*RESPIRATORY MEDICINE*

Cite as: Archiv EuroMedica. 2025. 15; 4. DOI 10.35630/2025/15/4.016

***Received 6 July 2025;***
***Accepted 25 August 2025;***
***Published 27 August 2025***

# FROM HYDRATION TO CARDIONEUROABLATION: A REVIEW OF TREATMENT MODALITIES IN VASOVAGAL SYNCOPE

***Karolina Paks[1]*** ✉, ***Zuzanna Gajda[2]***, ***Monika Pelczar[3]***, ***Barbara Starosta[2]***, ***Bartosz Brzychcy[4]***, ***Karolina Brzychcy[4]***, ***Natalia Musialik[5]***, ***Maciej Magiera[5]***, ***Michał Piotrowski[6]***, ***Paulina Hetnar[7]***

*[1]Independent Public Health Care Facility of the Ministry of Internal Affairs and Administration in Katowice named after sergeant Grzegorz Załoga, Katowice, Poland*
*[2]University Clinical Hospital no 2 in Lodz, Łódź, Poland*
*[3]T. Marciniak Lower Silesian Specialist Hospital - Emergency Medicine Centre, Wrocław, Poland*
*[4]Provincial Hospital Complex named after Dr. Roman Ostrzycki in Konin, Poland*
*[5]Central Teaching Hospital of the Medical University of Lodz, Poland*
*[6]Saint Barbara Provincial Specialist Hospital No. 5 in Sosnowiec, Poland*
*[7]Medical Centre in Piekary Slaskie, Poland*



✉ ***karolinapaks@gmail.com***

## ABSTRACT

Background: Vasovagal syncope (VVS) is the most common type of reflex syncope, characterized by transient loss of consciousness caused by cerebral hypoperfusion. Despite its frequency, the evidence on therapeutic management is heterogeneous, with interventions ranging from lifestyle modification and pharmacologic treatment to invasive procedures. The absence of uniform treatment standards highlights the need to summarize available data and assess the strength of evidence.

Aims: The aim of this review was to evaluate the effectiveness of therapeutic strategies for VVS and to identify directions for future research.

Methods: A literature review was conducted in PubMed and Google Scholar databases, covering articles published between 2015 and 2024. After applying predefined inclusion and exclusion criteria, 19 original research papers were selected for detailed analysis, including clinical trials and meta-analyses. An additional 18 references provided background and context.

Results: Invasive interventions, such as cardioneuroablation and dual-chamber pacing with closed-loop stimulation (CLS), demonstrated preventive effects in selected patients. Among non-invasive strategies, oral rehydration salts (studied in pediatric populations), vitamin D deficiency and its potential correction, psychotherapeutic interventions, and physical training including yoga showed supportive evidence, although sample sizes were limited. In pharmacotherapy, atomoxetine reduced positive tilt test responses, and

fludrocortisone demonstrated modest effects after dose stabilization.

Conclusions: Current VVS management requires a multimodal approach, including lifestyle and non-pharmacologic interventions, limited pharmacologic options, and invasive therapies in carefully selected patients. The heterogeneity of available studies and variability of outcomes underline the need for individualized strategies and further high-quality research to establish clear standards of care.

Keywords: vasovagal syncope, reflex syncope, tilt test, dual-chamber closed-loop stimulation, cardioneuroablation, psychotherapy, physical training, pacemaker, fludrocortisone, atomoxetine

## INTRODUCTION

Syncope is defined as a transient loss of consciousness due to cerebral hypoperfusion, characterized by rapid onset, brief duration, and spontaneous complete recovery [1], [2]. The most common form of syncope is vasovagal syncope (VVS), with a reported prevalence of up to 32% [1],[3]. VVS includes orthostatic syncope, typically induced by standing (less frequently by sitting), and emotional syncope triggered by fear, pain, or blood phobia [2]. Most patients with VVS report multiple identifiable triggering factors [5]. The condition affects both sexes, although women experience syncope more frequently [1], [5], [6]. The onset is typically sudden, with a median age at first episode of 14 years [1], [3]. Vasovagal syncope follows a bimodal age distribution, being most common among adolescents and older adults, while less frequent in middle age [7].

Although many individuals experience only one syncopal episode in their lifetime, over 35% will develop recurrences [8]. Notably, long asymptomatic intervals are often interrupted by sudden clusters of events [5]. A positive family history, especially maternal, increases the likelihood of experiencing VVS [1]. This condition involves both monogenic and polygenic inheritance patterns [9].

VVS, a neurally mediated syncope triggered by minimal stimuli such as pain, fear, or prolonged standing, is considered a uniquely human phenomenon. Several hypotheses attempt to explain why only humans seem to faint [5]. One theory proposes that the vasovagal reflex evolved as a protective mechanism against excessive sympathetic stimulation under emotional or physical stress [10]. If hypotension in VVS is viewed as a reflex-mediated regulatory response, then the expected physiological trigger should be hypertension or a related stimulus. Two explanations have been proposed: either the response is maladaptive, or it is in fact appropriate, implying the existence of a physiological challenge best addressed by transient cerebral hypoperfusion [11]. Research on acute stress-induced syncope and its molecular mechanisms involving α2B-adrenergic receptor (α2B-AR) gene polymorphisms suggests that this phenomenon may be an evolutionary byproduct of human bipedalism [12].

Syncope occurs as a result of a drop in systemic arterial pressure and a corresponding reduction in global cerebral blood flow. Even a brief cessation of cerebral perfusion lasting 6–8 seconds can cause complete loss of consciousness. A systolic pressure of 50–60 mmHg at heart level (equivalent to 30–45 mmHg at brain level in the upright position) is sufficient to induce syncope. Systemic arterial pressure is determined by the product of cardiac output and total peripheral resistance; thus, a decrease in either of these variables can precipitate syncope [2].

In VVS, there is a reduction in both systemic vascular resistance (SVR) and cardiac output (CO) [13], leading to hypotension and bradycardia. In orthostatic syncope, initial venous pooling reduces stroke volume, followed by a decline in heart rate (HR), which further exacerbates the drop in arterial pressure. While the efferent component of the VVS reflex is well understood, the afferent pathway remains unclear [11].

## AIMS

Given the current state of knowledge, the potential for effective treatment of vasovagal syncope (VVS) remains limited. Furthermore, there is no single therapy that is universally effective across all forms of reflex syncope. The aim of this review is to provide a comprehensive analysis of the existing evidence regarding therapeutic options and their efficacy in patients with vasovagal syncope. The analysis of available clinical trials and meta-analyses is intended to equip clinicians with essential, evidence-based data to support the selection of the most appropriate treatment strategy and to identify areas where further research is warranted.

## METHODS

This article is a narrative review based on a structured literature search. The primary objective was to identify and synthesize evidence on therapeutic strategies for vasovagal syncope (VVS).

### SEARCH STRATEGY

A structured search of PubMed and Google Scholar databases was conducted for articles published between January 2015 and December 2024. The following keywords and Boolean combinations were used: "vasovagal syncope" OR "reflex syncope" AND "treatment" OR "therapy" OR "tilt test". Reference lists of relevant publications were also screened to ensure completeness of the evidence base.

### STUDY SELECTION

The search initially yielded 170 records (PubMed = 60; Google Scholar = 110). After removal of duplicates, 107 records remained for screening. Titles and abstracts were evaluated for eligibility, and 87 full-text articles were assessed in detail. Nineteen original studies (randomized controlled trials, clinical trials, and meta-analyses) met the predefined criteria and were included in the core analysis. An additional 18 references (epidemiological studies, mechanistic research, and clinical guidelines) were used to provide context and background. In total, 37 references were cited in this review.

### INCLUSION CRITERIA

1. Original research articles specifically addressing vasovagal syncope and its therapeutic management
2. Clinical trials, randomized controlled trials, and meta-analyses
3. Human studies published in peer-reviewed journals between 2015 and 2023
4. Articles published in English

### EXCLUSION CRITERIA

1. Review articles, systematic reviews, case reports, editorials, and commentaries
2. Studies focusing on other types of syncope (e.g., cardiac, neurological, or unexplained syncope)
3. Non-English publications
4. Preclinical or animal studies

### DATA EXTRACTION AND APPRAISAL

From each included study, data were extracted on study design, patient population, type of intervention, follow-up duration, and main outcomes. The 19 original studies provided evidence on non-pharmacological interventions (oral rehydration salts, vitamin D supplementation, psychotherapy, physical training including yoga), pharmacological therapies (atomoxetine, fludrocortisone), pacing strategies with closed-loop stimulation, and catheter-based cardioneuroablation. Evidence was appraised descriptively according to study design, with randomized controlled trials and meta-analyses considered the most robust level of evidence.

## RESULTS

### NON-PHARMACOLOGIC THERAPY

### ORAL REHYDRATION SALTS (ORS)

Oral rehydration salts (ORS), administered in a volume of 500 mL, represent an effective method for preventing vasovagal syncope. During a 6-month follow-up period, syncope recurrence was absent in 56.3% of patients in the ORS group, compared to 39.2% in the group not receiving ORS. Upon repeat tilt-table testing, a negative result was observed in 65.5% of patients receiving ORS, compared to 35.4% in the control group [14].

### VITAMIN D SUPPLEMENTATION

It has also been demonstrated that individuals with VVS tend to have relatively low serum levels of vitamin D. In patients with a positive tilt-test result, the mean vitamin D level was significantly lower (17.5 ± 7.7 ng/mL) than in those without syncope (24.4 ± 9.1 ng/mL). Multivariate regression analysis indicated that low vitamin D levels increased the risk of syncope. In a separate study, it was shown that declining vitamin D levels are associated with reduced vagal tone, which may contribute to the occurrence of VVS [15].

### PSYCHOTHERAPY

Psychological factors play a significant role in patients with VVS. Quality of life, depression, and anxiety scales may serve as predictors of syncope episodes in these individuals. This suggests that psychotherapy, as well as pharmacological treatment of anxiety and depression, may reduce syncope frequency [16]. Another study evaluated whether weekly psychotherapy sessions could reduce the recurrence of syncope episodes and improve quality of life in VVS patients. The 12-month study demonstrated a significant reduction in annual syncope episodes—from 4.6 ± 0.9 to 1.0 ± 0.7—as well as improvement in quality of life [17].

## PHYSICAL EXERCISE

To assess the impact of physical exercise on VVS, a study was conducted involving a training program consisting of three weekly sessions, each lasting four hours. The program included tilt training, aerobic exercise, and standard counterpressure maneuvers. A significant reduction in syncope recurrence was observed in the training group. The median number of syncopal episodes during the 12-month follow-up was 0 in the training group versus 1 in the control group [4].

Yoga has been shown to exert a beneficial effect on the autonomic cardiovascular system. In a 14.3 ± 2.1 month observational period, the yoga group experienced significantly fewer symptoms compared to the control group [18]. Another study evaluating the effect of yoga on VVS incidence found that the mean number of syncopal or pre-syncopal episodes after 12 months was 0.7 ± 0.7 in the intervention group versus 2.52 ± 1.93 in the control group. In the yoga group, 43.3% of patients remained symptom-free, compared to 16.0% in the control group. Additionally, patients with VVS practicing yoga demonstrated a significant improvement in quality of life [19].

## PHARMACOLOGIC TREATMENT

Currently, few pharmacologic therapies have proven effective in treating VVS. Atomoxetine, a highly selective norepinephrine transporter (NET) inhibitor, enhances sympathetic tone and may thus contribute to a reduction in syncope frequency. In a study using a 40 mg dose of atomoxetine, 34.5% of patients experienced syncope during the tilt table test, compared to 70.4% in the placebo group. NET inhibition significantly reduced the 7 risk of tilt--induced syncope in VVS patients, primarily by attenuating reflex bradycardia, thereby preventing blood pressure drops [20].

## FLUDROCORTISONE

In a study evaluating fludrocortisone at daily doses ranging from 0.05 mg to 0.2 mg, the primary endpoint demonstrated only a marginal and statistically insignificant reduction in the number of syncopal episodes in the fludrocortisone group compared to placebo. A therapeutic benefit was observed only after dose stabilization at 0.2 mg for two weeks. However, the study failed to meet its primary objective of reducing the risk of VVS by 40%. During the 12-month follow-up, 44% of patients in the treatment group continued to experience VVS episodes, compared to 60.5% in the placebo group [21].

## PACEMAKER

A dual-chamber closed-loop stimulation (CLS) pacemaker significantly reduced the risk of syncope recurrence in patients aged ≥40 years with severe, recurrent reflex syncope and tilt-induced asystole. Syncope recurrence occurred in 16% of patients in the stimulation group versus 53% in the control group, with the estimated 2-year recurrence risk being 22% in the stimulation group and 68% in the control group over a mean follow-up of 11.2 months. Adverse events, mainly mild device-related incidents, were reported in 4% of cases. These findings support the utility of tilt-table testing in identifying candidates for cardiac pacing [22].

In another trial employing dual-chamber CLS pacing in patients ≥40 years with a high burden of syncopal episodes and a positive cardioinhibitory tilt-test response, participants were randomized to either 12 months of active stimulation followed by 12 months of sham stimulation, or vice versa. A ≥50% reduction in syncope frequency was observed in 72% of patients during active stimulation. Syncopal episodes occurred in 45.7% of patients during the sham phase, compared to only 8.7% during the active stimulation phase. Notably, pacing extended the time to first syncope recurrence by up to sevenfold [23].

A 2018 meta-analysis confirmed that closed-loop feedback pacing significantly reduces VVS recurrence by up to 80% compared to conventional pacing [24].

Furthermore, a study aimed at determining whether undiagnosed sinoatrial or atrioventricular node dysfunction might confound the assessment of pacing efficacy in VVS found no such interference. The therapeutic benefits of dual-chamber CLS pacing are attributed to the prevention of frequent vasovagal

episodes [25].

## CARDIONEUROABLATION

Catheter-based ablation of ganglionated plexi (GP) in the left atrium in patients with treatment-resistant vasovagal syncope (VVS) has shown high efficacy in preventing recurrence of syncope. In one study, 127 GP sites with a positive vasovagal response were ablated. Both high-frequency stimulation mapping and anatomical feature-based methods were used. During the follow-up period of 12 to 102 months, 91.2% of patients experienced no recurrence of syncope. A reduction in parasympathetic tone persisted for at least 12 months, and there was an improvement in tilt-table test tolerance. No statistically significant differences were found between the group treated with high-frequency stimulation and the group undergoing anatomical ablation [26].

Another study evaluated the efficacy and safety of catheter ablation for VVS using different GP mapping techniques—initially high-frequency stimulation, followed by anatomical mapping. Both mapping techniques were shown to effectively reduce the number of syncopal episodes, with 83.7% of patients remaining syncope-free during a follow-up period of 5 to 15 months [27].

Cardioneuromodulation, an ablative neuromodulation technique aiming to partially ablate the anterior right ganglionated plexus and achieve adequate vagolysis of the sinoatrial node, is a potentially beneficial method for VVS. This procedure was associated with a reduction in syncope frequency; 74% of patients experienced no syncopal episodes during the 12-month follow-up [28].

Ablation of autonomic ganglia in both the left and right atria also demonstrated benefits in another study. Syncope occurred in only 8% of patients in the ablation group over a 2-year follow-up period, compared to 54% in the control group. Furthermore, after the procedure, the mean sinus rhythm on 24-hour Holter monitoring was significantly faster, and heart rate variability parameters indicated a withdrawal of parasympathetic influence [29].

The effectiveness of cardioneuroablation was also confirmed in another case-control clinical study [30]. Table 1 summarizes current evidence on interventions for vasovagal syncope.

*Table 1. Treatment of vasovagal syncope*

| Category | Method/Intervention | Effect | Reference |
|---|---|---|---|
| Non-pharmacologic therapy | Oral Rehydratation Salts (ORS) | Absent in 56.3% vs 39.2% in the control group in 6 months | [14] |
| | Vitamin D Supplementation | Low vitamin D levels increased the risk of syncope | [15] |
| | Psychotherapy | Reduction in annual syncope episodes—from 4.6 ± 0.9 to 1.0 ± 0.7 | [17] |
| | Physical Exercise | The median number of syncopal episodes during the 12-month follow-up was 0 in the training group versus 1 in the control group. In the yoga group, 43.3% of patients remained symptom-free after 12 months, compared to 16.0% in the control group. | [4] |
| Pharmacologic Treatment | Fludrocortisone | During the 12-month follow-up, 44% of patients in the treatment group continued to experience | [21] |

| | | | |
|---|---|---|---|
| | | VVS episodes, compared to 60.5% in the placebo group | |
| | Atomoxetine | 34.5% of patients experienced syncope during the tilt-table test, compared to 70.4% in the placebo group | [20] |
| Non-pharmacological interventions | Dual-chamber closed-loop stimulation (CLS) | Syncope recurrence occurred in 16% of patients in the stimulation group versus 53% in the control group | [22] |
| | | Syncopal episodes occurred in 45.7% of patients during the sham phase, compared to only 8.7% during the active stimulation phase. Notably, pacing extended the time to first syncope recurrence by up to sevenfold | [23] |
| | | Closed-loop feedback pacing significantly reduces VVS recurrence by up to 80% compared to conventional pacing | [24] |
| | Cardioneuroablation | During the follow-up period of 12 to 102 months, 91.2% of patients experienced no recurrence of syncope. | [26] |
| | | 74% of patients experienced no syncopal episodes during the 12-month follow-up | [28]. |
| | | Syncope occurred in 8% of patients in the ablation group over a 2-year follow-up period, compared to 54% in the control group. | [29] |

## DISCUSSION

Despite the benign nature of vasovagal syncope (VVS), recurrent and unpredictable syncopal episodes may require treatment. The first-line therapy is non-pharmacological and includes education, lifestyle modifications, and reassurance regarding the benign course of the condition [2].

In our study, as part of non-pharmacological treatment, we analyzed the effect of oral rehydration salts, the administration of which was associated with a reduction in syncope episodes both during the 6-month observation period and during the tilt-table test. Moreover, a low level of vitamin D was significantly correlated with a positive tilt-test result, suggesting potential benefits of vitamin D supplementation in the management of VVS. Another intervention with a beneficial impact on patients with VVS is psychotherapy, which not only reduces the frequency of syncope but also improves quality of life [14], [15],[16], [17].

Psychotherapy may also be effective as part of a comprehensive treatment approach, since recurrent

syncopal episodes can worsen the psychiatric profile of affected individuals [31]. It has also been shown that people experiencing syncope have a higher risk of cardiovascular disease, depression, and reduced life expectancy [32].

Our study further demonstrated that regular physical activity plays an important role in the prevention of vasovagal syncope. Existing studies on this topic have focused on the positive effects of yoga, which indeed exerted a favorable influence on the autonomic nervous system, resulting in a reduction in VVS episodes [4], [18], [19].

However, available studies debate the strength of yoga's beneficial impact in this regard. One such study reported improvement in VVS symptoms in both the yoga group and the control group. These findings suggest that patients improved simply due to their participation in the study, while those in the yoga group improved to a greater extent due to stronger interpersonal interactions [8]. This study once again underscores the powerful role of psychological factors in VVS.

Additional treatment may be necessary in patients with severe syncopal episodes—those occurring very frequently, impairing quality of life, lacking a prodromal phase, or occurring during high-risk activities [33]. It is estimated that only 14% of a selected VVS population may require additional therapy [34]. Unfortunately, there is no single therapy suitable for all types of reflex syncope, and the most important factor guiding treatment decisions is age [2].

Various pharmacological agents have been tested in the treatment of reflex syncope, most often with disappointing outcomes [2]. In our study, we included scientific reports concerning fludrocortisone and atomoxetine to illustrate and highlight the potential role of pharmacotherapy in the management of VVS. However, a comprehensive evaluation of pharmacologic treatments in vasovagal syncope exceeds the methodological and volume limitations of this paper.

For example, fludrocortisone enhances sodium reabsorption in the kidneys, resulting in increased plasma volume—this mechanism is comparable to the administration of oral rehydration salts [2]. The benefits of fludrocortisone, based on the study we reviewed, were modest [21]. Atomoxetine, a potent and highly selective norepinephrine transporter (NET) inhibitor, was effective in reducing the number of tilt-induced syncopal episodes in patients with VVS by attenuating reflex bradycardia [20].

Parasympathetic activation, often coupled with transient sympathetic inhibition, can contribute to the occurrence of VVS. Therefore, atrial vagal ganglion ablation—resulting in vagal denervation—may reduce the frequency of vasovagal syncope [35].

We analyzed scientific reports investigating the effects of cardioneuroablation, and each demonstrated a significant reduction in the number of syncopal episodes during the follow-up period [26], [27], [28], [29], [30].

Permanent cardiac pacing therapy may be effective when asystole is the predominant feature of reflex syncope. Dual-chamber cardiac pacing should be considered to reduce syncope recurrence, primarily in patients aged 40 years and older [2].

The studies on cardiac pacing included in our review confirmed their beneficial impact on VVS. Closed-loop dual-chamber pacing is more effective than conventional pacing, and this benefit is attributed to the prevention of recurrent vasovagal episodes [22], [23], [24], [25].

According to the current literature, with increasing age, the contribution of cardioinhibition in VVS decreases, while vasodepression becomes more prominent. Asystolic pauses are less frequent in older individuals than in younger ones; however, when present, they are more often late-onset asystoles. The age-related decline in cardioinhibition may reduce the effectiveness of pacing therapy in older patients with VVS [13], [36], [37]. Therefore, when considering pacemaker implantation in the elderly, a balance between cardioinhibition and vasodepression should be taken into account [37].

## CONCLUSION

Dual chamber pacing with closed loop stimulation reduces recurrence of reflex syncope in carefully selected patients aged forty years and older with tilt induced asystole. Catheter based cardioneuroablation shows promising benefit across heterogeneous study designs, but the evidence base remains limited compared with pacing and requires further high quality trials. Among nonpharmacologic strategies, oral rehydration salts have supportive data in pediatric populations, psychotherapy and structured physical training including yoga improve symptoms and quality of life in small studies, and low vitamin D levels are associated with vasovagal syncope rather than proven therapeutic benefit of supplementation. Pharmacologic options remain limited. Atomoxetine decreases tilt induced syncope, and fludrocortisone shows modest and

inconsistent effects. Overall management should be individualized, with priority given to education, lifestyle measures, and careful selection of invasive therapies. High quality randomized studies are essential to validate noninvasive and pharmacologic approaches, to refine patient selection, and to define long term outcomes.

## AUTHOR CONTRIBUTIONS

Conceptualization: Karolina Paks, Monika Pelczar, Zuzanna Gajda; Methodology: Michał Piotrowski, Paulina Hetnar; Software: Maciej Magiera, Natalia Musialik; Check: Barbara Starosta, Bartosz Brzychcy, Karolina Brzychcy; Formal analysis: Natalia Musialik, Maciej Magiera, Paulina Hetnar; Investigation: Monika Pelczar, Paulina Hetnar; Resources: Zuzanna Gajda,; Data curation: Barbara Starosta, Bartosz Brzychcy; Writing - rough preparation: Karolina Paks; Writing - review and editing: Monika Pelczar, Zuzanna Gajda, Michał Piotrowski; Visualisation: Karolina Brzychcy, Natalia Musialik; Supervision: Karolina Paks; Project administration: Karolina Paks

All authors have read and agreed with the published version of the manuscript.

## USE OF AI

In preparing this work, the authors used Chat GPT by Open AI for the purpose of improving language clarity and formatting references. After using this tool, the authors reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

## FUNDING

This Research received no external funding.

## CONFLICT OF INTERESTS

The authors declare no conflict of interest

# REFERENCES

1. Serletis A, Rose S, Sheldon AG, Sheldon RS. Vasovagal syncope in medical students and their first-degree relatives. Eur Heart J. 2006;27(16):1965-1970. DOI: 10.1093/eurheartj/ehl147
2. Brignole M, Moya A, De Lange FJ, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J. 2018;39(21):1883-1948. DOI:10.1093/eurheartj/ehy037
3. Portuguesa De Cardiologia R, Almeida S. Cardioneuroablation: A game-changer for vasovagal syncope Cardioneuroablação: mudança de paradigma no tratamento da síncope vasovagal. Revista Portuguesa de Cardiologia. 2023;42:831-833. DOI:10.1016/j.repc.2023.02
4. Van Dijk JG, Sheldon R. Is there any point to vasovagal syncope? Clinical Autonomic Research. 2008;18(4):167-169. DOI:10.1007/s10286-008-0484-x
5. Wang S, Peng Y, Zou R, et al. The relationship between demographic factors and syncopal symptom in pediatric vasovagal syncope. Sci Rep. 2023;13(1). DOI:10.1038/s41598-023-49722-w
6. Brignole M, Rivasi G, Sutton R, et al. Low-blood pressure phenotype underpins the tendency to reflex syncope. J Hypertens. 2021;39(7):1319-1325. DOI:10.1097/HJH.0000000000002800
7. Raj SR, Sheldon RS. Vasovagal Syncope Needs the "Expert Touch." JACC Clin Electrophysiol. 2022;8(2):150-151. DOI:10.1016/j.jacep.2021.11.006
8. Matveeva N, Titov B, Bazyleva E, Pevzner A, Favorova O. Towards understanding the genetic nature of vasovagal syncope. Int J Mol Sci. 2021;22(19). DOI:10.3390/ijms221910316
9. Alboni P, Alboni M, Bertorelle G. The origin of vasovagal syncope: To protect the heart or to escape predation? Clinical Autonomic Research. 2008;18(4):170-178. DOI:10.1007/s10286-008-0479-7
10. van Dijk JG, van Rossum IA, Thijs RD. The pathophysiology of vasovagal syncope: Novel insights. Auton Neurosci. 2021;236. DOI:10.1016/j.autneu.2021.102899
11. Komiyama T, Hirokawa T, Sato K, et al. Relationship between human evolution and neurally mediated syncope disclosed by the polymorphic sites of the adrenergic receptor gene α2B-AR. PLoS One. 2015;10(4). DOI:10.1371/journal.pone.0120788
12. Stewart JM, Medow MS, Sutton R, Visintainer P, Jardine DL, Wieling W. Mechanisms of vasovagal syncope in the young: Reduced systemic vascular resistance versus reduced cardiac output. J Am Heart Assoc. 2017;6(1). DOI:10.1161/JAHA.116.004417

13. Chu W, Wang C, Wu L, Lin P, Li F, Zou R. Oral Rehydration Salts: An Effective Choice for the Treatment of Children with Vasovagal Syncope. Pediatr Cardiol. 2015;36(4):867-872. DOI:10.1007/s00246-015-1097-5
14. Zhang Q, Sun Y, Zhang C, Qi J, Du J. Vitamin D Deficiency and Vasovagal Syncope in Children and Adolescents. Front Pediatr. 2021;9. DOI:10.3389/fped.2021.575923
15. Atici A. The Relationship Between Clinical Characteristics and Psychological Status and Quality of Life in Patients with Vasovagal Syncope. North Clin Istanb. Published online 2020. DOI:10.14744/nci.2020.93753
16. de Barros e Silva RLA, Volich RM, de Barros e Silva PGM, da Costa Darrieux FC, Scanavacca MI, Hachul DT. Effect of psychotherapy on recurrence of events and quality of life in patients with vasovagal syncope. Sci Rep. 2022;12(1). DOI:10.1038/s41598-022-09513-1
17. Tajdini M, Tavolinejad H, Aghajani F, et al. Impact of Supervised Physical Training on Vasovagal Syncope; a Randomized Controlled Trial.; 2021. https://academic.oup.com/eurheartj/article/42/Supplement_1/ehab724.0618/6393001 DOI: https://doi.org/10.1093/eurheartj/ehab724.0618
18. Shenthar J, Gangwar RS, Banavalikar B, Benditt DG, Lakkireddy D, Padmanabhan D. A randomized study of yoga therapy for the prevention of recurrent reflex vasovagal syncope. Europace. 2021;23(9):1479-1486. DOI:10.1093/europace/euab054
19. Sharma G, Ramakumar V, Sharique M, et al. Effect of Yoga on Clinical Outcomes and Quality of Life in Patients With Vasovagal Syncope (LIVE-Yoga). JACC Clin Electrophysiol. 2022;8(2):141-149. DOI:10.1016/j.jacep.2021.09.007
20. Sheldon RS, Lei L, Guzman JC, et al. A proof of principle study of atomoxetine for the prevention of vasovagal syncope: The Prevention of Syncope Trial VI. Europace. 2019;21(11):1733-1741. DOI:10.1093/europace/euz250
21. Sheldon R, Raj SR, Rose MS, et al. Fludrocortisone for the Prevention of Vasovagal Syncope A Randomized, Placebo-Controlled Trial. J Am Coll Cardiol. 2016;68(1):1-9. DOI:10.1016/j.jacc.2016.04.030
22. Michele Brignole VRFAMO, Alonso Pedrote AAARSB, Jean Claude Deharo GMGN, Daniele Giacopelli AGMT. Cardiac pacing in severe recurrent reflex syncope and tilt-induced asystole. Eur Heart J. 2020;42(5):517-519. DOI:10.1093/eurheartj/ehaa975
23. Baron-Esquivias G, Morillo CA, Moya-Mitjans A, et al. Dual-Chamber Pacing With Closed Loop Stimulation in Recurrent Reflex Vasovagal Syncope The SPAIN Study.; 2017. DOI:10.1016/j.jacc.2017.08.026
24. Rattanawong P, Riangwiwat T, Chongsathidkiet P, et al. Closed-looped stimulation cardiac pacing for recurrent vasovagal syncope: A systematic review and meta-analysis. J Arrhythm. 2018;34(5):556-564. DOI:10.1002/joa3.12102
25. Russo V, Anguera I, de Lange FJ, et al. Heart rate distribution in paced and non-paced patients with severe recurrent reflex syncope and tilt-induced asystole: Findings from the BIOSync CLS study. Int J Cardiol. 2021;335:52-54. DOI: 10.1016/j.ijcard.2021.04.032
26. Sun W, Zheng L, Qiao Y, et al. Catheter Ablation as a Treatment for Vasovagal Syncope: Long-Term Outcome of Endocardial Autonomic Modification of the Left Atrium. J Am Heart Assoc. 2016;5(7). DOI:10.1161/JAHA.116.003471
27. Xu L, Zhao Y, Duan Y, et al. Clinical Efficacy of Catheter Ablation in the Treatment of Vasovagal Syncope. J Clin Med. 2022;11(18). DOI:10.3390/jcm11185371
28. Debruyne P, Rossenbacker T, Janssens L, et al. Durable Physiological Changes and Decreased Syncope Burden 12 Months after Unifocal Right-Sided Ablation under Computed Tomographic Guidance in Patients with Neurally Mediated Syncope or Functional Sinus Node Dysfunction. Circ Arrhythm Electrophysiol. 2021;14(6):E009747. DOI:10.1161/CIRCEP.120.009747
29. 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. DOI:10.1016/j.jacep.2022.08.011
30. Aksu T, Padmanabhan D, Shenthar J, et al. The benefit of cardioneuroablation to reduce syncope recurrence in vasovagal syncope patients: a case-control study. Journal of Interventional Cardiac Electrophysiology. 2022;63(1):77-86. DOI:10.1007/s10840-020-00938-0
31. Alhuzaimi A, Aljohar A, Alhadi AN, Aljenedil A, Hersi AS. Psychiatric traits in patients with vasovagal and unexplained syncope. Int J Gen Med. 2018;11:99-104. DOI:10.2147/IJGM.S157335
32. Aegisdottir HM, Thorolfsdottir RB, Sveinbjornsson G, et al. Genetic variants associated with syncope implicate neural and autonomic processes. Eur Heart J. 2023;44(12):1070-1080. DOI:10.1093/

eurheartj/ehad016

33. Michele Brignole AMFJ de L, Jean-Claude Deharo PMEAF. Practical Instructions for the 2018 ESC Guidelines for the Diagnosis and Management of Syncope. Vol 2. Poland; 2018. http://www.escardio.org/guidelines, DOI: 10.1093/eurheartj/ehy071
34. Brignole M, Ammirati F, Arabia F, et al. Assessment of a standardized algorithm for cardiac pacing in older patients affected by severe unpredictable reflex syncopes. Eur Heart J. 2015;36(24):1529-1535. DOI: 10.1093/eurheartj/ehv069
35. Aksu T, Brignole M, Calo L, et al. Cardioneuroablation for the treatment of reflex syncope and functional bradyarrhythmias: A Scientific Statement of the European Heart Rhythm Association (EHRA) of the ESC, the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS) and the Latin American Heart Rhythm Society (LAHRS). Europace. 2024;26(8). DOI: 10.1093/europace/euae206
36. Rivasi G, Torabi P, Secco G, et al. Age-related tilt test responses in patients with suspected reflex syncope. Europace. 2021;23(7):1100-1105. DOI: 10.1093/europace/euab024
37. van Dijk JG, van Rossum IA, van Houwelingen M, et al. Influence of Age on Magnitude and Timing of Vasodepression and Cardioinhibition in Tilt-Induced Vasovagal Syncope. JACC Clin Electrophysiol. 2022;8(8):997-1009. DOI: 10.1016/j.jacep.2022.05.009

back