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COMMENTARY

Quality of life improvement following cardioneuroablation for vasovagal syncope: expected or too early to say?

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Vasovagal syncope (VVS) remains the most common cause for syncope [1]. This common condition is mechanistically complex and widely thought to be secondary to a combination of parasympathetic activation and sympathetic inhibition, resulting in hypotension (vasodepression) and/or bradycardia (cardioinhibition) [1]. Although benign in many, recurrent VVS can be debilitating in some. Non-pharmacological approaches, including education on diagnosis and prognosis, avoiding known triggers, increasing salt and water intake, and physical counterpressure maneuvers, can be helpful in improving VVS [2]. Pharmacological treatment options include medications like midodrine and fludrocortisone [2]. Permanent pacing has been shown to reduce recurrent syncope in patients with recurrent cardioinhibitory (CI) VVS not responding to conservative therapy [3, 4].

Catheter ablation of ganglionated plexi (GPs) (cardioneuroablation (CNA)) is aimed at modulating the cardiac autonomic nervous system to mitigate the autonomic processes occurring in VVS, primarily parasympathetic activation, by using endocardial radiofrequency ablation in patients with predominant CI-VVS refractory to medical therapy [5, 6]. Observational studies and a small RCT have shown that CNA can significantly reduce syncope recurrence compared to conservative therapy in patients with CI-VVS [5–8]. A recent multicenter study showed that the syncope recurrence risk in CI-VVS patients who underwent CNA was similar to that of a population of patients undergoing pacemaker implantation with a similar safety profile [9].

VVS can result in poor health-related QOL and is associated with increased anxiety and depression [10, 11]. Various treatment strategies for VVS have been shown to have varying effects on QOL (Table 1). For CNA, the only available data on QOL is from a recent randomized controlled study comparing CNA vs. optimal nonpharmacologic therapy in 48 patients with CI-VVS. QOL was measured using the Impact of Syncope on Quality-of-Life Questionnaire [10]. The authors showed that QOL improved substantially in patients who underwent CNA whereas it remained the same in the control group [8].

In this issue of the journal, Baysal et. al report the results of a single-center, observational, single-arm study evaluating health-related QOL improvements in patients undergoing CNA [12]. Twenty-seven patients (age 34 ± 14 years; 48% female) with recurrent VVS (at least 3 syncopal episodes in the past 12 months) were enrolled and prospectively followed up for 12 months. Twenty (74%) had pure CI-VVS and the rest has mixed type VVS on head-up tilt table testing. All patients underwent QOL evaluation by telephone interviews using 36-Item Short Form Health Survey questionnaire (SF-36) and EQ-5D questionnaire at baseline and at 1 and 12 months post-ablation. The SF-36 provides a global measure of health-related QOL. Questionnaire results from each visit were summarized into physical (PCS) and mental component scores (MCS) using a 0–100 scoring scale. The EQ-5D evaluates impairment across 5 domains (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression) using a five-level grading system. QOL differences from pre-ablation to post-ablation were evaluated using paired *t*-tests.

CNA was performed using electroanatomic mapping–guided radiofrequency ablation, targeting fractionated electrograms in the regions consistent with probable GP locations in the left atrium. Additional ablation was done in

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Table 1 Randomized studies reporting the impact of different treatment strategies on quality of life in vasovagal syncope

Study	Treatment	No. of patients	Follow-up	QoL measurement tool	Headline results
Sharma et al. [14] (LIVE-Yoga)	Yoga practice	55	12 months	WHO-QOL-BREF and SF-30	QoL at 12 months showed significant improvement of all Syncope Functional Status Questionnaire scores and 2 domains of WHO QOL-BREF scores ($P < 0.05$)
Perez-Lugones et al. [15]	Fluoxetine vs. bisoprolol	96	6 months	General evaluation of QOL from 1 (very good) to 5 (very bad)	Patients' well-being was improved only in the fluoxetine-group (13.4 ± 0.7 vs. 15.4 ± 0.9 before treatment, $P < 0.01$)
Piotrowski et al. [8]	CNA	48	3, 12, 24 months	QOL questionnaire University of Calgary	QOL improved substantially in patients who underwent CNA whereas QOL in the control group remained the same during follow-up
Baron-Esquivias et al. [3]	Cardiac pacing	54	24 months	SF-36	Mean SF-36 scores were higher in the DDD-CLS group vs. the DDI group for the eight subdomains. DDD-CLS benefited both MCS and PCS components with significant differences in PCS when compared with the DDI group

QOL quality of life, *CNA* cardioneuroablation, *CLS* closed-loop stimulation, *MCS* mental component score, *PCS* physical component score

the right atrium if ablation endpoints were not met with left atrial ablation alone [5, 9]. Acute success was achieved in all patients, and all patients were free of syncope at 12-month follow-up.

Compared to baseline, significant improvement was noted in health-related QOL after ablation as assessed by both SF-36 and EQ-5D questionnaires. With SF-36, significant improvements were noted across the PCS and MCS domains. Age was a significant predictor of QOL improvement with SF-36 whereas gender or extent of heart rate improvement post-ablation was not. Improvement was noted in mobility, self-care, and activity domains by the EQ-5D questionnaire whereas no improvement was noted in the pain/discomfort and anxiety/depression domains. The authors concluded that CNA was associated with significant improvement in QOL in patients with predominantly CI-VVS.

The work from Baysal et al. is a welcome addition to the literature evaluating utility of CNA in improving health related QOL in VVS. Their results are comparable to the recent study from Piotrowski et al. [8], even though the QOL questionnaires used were different. However, several important limitations should be kept in mind. This is a single-center, unblinded observational study with a small number of patients who underwent CNA without a control group. In this scenario, placebo effect due to the procedure cannot be ruled out; this remains a big confounder and potentially limits the overall impact of the study results. It has been shown previously that health-related QOL in VVS patients improved significantly after consultation with a syncope expert and enrolling in a clinical trial, in spite of recurrent syncopal episodes or randomization to the placebo group [13]. There is also lack of clarity as to which questionnaire or tool accurately captures health-related QOL in VVS patients. Studies evaluating improvement in QOL in VVS patients have used various tools including WHO-QOL-BREF [14], Endicott questionnaire [15], and Impact of Syncope on Quality-of-Life Questionnaire by the University of Calgary [10]. This suggests that no "gold standard" tool exists for QOL assessment in VVS patients. Whether QOL assessment of different types of VVS patients (vasodepressive vs. CI-VVS) is best served by a specific questionnaire also remains unclear. Moreover, VVS patients could have other medical/psychological conditions that could potentially confound the QOL questionnaire results, and this could vary by type of questionnaire used. In the current study, 2 patients in the mixed VVS group had significant decrease in SF-36 score post-CNA, despite being free of recurrent syncope, pointing to confounding conditions.

In summary, Baysal et al. provide important hypothesis generating observations on the potential benefit of CNA on QOL in a cohort of patients with predominantly CI-VVS. This merits further exploration, ideally through multicenter, larger randomized studies with long-term follow-up.

Declarations

Conflict of interest Bosky Soni declares no conflict of interest. Dhiraj Gupta: principal investigator for institutional research grants from Boston Scientific and proctor for Abbott Ltd. Rakesh Gopinathannair: consultant/honoraria: Abbott Medical, Boston Scientific, and Sanofi: advisory board: PaceMate (no compensation).

References

1. Gopinathannair R, Salgado BC, Olshansky B. Pacing for vasovagal syncope. Arrhythm Electrophysiol Rev. 2018;7:95–102.
2. Shen WK, Sheldon RS, Benditt DG, Cohen MI, Forman DE, Goldberger ZD, Grubb BP, Hamdan MH, Krahn AD, Link MS, Olshansky B, Raj SR, Sandhu RK, Sorajja D, Sun BC, Yancy CW. 2017 ACC/AHA/HRS Guideline for the evaluation and management of patients with syncope: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2017;70:620–63.
3. Baron-Esquivias G, Morillo CA, Moya-Mitjans A, Martinez-Alday J, Ruiz-Granell R, Lacunza-Ruiz J, Garcia-Civera R, Gutierrez-Carretero E, Romero-Garrido R. Dual-chamber pacing with closed loop stimulation in recurrent reflex vasovagal syncope: the SPAIN Study. J Am Coll Cardiol. 2017;70:1720–8.
4. Brignole M, Menozzi C, Moya A, Andresen D, Blanc JJ, Krahn AD, Wieling W, Beiras X, Deharo JC, Russo V, Tomaino M, Sutton R. Pacemaker therapy in patients with neurally mediated syncope and documented asystole: third International Study on Syncope of Uncertain Etiology (ISSUE-3): a randomized trial. Circulation. 2012;125:2566–71.
5. Aksu T, Guler TE, Bozyel S, Golcuk SE, Yalin K, Lakkireddy D, Gopinathannair R. Medium-term results of cardioneuroablation for clinical bradyarrhythmias and vasovagal syncope: effects on QT interval and heart rate. J Interv Card Electrophysiol. 2021;60(1):57–68.
6. 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;13:1231–42.
7. Aksu T, Padmanabhan D, Shenthar J, Yalin K, Gautam S, Valappil SP, Banavalikar B, Guler TE, Bozyel S, Tanboga IH, Lakkireddy D, Olshansky RB, Gopinathannair R. The benefit of cardioneuroablation to reduce syncope recurrence in vasovagal syncope patients: a case-control study. J Interv Card Electrophysiol. 2022;63:77–86.
8. Piotrowski R, Baran J, Sikorska A, Krynski T, Kulakowski P. Cardioneuroablation for reflex syncope: efficacy and effects on autonomic cardiac regulation-a prospective randomized trial. JACC Clin Electrophysiol. 2023;9(1):85–95.
9. Gopinathannair R, Olshansky B, Turagam MK, Gautam S, Futyma P, Akella K, Tanboga HI, Bozyel S, Yalin K, Padmanabhan D, Shenthar J, Lakkireddy D, Aksu T. Permanent pacing versus cardioneuroablation for cardioinhibitory vasovagal syncope. J Interv Card Electrophysiol. 2022. https://doi.org/10.1007/s10840-022-01456-x.
10. Rose MS, Koshman ML, Ritchie D, Sheldon R. The development and preliminary validation of a scale measuring the impact of syncope on quality of life. Europace. 2009;11:1369–74.
11. Ng J, Sheldon RS, Ritchie D, Raj V, Raj SR. Reduced quality of life and greater psychological distress in vasovagal syncope patients compared to healthy individuals. Pacing Clin Electrophysiol. 2019;42:180–8.
12. Baysal E, Mutluer FO, Dagsali AE, Kumrulu UC, Huang HD, Aksu T. Improved health-related quality of life after cardioneuroablation in patients with vasovagal syncope. J Interv Card Electrophysiol. 2022. https://doi.org/10.1007/s10840-022-01420-9.
13. Ng J, Sheldon RS, Maxey C, Ritchie D, Raj V, Exner DV, Raj SR. Quality of life improves in vasovagal syncope patients after clinical trial enrollment regardless of fainting in follow-up. Auton Neurosci. 2019;219:42–8.
14. Sharma G, Ramakumar V, Sharique M, Bhatia R, Naik N, Mohanty S, Agarwal A, Meti M, Shukla A, Deepti S, Bansal R, Gupta A, Ahmed AS, Pandey RM, Narang R, Mishra S, Saxena A, Juneja R, Investigators LI-Y. Effect of yoga on clinical outcomes and quality of life in patients with vasovagal syncope (LIVE-Yoga). JACC Clin Electrophysiol. 2022;8:141–9.
15. Perez-Lugones A, Schweikert R, Pavia S, Sra J, Akhtar M, Jaeger F, Tomassoni GF, Saliba W, Leonelli FM, Bash D, Beheiry S, Shewchik J, Tchou PJ, Natale A. Usefulness of midodrine in patients with severely symptomatic neurocardiogenic syncope: a randomized control study. J Cardiovasc Electrophysiol. 2001;12:935–8.