holter monitoring, change in electrophysiological parameters (Wenckebach point, AV ERP, and cSNRT), improvement in health-related quality of life, and freedom from PPM implantation at 12 months.

The protocol-specified visit schedule included assessments at 3, 6, 12, and 24 months post-procedure. Actual follow-up duration ranged from 4 to 25 months (mean: 14.5 months), reflecting ongoing enrollment. No patients were lost to follow-up; all 21 patients completed at least one post-procedural assessment. Throughout this period, no episodes of syncope were documented across the cohort.

In most cases, marked increase of sinus rhythm rate was noted post-CNA. However, the positive clinical effect was not maintained in one patient. Despite a modest intra-procedural acceleration of the sinus rhythm, post-procedural Holter monitoring revealed a sinus pause of up to 3,318 ms driven by SA block. This necessitated the subsequent implantation of a PPM. Retrospective analysis suggested the presence of underlying structural SND in this patient.

In another patient who underwent CNA for a second-degree AV block, a late recurrence of second-degree AV block Mobitz type II was recorded via ambulatory ECG monitoring 14 months after the intervention. This recurrence was characterized by frequent pauses exceeding 2,000 ms and associated clinical symptoms, eventually leading to the implantation of a PPM.

No procedure-related complications were recorded during or after CNA. Monitored adverse events included: cardiac tamponade, pericardial effusion, stroke or transient ischemic attack, pulmonary vein stenosis, vascular access complications (hematoma, arteriovenous fistula, and retroperitoneal bleeding), atriopharyngeal fistula, complete AV block requiring PPM as a complication (distinct from PPM for procedural failure), significant proarrhythmia (sustained atrial tachyarrhythmia or ventricular arrhythmia), and death. Monitoring was performed by continuous intraoperative ECG

and hemodynamic recording, immediate post-procedural transthoracic echocardiography, and 24-hour in-hospital telemetry. None of the above events was observed in any patient. There was no evidence of proarrhythmia or new clinically meaningful arrhythmias attributable to the ablation.

DISCUSSION

Efficacy of CNA for Sinus Bradycardia and AV block

This research demonstrated a statistically significant increase in mean HR, as observed on Holter monitoring ($p < 0.001$). This outcome provides direct evidence of the attenuation of excessive vagal influence on the sinus node, resulting in the restoration of its physiological automaticity. A meaningful reduction in the cSNRT further supports the improvement in sinus node automatic function and vagal withdrawal [9].

Although mean minimal and maximal HR metrics depict the general trend, they do not fully capture the true clinical efficacy of CNA (Figure 2). These measures may be influenced by multiple external and physiological factors, including physical and emotional stress, sleep quality, circadian variation, and concomitant conditions [10].

Expanded analysis of electrophysiological indices demonstrated significant improvement in antegrade conduction (Wenckebach point: -148.1 ms; 95% CI: -207.1 to -89.1 ; $p < 0.001$; $d = 1.34$) and AV nodal ERP (ERP: -88.0 ms; 95% CI: -138.0 to -38.0 ; $p = 0.003$; $d = 1.26$), confirming attenuation of vagal tone and enhanced AV nodal conduction (Figure 5). cSNRT also decreased significantly ($p = 0.030$; Wilcoxon $p = 0.001$), reflecting improved sinus node automaticity. Critically, PR, AH, and HV intervals showed no statistically significant changes (all $p > 0.05$), confirming that CNA selectively modifies



Figure 6. Pre- and post-procedural ECG findings (note the resolution of the second-degree AV block and the subsequent shortening of the PR interval to 240 ms post-intervention: (A) pre-procedural ECG [upper panels] & (B) post-procedural ECG [lower panels] (created by the authors)

parasympathetic innervation of the sinus and AV nodes without affecting infra-Hisian or His-Purkinje conduction.

A pronounced improvement in health-related quality of life was observed. According to the SFSQ, all patients with a prior history of syncope achieved complete resolution of syncope, with the dysfunction score dropping from 51 to 17.2. Moreover, the EQ-5D questionnaire showed a marked improvement across most domains, particularly mobility, self-care, usual activities, pain/discomfort, and anxiety/depression ($p < 0.05$). These results directly correlate with a reduction in syncope burden and enhanced general well-being, representing a clinically consequential outcome. However, the Wayne questionnaire for assessment of autonomic status showed no statistically significant change (pre: 42.57; post: 41.76; $p = 0.304$). This finding is physiologically consistent and should not be misinterpreted as procedural failure. The Wayne instrument assesses a broad spectrum of autonomic symptoms spanning both cardiac and extra-cardiac domains (perspiration, headache, sleep, gastrointestinal, and respiratory symptoms). CNA selectively targets cardiac ganglionated plexi, modifying parasympathetic innervation of the sinus and AV nodes without altering systemic autonomic regulation or extra-cardiac vagal projections. The dissociation between cardiac-specific outcomes (objective Holter-based HR and EP parameters) and systemic autonomic outcomes (Wayne score) reflects the anatomically confined scope of CNA and is consistent with prior observations in [7, 11], which similarly noted that CNA does not normalize systemic autonomic tone.

Among the patients with transient second-degree AV block, a recurrent AV block Mobitz type II second-degree AV block was recorded on Holter monitoring following CNA. The recurrence was characterized by frequent pauses over 2000 ms and clinical manifestations, necessitating the implantation of a PPM. Notably, the procedure yielded only a partial effect in this patient, as a first-degree AV block with a mean PR interval of

238 ms persisted after the intervention. Post-procedural intra-operative readings were 140 ms and 60 ms for the AH interval and HV interval, respectively. Pre-operatively, Holter monitoring predominantly demonstrated Mobitz type I and type II second-degree AV block, with episodes of 2:1 conduction. Additionally, intermittent first-degree AV block was observed, with a mean PR interval of 276 ms. Baseline values before CNA were 170 ms and 62 ms for the AH and HV intervals, respectively (Figure 6).

The atropine test performed before CNA was defined as positive if AV conduction was completely restored following atropine administration with a PR interval between 190 and 200 ms. Based on these results, the patient was referred to the interventional treatment. During the intraoperative high-density mapping of the right atrium, a considerable cluster of parasympathetic ganglionated plexi was identified in the coronary sinus ostium region. An RFA line was created extending from the fossa ovalis to coronary sinus ostium, and further towards inferior vena cava (Figure 7).

The cause of the recurrent second-degree AV block in this patient during the longitudinal observation remains to be fully elucidated. In this research, the majority of patients had sinus node autonomic dysfunction rather than different degrees of AV block. In addition, we had a limited experience with CNA particularly in patients with isolated AV blocks, which could also have an impact on the outcomes. However, as noted in [11], biatrial ablation, involving both the right and left atria, demonstrated superior efficacy compared to isolated right atrial ablation. Nevertheless, this approach needs to be investigated to establish its long-term superiority [12].

A paradoxical response was recorded during CNA in a patient with severe bradycardia (HR = 40 bpm) initially. HR acceleration reached 80 bpm during the RFA of ganglionated plexi, and it was accompanied by the prolongation of the PR interval to 240 ms, despite the absence of prior AV conduction

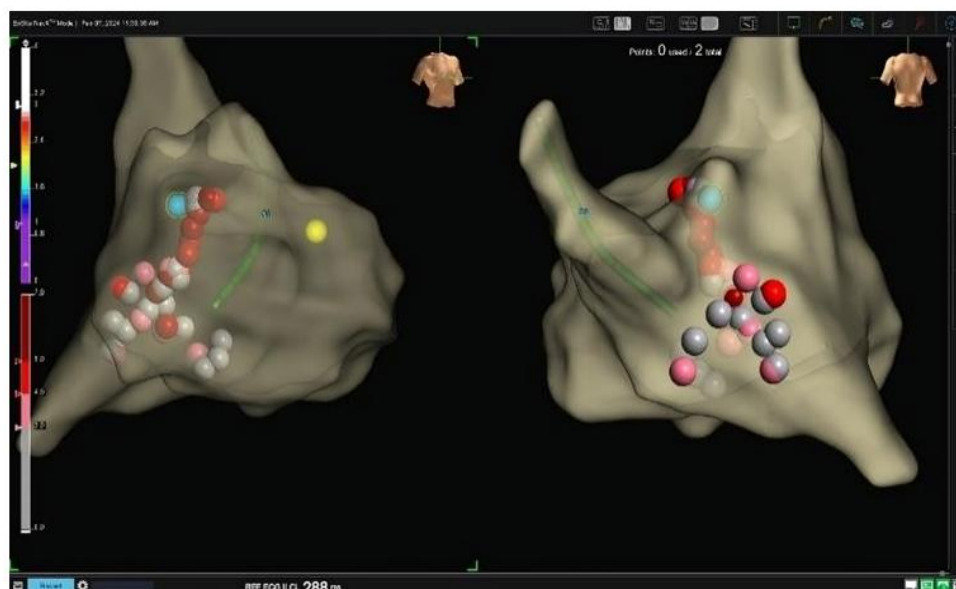


Figure 7. Radiofrequency ablation application sites (created by the authors)

disturbances. This observed phenomenon may illustrate a personalized autonomic response after denervation. Similar patterns were seen in two other patients.

The PR interval prolongation after CNA may be functional and adaptive in nature. Considering that the procedure is primarily aimed at elimination of parasympathetic influence on the sinus node, HR acceleration is commonly identified in the post-ablation period. Under these conditions, the AV node, which previously functioned under intense vagal control, appears to be not fully adapted to increased frequency of atrial impulses. It causes PR interval prolongation due to decremental conduction within the AH interval. Consequently, these changes may transiently manifest as moderate slowing of AV nodal conduction without underlying structural damage. Thus, recorded PR interval prolongation probably reflects temporary physiological dissociation in adaptive processes between the sinus node and AV node rather than organic destruction of the cardiac conduction system [13, 14].

Study Limitations and Perspectives of Further Research

This study has several important limitations. First, the small sample size ($n = 21$ overall; $n = 3$ in the isolated AV block subgroup) limits statistical power and generalizability, particularly for subgroup analyses. Second, as a single-center pilot study conducted at a specialized cardiac interventional unit, external validity is inherently constrained; patient selection criteria, operator experience, and post-procedural monitoring may differ across institutions, and multicenter studies are required to confirm these findings. Third, head-up tilt-table testing was not routinely performed; differentiation between vagal and intrinsic conduction disease relied on the atropine test, Holter monitoring, and standard exclusion criteria, which may not identify all cases of mixed etiology. Fourth, the absence of a concurrent control group precludes causal attribution of outcomes to CNA. Fifth, variable follow-up duration (4-25 months) limits long-term outcome assessment for the full cohort. Sixth, the paradoxical responses observed in a subset of patients and the late recurrence of AV block in one patient indicate that predictors of durable procedural success remain incompletely defined and require prospective investigation. The role of biatrial ablation and more precise

electrophysiological criteria for ganglionated plexus targeting also require further study.

The research demonstrates promising initial results; however, several aspects require further studies in order to strengthen the evidence base of CNA and support its wider implementation.

CONCLUSION

In selected patients with confirmed vagally mediated bradyarrhythmias, CNA represents a feasible and potentially effective catheter-based treatment modality. In the present single-center pilot cohort ($n = 21$), CNA was associated with significant improvements in mean HR, electrophysiological parameters, and health-related quality of life, and all patients with prior syncope remained syncope-free throughout follow-up. These findings suggest that CNA may reduce the need for PPM implantation in carefully selected patients with vagally mediated bradyarrhythmias, particularly younger individuals who face the long-term sequelae of device therapy. However, given the preliminary, single-arm design, these results are hypothesis-generating and require confirmation in larger, multicenter, prospective studies—ideally with concurrent control comparators—before CNA can be recommended for wider clinical implementation.

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APPENDIX A: EQ-5D HEALTHQUESTIONNAIRE

Under each heading, please tick the **ONE** box that best describes your health **TODAY**.

MOBILITY

- ☐ I have no problems in walking about.
☐ I have some problems in walking about.
☐ I am confined to bed.

SELF-CARE

- ☐ I have no problems with self-care.
☐ I have some problems washing or dressing myself.
☐ I am unable to wash or dress myself.

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

- ☐ I have no problems with performing my usual activities.
☐ I have some problems with performing my usual activities.
☐ I am unable to perform my usual activities.

PAIN / DISCOMFORT

- ☐ I have no pain or discomfort.
☐ I have moderate pain or discomfort.
☐ I have extreme pain or discomfort.

ANXIETY/DEPRESSION

- ☐ I am not anxious or depressed.
☐ I am moderately anxious or depressed.
☐ I am extremely anxious or depressed.

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Table A1. Questionnaire for identifying signs of autonomic (vegetative) changes (A. M. Wayne)

Patient: _____ Date: _____

	Yes	S	No
1. Please indicate whether you (in any situation of emotional stress) have a tendency to:			
A) facial flushing (redness of the face)	Yes	3	No
B) facial pallor	Yes	3	No
2. Do you experience numbness or a sensation of coldness:			
A) of the fingers of the hands and feet	Yes	3	No
B) of the entire hands and feet	Yes	4	No
3. Do you experience changes in skin color (pallor, redness, cyanosis):			
A) of the fingers of the hands and feet	Yes	5	No
B) of the entire hands and feet	Yes	5	No
4. Do you experience increased sweating? If the answer is yes», underline constant or during emotional stress.	Yes	4	No
5. Do you often experience sensations of palpitations, fluttering or stopping of the heart?	Yes	7	No
6. Do you often experience difficulty breathing, a feeling of lack of air, rapid breathing? If the answer is «yes», specify: during emotional stress, in a stuffy room (underline as appropriate).	Yes	7	No
7. Is dysfunction of the gastrointestinal tract characteristic for you: a tendency to constipation, diarrhea, abdominal bloating, abdominal pain?	Yes	6	No
8. Do you experience fainting episodes (sudden loss of consciousness or a feeling that you might lose consciousness)? If yes, specify the conditions: stuffy room, emotional stress, prolonged standing position (underline as appropriate).	Yes	7	No
9. Do you experience paroxysmal (attack-like) headaches? If yes, specify: diffuse or only in one half of the head: squeezing or pulsating (underline as appropriate).	Yes	7	No
10. Do you currently note decreased working capacity and rapid fatigability?	Yes	5	No
11. Do you note sleep disturbances? If the answer is «yes», specify: A) difficulty falling asleep; B) shallow, non –restorative sleep with frequent awakenings; C) feeling of sleep deprivation and fatigue upon waking in the morning.	Yes	5	No

Note. If the total number of points is equal to or greater than 15, the presence of autonomic dystonia syndrome is assumed & S: Scores

SFSQ Questionnaire—Syncope Functional Status Questionnaire

Linzer M, Gold DT, Pontinen M, Divine GW, Felder A, Brooks WB. Recurrent syncope as a chronic disease: preliminary validation of a disease-specific measure of functional impairment. *J Gen Intern Med.* 1994;9(4):181-6.

Last name:

First name:

Patient code:

I) Please answer each question: Y – yes, N – no, or N/A – not applicable

These episodes interfere with my life and daily activities:

- () Interfere with my life or daily activities
 () Prevent me from driving a car
 () Reduce my ability to take daily walks (including shortening the distance)
 () Interfere with my use of public transportation (bus, subway, train, etc.)
 () Interfere with my household activities (shopping, cleaning, housekeeping)
 () Interfere with my physical activities (recreation, sports)
 () Interfere with my job duties
 () Affect my relationship with my spouse/partner
 () Affect my relationship with my family
 () Affect my relationship with friends
 () Affect my sexual relationships

II) How much do these episodes bother you? Please circle the number that corresponds to your level of concern.

1	2	3	4	5	6	7	8
Always bother me							Never bother me

III) How afraid are you of having another episode?

Please circle the number that best describes you.

1	2	3	4	5	6	7	8
Terrified			Neutral attitude				Not afraid at all

IV) How does worry about another episode affect your daily life?

On the scale below, circle the number that best applies to you.

1	2	3	4	5	6	7	8
All I do is worry (so anxiety completely distracts me from my normal life), I never worry (so anxiety does not interfere with me)							

Instructions for scoring the syncope functional status questionnaire: The functional impairment score is calculated as the percentage of affected areas out of the 11 possible, where the patient reports being affected by syncope. For example, if the patient is unemployed, making the item “job duties” not applicable, the score will be based on 10 items.

If the patient answers “yes” to 3 of those 10 items, the functional impairment score would be 30 or 30%. The fear/worry score is based on the mean value of the three Likert-scale items, after converting their range from 1-8 to 100-0. For example: If a patient answers 2, 6, and 3 on the three questions, the converted values will be 85.7, 14.3, and 71.4, respectively. The average of these will give a fear/worry score of 61.9 (note that it may be more efficient to average the three Likert values first before scaling). The SDS equals the average of the functional impairment score and the fear/worry score.

For the hypothetical patient above, SDS = 46.

Conversion formula: Score = $100 \times (8 - \text{Likert value}) / 7$.