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Prevalence and symptom characteristics of Postural Orthostatic Tachycardia Syndrome (POTS) in patients with orthostatic intolerance

Prevalencia a prejavy syndrómu ortostatickej tachykardie (POTS) u pacientov s ortostatickou intoleranciou

Monika Lukáčová, Peter Mitro, Kristína Valová

I. kardiologická klinika LF UPJŠ a VÚSCH, a. s., Košice, Slovenská republika

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Abstract. *Introduction:* Postural orthostatic tachycardia syndrome (POTS) is a form of orthostatic intolerance characterized by an excessive increase in heart rate upon standing in the absence of orthostatic hypotension.

Aim: To assess the prevalence of POTS among patients evaluated for orthostatic intolerance and to analyze symptom characteristics across different POTS phenotypes.

Methods: Between 2021 and 2024, a total of 816 head-up tilt (HUT) tests were performed at our institution for the evaluation of orthostatic intolerance. POTS was diagnosed in 27 patients (3.5%), of whom 17 underwent comprehensive autonomic testing, including the active standing test and the Valsalva maneuver. Symptom burden was assessed using the Malmö POTS Symptom Score.

Results: The mean age of patients was 30.4 ± 7.7 years, and women accounted for 70.6% of the cohort. The most common symptoms were palpitations, presyncope, dyspnea, chest pain, and gastrointestinal complaints. A concomitant vasovagal response during HUT testing was documented in 47% of patients, supporting the existence of an overlap syndrome between POTS and vasovagal syncope. Based on autonomic testing, 57% of patients were classified as having the non-neuropathic POTS phenotype, 36% the neuropathic phenotype and 7.1% the undefined POTS phenotype. No statistically significant differences in symptom profiles were observed among the individual phenotypes.

Conclusion: POTS is a markedly less common form of orthostatic intolerance than reflex or orthostatic syncope. Its clinical presentation is highly heterogeneous and encompasses a broad spectrum of cardiovascular symptoms. Therefore, POTS should be considered in the cardiovascular differential diagnosis of patients without evident structural heart disease. Autonomic cardiovas-

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Corresponding author: prof. MUDr. Peter Mitro, DrSc., FESC, I. Kardiologická klinika LF UPJŠ a VÚSCH, a. s., Ondavská 8, 040 11 Košice, Slovakia, email: peter.mitro@upjs.sk

cular function testing enabled the classification of most patients into distinct POTS phenotypes, whereas symptomatology alone did not allow reliable differentiation between them. Fig. 2, Tab. 3, Ref. 24, on-line full text (Free, PDF), www.cardiologyletters.sk
Keywords: postural orthostatic tachycardia syndrome – POTS – orthostatic intolerance – autonomic dysfunction – Malmö POTS Symptom Score

Orthostatic intolerance is defined as the development of characteristic symptoms during standing that improve significantly after assuming a supine position (1). These symptoms may be cardiovascular in nature – including palpitations, lightheadedness, presyncope, dyspnea, chest pain, and blurred vision, as well as non-cardiovascular manifestations such as fatigue, generalized weakness, nausea, gastrointestinal complaints, and other nonspecific symptoms (2).

Orthostatic intolerance syndromes include specific forms of reflex syncope (namely vasovagal syncope), orthostatic hypotension, and postural orthostatic tachycardia syndrome (POTS).

POTS is a chronic heterogeneous syndrome characterized by a sustained increase in heart rate of at least 30 beats per minute within 10 minutes of standing (or more than 40 beats per minute in adolescents aged 12–19 years), in the absence of orthostatic hypotension. Orthostatic hypotension is defined as a decrease in systolic blood pressure of at least 20 mmHg or a decrease in diastolic blood pressure of more than 10 mmHg. A sustained heart rate increase is defined as the presence of such an increase in at least two measurements obtained one minute apart. In most patients, heart rate exceeds 120 beats per minute during orthostasis (2). The minimum resting supine heart rate should be at least 60 beats per minute to avoid diagnosing POTS in individuals with a naturally low resting heart rate that increases into the normal range upon standing (3). The diagnostic criteria for POTS are summarized in **table 1**.

The typical age of symptom onset ranges from 15 to 45 years, and approximately 80% of patients are women (2).

Most patients with POTS have a normal or high-normal resting heart rate. In individuals exhibiting persistent tachycardia regardless of body position, inappropriate sinus tachycardia should be considered. This condition is defined by a resting heart rate exceeding 100 beats per minute or an average heart rate above 90 beats per minute on 24-hour Holter ECG monitoring (3).

Not all patients with orthostatic tachycardia have POTS. For the diagnosis of POTS, other causes of sinus tachycardia must be excluded, including anemia, acute hypovolemia, endocrinopathies, medication-related effects (e.g., diuretics, vasodilators, antipsychotics, anticholinergics), anxiety disorders, and other conditions (3).

According to Feigofsky, cardiac dysautonomias (including POTS, inappropriate sinus tachycardia, orthostatic hypotension, reflex syncope, and chronotropic incompetence) occur with varying prevalence throughout life and frequently coexist, posing significant diagnostic and therapeutic challenges (4).

Table 1 Diagnostic criteria for postural orthostatic tachycardia syndrome (adapted from 2, 3)

Diagnostic Criteria for POTS
Sustained heart rate increase of ≥ **30 beats/min** within 10 minutes of assuming the upright position ≥ 40 beats/min in adolescents aged 12–19 years).
Absence of orthostatic hypotension (systolic blood pressure decrease ≥ 20 mmHg or diastolic blood pressure decrease ≥ 10 mmHg).
Presence of orthostatic intolerance symptoms that worsen during standing and improve upon recumbency (e.g., lightheadedness, palpitations, weakness, blurred vision, fatigue, syncope).
Symptom duration of **more than 3 months**.
No alternative condition explaining the sinus tachycardia.

A relatively common clinical scenario is the overlap syndrome between POTS and vasovagal syncope (VVS) in patients with orthostatic symptoms related to impaired cardiovascular adaptation to blood volume redistribution during standing. Hamrefors et al. reported that up to 65% of patients diagnosed with POTS also exhibited vasovagal syncope during head-up tilt testing (HUT). Accurate differentiation between isolated VVS and POTS-VVS overlap syndrome is essential for successful treatment of these patients (5).

Due to the marked increase in heart rate upon standing, the nature of symptoms, and elevated plasma norepinephrine concentrations observed in a substantial proportion of patients, POTS was initially characterized as a predominantly hyperadrenergic state. However, some patients demonstrate impaired norepinephrine release in the lower extremities and reduced sweating capacity in the legs (6). These findings are consistent with partial sympathetic denervation of the lower limbs and led to the designation of this subgroup as neuropathic POTS.

Based on the underlying pathophysiological mechanisms, three major POTS phenotypes are recognized in the literature: hyperadrenergic, neuropathic, and hypovolemic (2). These phenotypes do not necessarily exist as isolated entities; rather, their mechanisms frequently overlap and interact (7).

The mechanism of underlying autonomic neuropathy (neuropathic POTS) is thought to involve excessive venous pooling due to inadequate vasoconstriction of the venous system in the lower extremities. This results in reduced cardiac output and necessitates enhanced sympathetic activation to maintain blood pressure, ultimately producing excessive orthostatic tachycardia (7). These patients likely exhibit significantly reduced sympathetic nervous system activity in the lower body (8).

The mechanism responsible for hypovolemic POTS is similar. Hypovolemia contributes to reduced venous return and decreased cardiac output, thereby requiring compensatory sympathetic activation through baroreceptor-mediated pathways to maintain blood pressure (7). Physical deconditioning is an important comorbidity frequently observed in patients with POTS due to the high prevalence of hypovolemia (8).

In most cases, the hyperadrenergic state is secondary either to compensatory vasoconstriction associated with peripheral neuropathy or to excessive sympathetic activation resulting from hypovolemia (7). Its principal feature is elevated plasma norepinephrine levels (8).

Several authors have also described symptom profiles associated with individual POTS phenotypes. The hyperadrenergic phenotype is characterized by anxiety, cold and sweaty extremities, tremor, and increased urinary frequency. The neuropathic phenotype is associated with weakness, dependent acrocyanosis during standing, restless legs syndrome, neuropathic pain, headaches, and insomnia. The hypovolemic phenotype is typically characterized by fatigue, exercise intolerance, lightheadedness, impaired concentration, and cognitive dysfunction ("brain fog") (9).

Objective differentiation of POTS phenotypes can be achieved using several diagnostic tests. Hyperadrenergic POTS is characterized by orthostatic hypertension, standing plasma norepinephrine levels exceeding 600 pg/mL, and an exaggerated phase IV blood pressure overshoot during the Valsalva maneuver (10), or by an increase in systolic or diastolic blood pressure of more than 10 mmHg during HUT testing (11). Neuropathic POTS may be identified by quantitative sudomotor axon reflex testing, distal abnormalities on thermoregulatory sweat testing, or abnormal epidermal skin biopsy findings. Patients with hypovolemic POTS exhibit reduced standing renin and aldosterone concentrations compared with normovolemic individuals (10) or a 24-hour urinary sodium excretion below 100 mmol (11).

To objectively assess symptom burden and severity, the Malmö POTS Symptom Score questionnaire was developed. This instrument evaluates the 12 most common symptoms associated with POTS, including five cardiovascular symptoms (palpitations, lightheadedness, presyncope, dyspnea, and chest pain) and seven non-cardiovascular symptoms (gastrointestinal complaints, insomnia, concentration difficulties, headache, muscle pain, nausea, and fatigue). Patients rate the severity of each symptom on a visual analogue scale ranging from 0 ("symptom absent") to 10 ("extremely bothersome symptom") (12). The questionnaire was developed to capture both the frequency and severity of symptoms typical of orthostatic intolerance that significantly affect patients' quality of life (13). A visual representation of the symptom score is shown in **figure 1**.

This quantification is important not only for diagnosis but also for monitoring disease progression and evalu-

Malmö POTS Symptom Score: Assessing Symptom Burden in Postural Orthostatic Tachycardia Syndrome											
Symptom	**Self-rating scale**										
Dizziness	0	1	2	3	4	5	6	7	8	9	10
Palpitations	0	1	2	3	4	5	6	7	8	9	10
Chest pain	0	1	2	3	4	5	6	7	8	9	10
Presyncope	0	1	2	3	4	5	6	7	8	9	10
Memory/concentration difficulty	0	1	2	3	4	5	6	7	8	9	10
Dyspnea	0	1	2	3	4	5	6	7	8	9	10
Gastrointestinal problems	0	1	2	3	4	5	6	7	8	9	10
Abnormal tiredness	0	1	2	3	4	5	6	7	8	9	10
Nausea	0	1	2	3	4	5	6	7	8	9	10
Muscle pain	0	1	2	3	4	5	6	7	8	9	10
Headache	0	1	2	3	4	5	6	7	8	9	10
Insomnia	0	1	2	3	4	5	6	7	8	9	10
Score	**- total score -**										

Figure 1 Visual representation of the Malmö POTS Symptom Score (adapted from 12)

ating therapeutic effectiveness (13). In clinical practice, the Malmö POTS Symptom Score represents a simple and time-efficient tool that provides a rapid overview of the patient's current symptom burden.

The diagnostic evaluation of patients with suspected POTS should include electrocardiography, echocardiography, and 24-hour Holter ECG monitoring. The primary objective of these investigations is to exclude structural heart disease, inappropriate sinus tachycardia, or other clinically significant arrhythmias (10).

Cardiovascular autonomic testing should be considered in patients with suspected POTS to confirm the diagnosis and facilitate phenotypic classification. Evaluation may be performed using either the active stand test or head-up tilt testing (HUT), ideally combined with continuous non-invasive monitoring of blood pressure and heart rate (14).

Within autonomic testing, blood pressure measurements obtained during HUT or active stand test are used to identify orthostatic hypertension, while the Valsalva maneuver (VM) contributes to phenotypic classification. Patients with neuropathic POTS may exhibit a blunted phase IV overshoot, an exaggerated blood pressure decline during early phase II (15), or delayed blood pressure recovery during late phase II (16). In contrast, patients with hyperadrenergic (or hypovolemic) POTS typically demonstrate an exaggerated phase IV overshoot (17). Hyperadrenergic POTS is defined by the presence of orthostatic hypertension together with an exaggerated phase IV overshoot during the Valsalva maneuver. Orthostatic hypertension is defined as an increase in systolic blood pressure of more than 20 mmHg upon standing or a standing systolic blood pressure exceeding 140 mmHg in normotensive individuals. Assessment of diastolic blood pressure is considered less reliable in this context (18).

Methods

Between 2021 and 2024, a total of 816 head-up tilt tests (HUT) were performed at our institution in patients with orthostatic intolerance symptoms (syncope, presyncope, vertigo and orthostatic tachycardia / palpitations).

All patients underwent HUT according to the standard Italian protocol using a tilt angle of 60° (20-minute passive phase followed by a 15-minute pharmacological phase) with administration of 400 µg sublingual nitroglycerin.

Patients diagnosed with POTS subsequently underwent functional cardiovascular autonomic testing using continuous non-invasive blood pressure (Finometer NOVA, Finapres Medical Systems). Including active standing test and Valsalva maneuver.

For active standing test participants were instructed to stand abruptly from supine position and remain

standing for 5 minutes. Blood pressure and heart rate were recorded in the supine position and after standing.

The Valsalva maneuver was conducted in the sitting position following a short resting period of approximately 3–5 minutes. Patients were instructed to take a deep breath and then perform a forced expiration against resistance for 15 seconds while maintaining an intrathoracic pressure of 40 mmHg. Mean arterial pressure (MAP) was recorded at baseline (before the maneuver), during the early peak response (phase I), the minimum blood pressure response (early and late phase II), the recovery phase (phase III), and the overshoot phase (phase IV). The Valsalva ratio was subsequently calculated.

Based on the results of the active stand test and the Valsalva maneuver, POTS phenotypes were classified into four categories:

- **Neuropathic phenotype** – patients with POTS exhibiting a blunted phase IV blood pressure overshoot during the Valsalva maneuver or an exaggerated blood pressure decrease during phase II of the Valsalva maneuver
- **Non-neuropathic POTS phenotype** – patients with POTS demonstrating an exaggerated phase IV blood pressure overshoot during the Valsalva maneuver This group may include individuals with either hyperadrenergic or hypovolemic forms of POTS; further testing would be required for more precise phenotypic characterization)
- **Hyperadrenergic phenotype** – defined in our study by the presence of orthostatic hypertension. Orthostatic hypertension is defined as an increase in systolic blood pressure of more than 20 mmHg upon standing during HUT
- **Undefined phenotype** – Valsalva maneuver findings within normal limits and absence of orthostatic hypertension

The standardized Malmö POTS Symptom Score questionnaire was completed by 14 patients.

All patients underwent routine laboratory testing (complete blood count and biochemistry), had no significant structural heart disease documented by echocardiography, and most completed Holter ECG monitoring without evidence of hemodynamically significant arrhythmias.

Statistical analysis was performed using JMP Pro 17 Statistical Discovery software (SAS Institute, Cary, NC, USA). Comparisons between groups were conducted using Fisher's exact test and chí-square test. Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test. Data sets were checked fo the normality of the distribution.

Results

Among 816 patients, 510 (62%) were diagnosed as vasovagal syncope, while orthostatic hypotension was identified in 52 cases (approximately 7%). A total of 240 patients (29%) had a negative HUT result with respect to both vasovagal reaction and orthostatic hypotension.

Within this cohort, 27 patients (approximately 3.5%) fulfilled diagnostic criteria for POTS. Of these, 10 patients either declined further evaluation, failed to attend follow-up examinations, or were lost to follow-up. The patient selection process is illustrated in **figure 2**.

A total of 17 adult patients (5 men and 12 women, mean age 30.4 ± 7.7 years) with confirmed POTS underwent cardiovascular autonomic testing and symptom evaluation by Malmo questionnaire.

The most common comorbidities were thyroid disease (with euthyroidism achieved at the time of assessment) and bronchial asthma. Three patients were receiving chronic heart rate-lowering therapy (beta-blockers or ivabradine) for palpitations or sinus tachycardia.

Eight patients demonstrated a positive HUT result consistent with a vasovagal reaction. Among them, two women exhibited a mixed vasovagal response (VASIS I), four women and one man developed a vasodepressor response (VASIS III), and one man experienced a cardioinhibitory vasovagal reaction associated with a 15-second asystole. These patients had a documented history of recurrent syncope or a history of syncope accompanied by typical vasovagal prodromal symptoms. Detailed HUT findings are presented in **table 2**.

Nine patients (six women and three men) had a negative HUT result with respect to vasovagal response.

The diagnosis of POTS was confirmed by active stand testing (AST) in all 14 patients who underwent the examination. Orthostatic hypertension, one of the characteristic features of the hyperadrenergic POTS phenotype, was observed in seven patients.

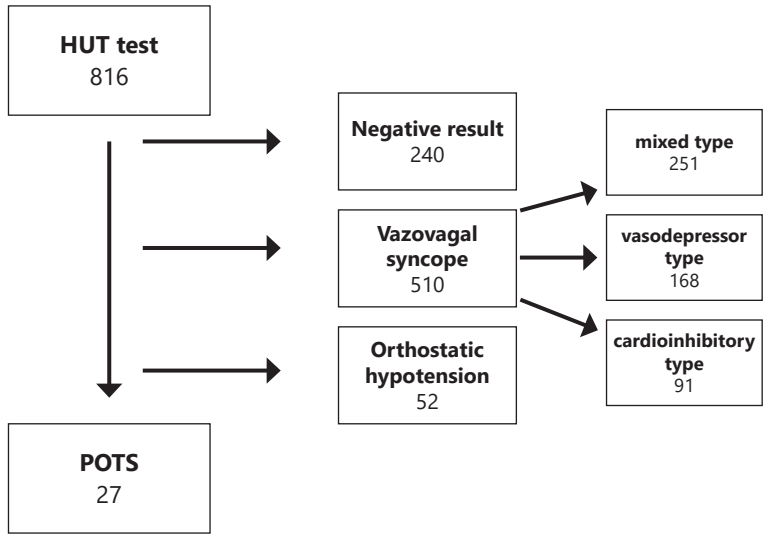

Figure 2 Flow chart of patient selection

Based on the results of the Valsalva maneuver (VM), the following POTS phenotypes were identified:

- Neuropathic phenotype: 5 patients (36%)
- Non-neuropathic phenotype: 8 patients (57%) (7 patients with hyperadrenergic phenotype and 1 patient with undefined non-neuropathic phenotype)
- Undetermined phenotype: 1 patient (7.1%)

Analysis of clinical history and the Malmö POTS Symptom Score questionnaire revealed that the most prominent symptoms in our cohort were palpitations, presyncope, dyspnea, chest pain, and gastrointestinal complaints (primarily diarrhea and constipation). Additional, less frequent symptoms included dizziness, fatigue, and insomnia. In two cases, symptoms resulted in significant disability, rendering the patients unable to continue their professional activities due to symptom severity. No alternative diagnosis could adequately explain the clinical presentation in these patients.

Comparison of symptom characteristics among the individual POTS phenotypes did not reveal statistically significant differences. Thus, symptom profiles alone were insufficient to distinguish between phenotypes.

Table 2 Basic hemodynamic characteristics and HUT findings in the study cohort

Patient number	Sex	Baseline BP	Baseline HR	Maximal HR	Δ HR	Minimal BP	Time until the minimal BP	HUT test result/ VASIS classification
1	M	160/100	100	156	56	110/80	6.min	negat
2	F	100/60	100	160	50	70/-	3.min	I
3	F	110/60	70	150	80	110/70	whole time	negat
4	F	95/60	69	115	46	95/65	3.min passive	negat
5	F	100/60	70	100	30	70/40	3.min	I
6	M	130/80	60	140	80	90/60	2.min	negat
7	F	130/80	70	113	43	110/75	whole time	negat
8	F	120/70	93	135	42	77/40	4.min	negat
11	F	120/70	70	150	80	90/60	5.min	negat
12	F	105/75	90	135	45	70/40	5.min	III
13	M	110/80	68	125	57	70/40	2.min	IIb (15sec)
14	M	125/80	101	140	39	90/70	5.min	negat
15	M	120/80	72	137	65	60/40	5.min	III
16	F	130/80	65	120	55	90/50	3.min	negat
17	F	125/60	80	122	42	70/50	4.min	III

Table 3 Symptom characteristics of neuropathic and non-neuropathic POTS phenotypes and Malmö POTS Symptom Score

Symptom	Neuropathic POTS (n=5)	Non-neuropathic POTS (n=8)	p-value
Dizziness	4 (80 %)	5 (62,5 %)	n.s.
Palpitation	4 (80 %)	6 (75 %)	n.s.
Chest pain	2 (40 %)	3 (37,5 %)	n.s.
Presyncope	5 (100 %)	7 (87,5 %)	n.s.
Memory/concentration difficulty	4 (80 %)	3 (37,5 %)	n.s.
Dyspnea	2 (40 %)	3 (37,5 %)	n.s.
Gastrointestinal	2 (40 %)	5 (62,5 %)	n.s.
Fatigue	4 (80 %)	7 (87,5 %)	n.s.
Nausea	2 (40 %)	4 (50 %)	n.s.
Muscle pain	3 (60 %)	3 (37,5 %)	n.s.
Headache	2 (40 %)	2 (25 %)	n.s.
Insomnia	4 (80 %)	3 (37,5 %)	n.s.
Exercise intolerance	3 (60 %)	2 (25 %)	n.s.
Malmö POTS Symptom Score - average	49,2 ± 28,8	33,9 ± 11,2	p = 0,3

The largest, although non-significant, differences were observed for memory/concentration difficulties (80% vs. 37.5%, p = 0.266), insomnia (80% vs. 37.5%, p = 0.266), and exercise intolerance (60% vs. 25%, p = 0.293). A comparison of symptom characteristics between neuropathic and non-neuropathic POTS phenotypes and the corresponding p-values is shown in **table 3**.

Summation score of Malmö POTS Symptom Score tended to be higher in patients with neuropathic POTS (neuropathic POTS phenotype 49.2 ± 28.8 points) in comparison to non-neuropathic POTS phenotype 33.9 ± 11.2 points) but the difference was statistically significant.

A history of syncope was present in 10 patients. Seven patients reported recurrent syncopal episodes (two or more), accompanied by typical prodromal symptoms such as warmth, cold sweating, tinnitus, visual dimming, and palpitations. These symptoms had often been present for several years, in some cases since childhood or early adolescence.

Based on clinical history and/or HUT findings, seven patients were classified as having a POTS–vasovagal syncope overlap syndrome rather than syncope attributable solely to POTS. In the remaining three patients, a single isolated reflex syncope episode was identified, each associated with a recognizable trigger such as a medical procedure, febrile illness, or gastroenteritis.

Two female patients experienced severe disability related to their condition, characterized by inability to continue employment and debilitating symptoms present throughout most of the day, significantly limiting routine daily activities. One of these patients had neuropathic POTS, while the second exhibited a mixed phenotype with neuropathic features. These observations suggest that patients with neuropathic characteristics may experience a more severe clinical course and greater symptom burden.

Discussion

The prevalence of POTS in the general population was estimated at approximately 1.73% before the COVID-19 pandemic and has increased to approximately 3.42% thereafter (19). In our population of patients referred for evaluation in Post COVID-19 era mostly because of syncope/presyncope the prevalence of POTS was 3.5% – not different from the general population. Syncope is not a common manifestation of POTS.

The most common cardiovascular manifestations of POTS include palpitations, weakness, fatigue, dyspnea, presyncope, and chest pain (2, 3, 12). These findings are consistent with the symptom profile observed in our cohort.

The coexistence of POTS and vasovagal reactions during head-up tilt testing is both possible and

relatively common. Syncope itself is not considered a typical manifestation of isolated POTS; instead, the presence of syncope should prompt consideration of a POTS–vasovagal syncope overlap syndrome. Presyncope, however, is a common component of the POTS symptom complex.

Several studies have demonstrated that approximately 30–45% of patients with POTS exhibit concurrent vasovagal syncope (20, 21). This observation may suggest that these conditions are not entirely distinct clinical entities but rather represent a continuum of autonomic dysfunction.

Cardiovascular autonomic testing can be effectively utilized for phenotypic classification of POTS. In our cohort, autonomic testing enabled phenotype identification in 13 of 14 evaluated patients.

No differences in symptom presentation were observed among individual POTS phenotypes. Although our sample is small, these findings are in agreement with the study by Angeli et al. (378 POTS patients were evaluated), in which lightheadedness was the most common symptom, followed by palpitations, headache, dizziness, cognitive impairment, weakness, visual disturbances, exercise intolerance, dyspnea, chest pain, orthostatic fatigue, and anxiety. No significant differences in symptom presentation were observed among the different POTS phenotypes (11). Similarly, Okamoto et al. evaluated 28 patients and found no differences in symptom severity or frequency between patients with hyperadrenergic and non-hyperadrenergic POTS. Furthermore, there were no differences in the impact of symptoms on daily activities, chronic fatigue, or manifestations associated with autonomic nervous system dysfunction (22).

Therapeutic approaches may differ among POTS phenotypes. As tachycardia is an essential symptom, treatment is commonly initiated with beta-blockers If beta-blockers are contraindicated, ivabradine may be considered. If this treatment is not effective further considerations should include the phenotype of POTS.

In neuropathic POTS, especially if hypotension coexists, alpha mimetics midodrine is a preferred drug. Another therapeutic option is pyridostigmine, which enhances cholinergic activity and directly influences parasympathetic nervous system tone.

In hyperadrenergic POTS centrally acting sympatholytic agents such as clonidine and methyldopa may be useful in selected patients. Their therapeutic effect is mediated through attenuation of central sympathetic outflow (8).

In hypovolemic POTS, fludrocortisone may be prescribed to increase circulating blood volume. This synthetic mineralocorticoid promotes renal sodium retention; however, its long-term safety remains insufficiently studied, and regular monitoring of serum electrolytes, particularly potassium, is recommended. Desmopressin, a synthetic vasopressin analogue, may also be used to improve renal free-water retention (3, 8, 9, 23).

Some patients with hypovolemic POTS respond favourably to increased dietary sodium intake, chronic administration of intravenous saline, or albumin infusions. Infusion-based therapies are generally reserved for clinically decompensated patients and are not recommended as routine long-term treatment strategies (24).

Phenotypic characterization appears particularly valuable in patients with treatment-resistant POTS who fail to respond adequately to conventional non-pharmacological and pharmacological interventions, especially when symptoms are severe or disabling.

For monitoring treatment response, symptom assessment questionnaires such as the Malmö POTS Symptom Score may be useful. These instruments primarily reflect symptom burden and severity rather than serving as diagnostic tools, as no validated diagnostic cut-off values currently exist. They are, however, valuable for monitoring disease progression and evaluating therapeutic efficacy over time.

Conclusion

Postural orthostatic tachycardia syndrome represents a less common form of orthostatic intolerance than reflex syncope or orthostatic hypotension. Its clinical presentation is highly heterogeneous and encompasses a broad spectrum of cardiovascular and non-cardiovascular symptoms. Therefore, POTS should be considered in the differential diagnosis of cardiovascular symptoms in patients without evident structural heart disease.

The absence of significant differences in symptomatology among individual POTS phenotypes indicates that clinical manifestations alone are insufficient for phenotype differentiation. This finding highlights the

importance of autonomic testing within the diagnostic process.

Simple tests as standing test Valsalva maneuver enabled phenotypic classification in the majority of patients in our cohort. This has important clinical implications, as treatment strategies may differ according to the underlying phenotype. On the other hand it should be acknowledged that additional tests may be required in a proportion of POTS patients.

The use of standardized symptom questionnaires proved to be a practical and effective method for objectively assessing subjective symptom burden in our patients.

Our findings also emphasize the need for an individualized approach to patient management, as POTS may lead to substantial functional impairment and significant reductions in quality of life.

Despite considerable advances in recent years, POTS remains a complex and incompletely understood syndrome. Further research is required to improve understanding of its pathophysiology, optimize phenotypic classification, and develop more targeted therapeutic strategies.

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