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ORIGINAL ARTICLE

Deep abdominal breathing reduces heart rate and symptoms during orthostatic challenge in patients with postural orthostatic tachycardia syndrome

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Abstract

Background and purpose: This study investigated the effects of deep abdominal breathing on cardiovascular parameters and symptoms in patients with postural orthostatic tachycardia syndrome (POTS) during head-up tilt-table (HUT) challenge.

Methods: Thirty POTS patients completed two consecutive rounds of 10-min HUT in a crossover design. One round was HUT without intervention, and one round combined the HUT with deep breathing at a rate of 6 breaths/min. Cardiovascular parameters, including mean blood pressure and maximum and mean heart rate (HR), were measured supine and standing. Symptoms were assessed using the Vanderbilt Orthostatic Symptom Score (VOSS).

Results: During the breathing technique, the mean HR increase was -7.35 bpm (95% confidence interval [CI] = -11.71 to -2.98), and the maximum HR increase was -6.27 bpm (95% CI = -11.85 to -0.68, p = 0.041), significantly lower compared to normal breathing. Additionally, improvements were observed in all absolute cardiovascular parameters during standing, with VOSS symptoms simultaneously and significantly decreasing by -5.38 (95% CI = -10.43 to -0.36).

Conclusions: Slow deep abdominal breathing can act as a simple technique to reduce the standing HR increase upon HUT in patients with POTS. This suggests that modulation of the cardiopulmonary neurocircuits and the respiratory pump may reduce HR increase and symptoms in patients with POTS. The findings of this study highlight the use of a safe, zero-cost, and simple behavioral tool to suggest to POTS patients for symptom relief apart from standard treatment. The observed improvements in cardiovascular parameters and symptoms offer a promising therapeutic approach for patients in times of inadequate treatment options.

KEYWORDS

breathing technique, deep abdominal breathing, heart rate, postural tachycardia syndrome, Vanderbilt Orthostatic Symptom Score, yoga

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INTRODUCTION

Postural orthostatic tachycardia syndrome (POTS) is a dysfunction of the autonomic nervous system (ANS) that predominantly affects female (5:1) adolescents or young adults [1]. POTS is characterized by symptoms of orthostatic intolerance for at least 3 months accompanied by a sustained heart rate (HR) increase of at least 30 beats/ min without orthostatic hypotension during 10min of standing [2]. There are still no epidemiological data available concerning the exact prevalence, but prepandemic studies suggest a prevalence between 0.1% and 1% [3, 4]. Current evidence indicates a link with COVID-19 infections, suggesting an increased prevalence due to the pandemic [5].

The appearance of POTS is clinically heterogenous; several conditions are associated with small fiber neuropathy [6, 7]. However, the following aspects contribute to its pathophysiology. Upright, the disturbed ANS may cause arteriolar dysfunction, leading to abnormal blood pooling in the lower part of the body [4, 8]. The resulting decreased venous return leads to reduced stroke volume, blood pressure (BP), and both thoracic and cerebral perfusion [4, 8, 9]. The increased baroreceptor activity results in an exaggerated sympathoneural response, resulting in compensatory reflex tachycardia [8, 10].

It was described that approximately 80%–90% of patients with POTS presented with dysfunctional breathing (DB) and up to 65% with severe breathlessness at rest [11]. DB is classified as a combination of hyperventilation, periodic deep sighing, thoracic dominant breathing, forced abdominal expiration, and thoracoabdominal asynchrony [12]. Hereby, DB is considered a symptom and not an etiology of POTS.

Breathing, unlike other autonomic functions, can be consciously perceived and specifically modulated by higher brain centers. This makes it a great therapeutical target for behavioral interventions to influence the ANS [13]. Today, behavioral therapies are becoming an increasing part of scientific research. On PubMed, the results for "breathing techniques" per year have tripled since the year 2000 (8150 publications in 2022) [14].

The contrasting breathing pattern to hyperventilation, characterized by deep and slow breathing, is linked to the activation of the parasympathetic nervous system [13]. Already after 5 min of deep breathing, a slight fall of resting HR was detected in a study with healthy subjects [15]. Even though the effect on resting HR was small, it may increase dramatically in patients with tachycardia and sympathetic overactivity.

All POTS pathomechanisms culminate in a common pathway, sympathetic overactivity. POTS is mainly treated symptomatically with behavior modification, increased fluid and salt intake, compression garments, and off-label medications. Lifestyle changes for symptom reduction were ranked the number one research priority from patients' point of view [16].

Consistent with this patient desire and need for evidence-based suggestions concerning lifestyle modification, in this study the therapeutic approach of implementing a slow deep breathing technique that reduces POTS symptoms and the HR increase during head-up tilt (HUT) was investigated. This approach has never been studied before but is of great interest due to its low complexity and ease of implementation. Can deep slow breathing significantly reduce orthostatic symptoms and HR?

METHODS

The study was carried out between May 2022 and February 2023 at the autonomic ambulatory outpatients clinic, as part of a prospective study for the investigation of autonomic neuropathies (ProANS Study, ClinicalTrials.gov identifier: NCT04310644, 17 March 2022). This prospective investigation was performed in accordance with the Declaration of Helsinki and was approved by the institutional review board (ethics committee) of the Medical Faculty of RWTH Aachen University (EK 092/19). All participants gave their written informed consent prior to study inclusion.

All subjects were diagnosed with POTS by an experienced physician, based on the following parameters:

- (i) Symptomatic and sustained increase in HR of ≥30 beats/min (or an absolute HR > 120/min within the first 10min of HUT) by the absence of orthostatic hypotension.
- (ii) Orthostatic complaints for at least 3 months that ameliorated on return to the supine position.

We defined "sustained" such that at least 50% of all standing HR values had to be elevated by >30 bpm compared to the mean supine HR. The HUT was utilized in this context as a wellestablished standardized method to reaffirm the diagnosis of POTS on the study day [1, 2]. Unlike active standing, it significantly diminishes the risk of injury in the case of syncope, thanks to the inclusion of Velcro straps and the ability to tilt the patient back if they faint.

Beforehand, questionnaires were collected for a better characterization of the subjects, including Beck Depression Inventory [17] for signs of clinical depression, Back Anxiety Inventory [18] for the severity of anxiety symptoms, and COMPASS-31 (Composite Autonomic Symptom Score 31) [19] as a quantitative measure of autonomic symptoms. Additionally, we used a German translation of the Malmö POTS Symptom Score (MAPS), which was recently developed by Spahic et al. [20], to assess the symptom burden in POTS. MAPS is a self-assessment tool consisting of 12 items rated on a scale of 0–10 per item (total range=0–120), which relies on patients' own perception of symptoms evaluated through visual analogue scale assessment [20] (see Table 1).

The frequency of Ehlers–Danlos syndrome and mast cell activation syndrome was assessed using medical history questionnaires. Neuropathic POTS was defined as when patients had a classic length-dependent small fiber neuropathy according to the NEURODIAB criteria [21]. Hyperadrenergic POTS patients had standing norepinephrine levels of >600 pg/mL. **TABLE 1** Demographic characteristics,sex, comorbid conditions, andquestionnaire data for group 1, group 2,and combined analysis.

Characteristic	Total, $n = 30$	Group 1, <i>n</i> = 16	Group 2, <i>n</i> = 14		
Demographics, mean \pm SEM ^a					
Age, years	33.50 ± 1.8	31.44 ± 1.7	35.86±3.3		
Height, cm	169.83 ± 1.5	168.75 ± 2	171.07 ± 2.1		
Weight, kg	65.47 ± 2.2	65.63 ± 3.4	65.29 ± 2.8		
Sex, n (%)					
Female	22 (73)	13 (81)	9 (64)		
Male	8 (27)	3 (19)	5 (36)		
Comorbid conditions, n (%)					
EDS	14 (43)	10 (63)	7 (50)		
MCAS	7 (23)	4 (25)	3 (21)		
Neuropathic POTS[SFN; NEURODIAB criteria]	9 (30)	2 (13)	7 (50)		
Hyperadrenergic POTS [Noradrenalin > 600 pg/mL]	19 (63)	10 (63)	9 (64)		
Maximum HR increase, beats/min	47.7±2.8	49.2±4.6	45.9±2.5		
Questionnaires, total scores, mean ±SEM ^a					
MAPS (0-120)	$63.04 \pm 3.8, n = 27$	$65.07 \pm 5.9, n = 14$	$60.85 \pm 4.8, n = 13$		
COMPASS-31 (0-100)	$55.76 \pm 2.8, n = 25$	$55.69 \pm 4.5, n = 12$	55.83 ± 3.5 , n=12		
BDI (0-63)	$14.21 \pm 1.9, n = 24$	$16.58 \pm 3.1, n = 11$	$11.83 \pm 2, n = 13$		
BAI (0-63)	$22 \pm 2.1, n = 23$	$23.17 \pm 3.4, n = 11$	$20.73 \pm 2.7, n = 12$		

Note: Groups 1 and 2 did not differ in terms of demographics and questionnaire scores (p > 0.05). HR increase and scores are presented as mean \pm SEM. The maximum HR increase was determined without breathing technique (round A) based on the average HR while lying down. The numbers in parentheses after the questionnaires indicate the range of the respective scores. Criteria for the diagnosis of SFN is according to Tesfaye et al. [21].

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; COMPASS-31, Composite Autonomic Symptom Score 31; EDS, Ehlers-Danlos syndrome; HR, heart rate; MAPS, Malmö POTS Symptom Score; MCAS, mast cell activation syndrome; SFN, small fiber neuropathy. ^aNo significant difference.

On the study day, investigations were always performed between 9 and 12 a.m. on an empty stomach without caffeine or nicotine intake and without medications that might influence the function of the ANS for at least 48 h prior to the investigation. The room temperature was kept constantly between 20°C and 24°C.

Exclusion criteria were cardiac pacemakers, pregnancy, moderate to severe sensorimotor polyneuropathy, neurodegenerative diseases, severe heart failure, diabetes mellitus, drug abuse, hypovitaminosis, anemia, and untreated hyperthyroidism.

Study protocol

As illustrated in Figure 2, the study protocol comprised two rounds in each participant, round A and round B. All participants performed both rounds, with group 1 (14 participants) starting with round A and group 2 (16 participants) with round B.

In round A, the procedure included a standard HUT consisting of an initial resting period of at least 7 min, followed by 10 min of tilt at 70°. Before tilting back, the Vanderbilt Orthostatic Symptom Score (VOSS) was filled out. In round B, the HUT was coupled with a deep abdominal breathing technique. The VOSS was likewise administered after the 10-min HUT (Figure 2).

Between the two rounds, the subjects remained lying on the tilt table, and during this 30-min break in the supine position, a detailed orthostatic symptom medical history was performed.

Head-up tilt

Autonomic testing was performed using the equipment Testworks 3 from WR Medical Electronics Co. (Maplewood, MN, USA), and BP was measured continuously on the left side with noninvasive beatto-beat arterial BP finger cuff (CNAP; CNSystems, Graz, Austria) on digits three and four to assess autonomic impairment standardized with the Composite Autonomic Severity Score. Continuous BP measurement is highly error-prone due to calibration artifacts, and data acquisition may be incomplete. Thus, for the purpose of this study, the BP at the upper right arm was collected and analyzed every minute using a manual cuff (BP Cuff; Welch Allyn, Skaneateles Falls, NY, USA) during lying and standing. Simultaneously, an HR value was documented every minute from single-channel electrocardiography. A chest strap at the costal arch level was used to track thoracic excursions for respiration rate and pattern. The HUT included a 7-min supine period followed by 10-min passive standing at 70°.

Special care was taken not to record any outliers and to analyze only reliable measured values. The initial vitals were recorded at the same time as the start of the 7-min lying period, resulting in the collection of eight data points in both rounds during lying and 10 data points during standing. These data points were then used to calculate the highest HR value as the "max. HR" and the lowest value as the "min. HR" for both the lying and standing positions.

Subsequently, the following values for the lying and standing time were determined for the analysis. The mean value of HR was calculated once for the 7 min of lying and 10 min of standing. The mean HR provides a broader representation and improves the estimation of the change in tachycardia during the intervention. Max. HR and min. HR were noted on the evaluation form. Systolic and diastolic BP (DBP) values were utilized corresponding to the moment of maximum HR. Mean BP (MBP) was calculated using the formula (2 * diastolic + systolic) / 3. Furthermore, the baseline for calculating the mean and maximum HR increase in both rounds was established as the average supine resting HR in the absence of the breathing technique (round A).

Vanderbilt Orthostatic Symptom Score

The VOSS was developed by the Vanderbilt Autonomic Dysfunction Center [22]. It captures the following nine symptoms: mental clouding, brain fog, shortness of breath, palpitations, tremor, headache, tightness in the chest, blurred vision, and nausea.

VOSS was assessed standing, or if symptoms were severe, after tilting back. The participants were asked to indicate the expression of the symptoms on a scale of 0–10. The number 0 represents the absence of the respective symptom and the number 10 the maximum expression. The individual symptom points were added to a score.

HR response to deep breathing

Round B was started with the HR response to deep breathing (HRDB). Subjects were instructed to synchronize their breathing with a moving bar on the HR variability (HRV) Acquire device (WR Medical Electronics Co., Saint Paul, MN, USA). This bar ascended for 5 s and descended for 5 s. Participants were directed to inhale when the bar rose and exhale when it fell. The objective was to achieve a breathing rate of 6 breaths/min. HRDB aimed to evaluate the accurate execution of the breathing technique, which aligns with the HRDB measurement's breathing pattern.

Breathing technique

Subsequently, the HRV Acquire device was replaced with an iPad displaying a video featuring the same rising and falling bar pattern.

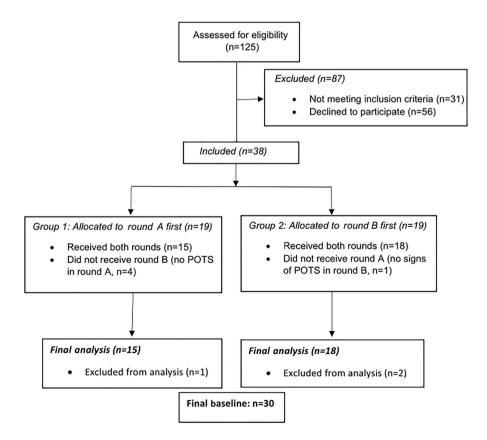


FIGURE 1 Consort flow diagram. POTS, postural orthostatic tachycardia syndrome.

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Participants were instructed to maintain the learned breathing pattern while following the video. This breathing pattern was to be sustained until the end of the HUT in round B.

Throughout the breathing technique phase, the recording included the type of breathing (nasal or diaphragmatic) and any instances of early termination.

Statistical analyses

Statistical analyses were performed with IBM (Armonk, NY, USA) SPSS (v29). The Shapiro–Wilk test was used to screen for normal distribution. A paired *t*-test was used to evaluate normally distributed parameters of HUT and VOSS. For the remaining not normally distributed parameters, the nonparametric Wilcoxon test was used. For one subject, the VOSS was not queried after the second tilt table (round A, normal breathing). Thus, significance tests were performed with n = 29. An unpaired *t*-test was used for the evaluation of all data presented in Table 1.

Data are presented as mean \pm SEM. The alpha level of significance was set to p < 0.05.

RESULTS

Out of 125 patients screened in our outpatient clinic, 30 patients with POTS (22 women, eight male, $age=33.50\pm1.8$ years) fulfilled inclusion criteria (Figure 1) and completed the whole study procedure. Groups did not differ significantly concerning demographic data and questionnaire scores (Table 1).

The mean HR increase in round B with the breathing technique was -7.35 bpm (95% confidence interval [CI] = -11.71 to -2.98) and

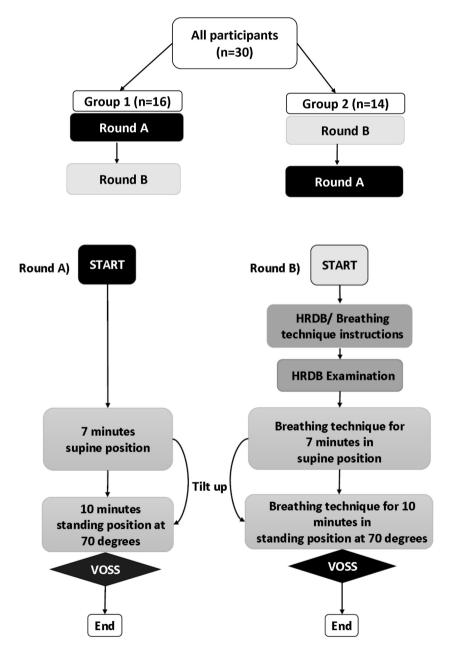


FIGURE 2 Group 1 was allocated to round A first, and group 2 was allocated to round B first. Round A was without breathing technique, and round B was with breathing technique. HRDB, heart rate response to deep breathing; VOSS, Vanderbilt Orthostatic Symptom Score.

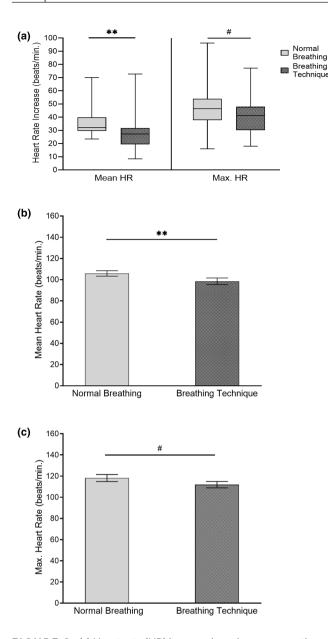


FIGURE 3 (a) Heart rate (HR) increase based on mean resting HR while lying down with normal breathing. The breathing technique reduced the mean and maximum HR increase while standing. (b, c) Standing tilt table parameters. Compared to the round with normal breathing, the participants showed a reduced (b) mean and (c) maximum HR performing the breathing technique while standing. *t*-test: **p < 0.01. Wilcoxon rank test: ${}^{\#}p$ < 0.05.

the max. HR increase was -6.27 bpm (95% CI = -11.85 to -0.68) compared with round A (Figure 3a), with a statistically significant difference observed between the two rounds (mean p=0.002, maximum p=0.041).

There was a significant decrease of the max. HR (round A: 118.17 ± 3.3 , round B: 111.90 ± 3 , p=0.041), the mean HR (A: 105.9 ± 2.6 , B: 98.5 ± 3.1 , p=0.002; Figure 3b,c), and the min. HR (92.9 ± 2.6 , 83.3 ± 2.9 , p<0.001) performing the breathing technique during standing compared to normal respiration.

Moreover, the standing DBP changed by -5.77 mmHg (95% CI = -8.91 to -2.61, p < 0.001), the standing MBP by -4.89 mmHg (95%

CI = -8.52 to -1.25, p=0.010), and the supine DBP by -1.7 mmHg (95% CI = -3.32 to -0.07, p=0.041) using the breathing technique (Table 2).

Concerning the VOSS, all symptoms were reported as less severe with the breathing technique, except for blurred vision and brain fog (Figure 4). The total score was reduced significantly by -5.38 (95% CI = -10.43 to -0.36, p=0.036) while performing the breathing technique, indicating less severe symptoms. The breathing technique notably reduced shortness of breath by -1.79 (95% CI = -2.96 to -0.62, p=0.004) and palpitations by -1.69 (95% CI = -2.72 to -0.65, p=0.002), as illustrated in Figure 4.

DISCUSSION

This study for the first time investigated the short-term effect of a deep breathing technique on the symptoms and standing HR in POTS. Slow deep breathing could reduce the standing HR increase in patients with POTS. In addition to the increase, the breathing technique also resulted in a reduction of all absolute vital parameters while standing. The general reduction in mean HR and DBP is consistent with studies that have investigated breathing techniques in healthy subjects [15, 23]. These findings indicate an increase in parasympathetic tone, suggesting undisturbed functioning of neurocircuits modulating the ANS in this POTS cohort.

More important, however, was to demonstrate that participants experienced a subjective relief of symptomatology, especially shortness of breath and palpitations. Because palpitations are one of the most reported orthostatic symptoms, this may contribute to improved disease management and quality of life [24, 25].

Several conceivable mechanisms, such as the activation of pulmonary stretch receptors [26, 27] and modulation of intravascular volume (respiratory pump) [28], may interact to produce the positive effects of deep breathing, influencing the autonomic state and HR regulation [11]. Moreover, standing induces stress for POTS patients, often leading to anxiety, whereas deep breathing may alleviate stress by engaging pulmonary and baroreceptorafferent neurons [11]. Additionally, focusing on breath can divert attention from distressing thoughts, potentially reducing both stress and HR.

During the conduct of our study, Balban et al. [29] published a paper on a randomized controlled trial that compared the psychophysiological effects of 5-min daily practice of three different breathing exercises and mindfulness meditation over 1 month. The authors concluded that a daily 5-min breathwork practice improves mood and physiological arousal and reduces respiratory rate in healthy individuals.

Given that the breathing technique is generally deemed safe but not entirely devoid of side effects, POTS patients should closely collaborate with their physicians when integrating it into their standing symptom management strategies. However, patients must receive thorough instruction, as improper implementation could potentially exacerbate symptoms. In summary, adopting the breathing DEEP ABDOMINAL BREATHING REDUCES HEART RATE AND SYMPTOMS DURING ORTHOSTATIC CHALLENGE IN PATIENTS WITH POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

TABLE 2Cardiovascular parametersduring tilt test (supine and standing)without (round A) and with breathingtechnique (round B).

	Supine		Standing	
	Normal breathing	Breathing technique	Normal breathing	Breathing technique
Respiration, breath	ns/min			
Mean RR	15.5 ± 0.6	6.00±0	17.7 ± 0.6	6±0.1
Heart rate, beats/r	nin			
Maximum HR	73.7 ± 2.1	76.7±2.2	$118.17 \pm 3.3^{\#}$	$111.90 \pm 3^{\#}$
Minimum HR	66.3 ± 1.7	65.5 ± 2	92.9±2.6 ^{###}	83.3±2.9 ^{###}
Mean HR	70.43 ± 1.65	70.97 ± 2.1	$105.9 \pm 2.6^{**}$	98.5±3.1**
Blood pressure, m	mHg			
SBP	114 ± 1.9	112.5 ± 1.9	117.5 ± 2.2	112.2 ± 2.4
DBP	$73.2 \pm 1.3^{*}$	$71.5 \pm 1^{*}$	$81.2 \pm 1.3^{***}$	$75.4 \pm 1.4^{***}$
MBP	87±1.4	83.2±2.9	$93.5 \pm 1.6^{*}$	$88.6 \pm 1.6^{*}$

Note: Data are presented as mean \pm SEM. The vital signs were compared between the rounds (round A: normal breathing and round B: breathing technique). The comparison was made for the values in standing and in supine position. *t*-test: *p <0.05, **p <0.01, ***p <0.001; Wilcoxon rank test: *p <0.05, **p <0.05, **p <0.01. Adapted from Tesfaye et al. [21].

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; MBP, mean blood pressure; RR, respiratory rate; SBP, systolic blood pressure.

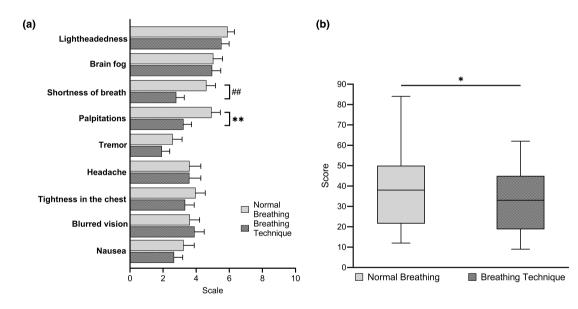


FIGURE 4 Vanderbilt Orthostatic Symptom Score: symptom scale (0–10) and total score (0–90). Shortness of breath and palpitations were significantly reduced (a) and the total score showed a significant reduction (b) when applying the breathing technique. *t*-test: *p < 0.05, **p < 0.01. Wilcoxon rank test: #p < 0.01.

technique may mitigate the sympathoneural response to upright posture and aid in symptom alleviation.

Limitations

The abovementioned possible mechanisms suggest a complex interplay that we did not further address in more detail in our study, which was primarily designed as a proof of concept to showcase the feasibility of the breathing intervention in reducing symptoms, addressing the immediate clinical needs of patients. The VOSS, although efficient and brief, lacks psychometric validation and does not account for symptom fluctuations during the 10-min examination period. Participants often struggled to assign a single number due to varying symptom intensity throughout the standing duration, prompting them to provide an average value when necessary.

The breathing technique could have been enhanced by incorporating prolonged expiration, which has been noted to induce greater relaxation and reduce arousal [30]. However, we deliberately simplified the breathing technique to facilitate its integration into daily life. Nonetheless, some patients encountered challenges in maintaining focus on the technique, leading to shallow breathing or brief interruptions. With practice, these occurrences may diminish, and the individual effects may be amplified. The absence of $ETCO_2$ measuring equipment leaves uncertainty regarding whether the breathing technique ensures CO_2 normalization or might induce moderate hyperventilation, as observed by others [31]. Previous studies suggest that hyperventilation-induced hypocapnia can lower BP in patients with autonomic failure (orthostatic hypotension) [11, 32]. Nevertheless, it remains unclear whether the notable decline in MAPS results from this hypocapnia or a reduction in sympathetic tone by the deep breathing technique. The latter seems more plausible, as evidenced by the concurrent decrease in HR and symptom burden.

Furthermore, although continuous BP monitoring was employed to assess baseline autonomic characteristics in our cohort, it was not performed during both rounds of HUT due to practical limitations. This represents a potential missed opportunity for gaining further mechanistic insights. Based on these study findings, one might speculate that daily utilization of this or a similar breathing technique could yield enduring effects in POTS patients. Future research endeavors should incorporate several enhancements to bolster the robustness and relevance of our findings. First, considering a larger sample size would ensure a more comprehensive representation of the POTS population. Moreover, patients should be afforded ample opportunity to practice the breathing technique extensively to familiarize themselves with the slow frequency and depth of breathing. Additionally, exploring whether there is an adaptation of the autonomic nervous system with daily practice over weeks or months would be insightful. Lastly, it remains uncertain whether the breathing technique can alleviate the severity of pre-existing symptoms.

Conclusions

The outcome of this study may provide physicians a cost-effective, nonpharmaceutical, and straightforward behavioral intervention to recommend to their patients for alleviating symptoms alongside standard symptomatic treatment for POTS. Although further research is warranted, POTS patients could readily adopt and tailor the breathing technique according to their requirements. The observed improvements in cardiovascular parameters and symptoms offer a promising therapeutic approach for patients in times of inadequate treatment options.

AUTHOR CONTRIBUTIONS

Moritz Stick: Conceptualization; investigation; writing – original draft; methodology; visualization; writing – review and editing; formal analysis; software. **Ariane Leone:** Writing – review and editing; conceptualization. **Fiona Fischer:** Writing – review and editing; data curation; methodology. **Jörg B. Schulz:** Resources; writing – review and editing; funding acquisition. **Andrea Maier:** Conceptualization; investigation; funding acquisition; methodology; validation; writing – review and editing; formal analysis; project administration; supervision; data curation.

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CONFLICT OF INTEREST STATEMENT

On behalf of all authors, the corresponding author states that there is no conflict of interest in the performing of this study. A.M. works on the advisory board for "Deutsche EDS Initiative" and "PoTS und andere Dysautonomien" and has received grants from Takeda Pharmaceuticals, the Standing Up to PoTS Research Fund, and Centogene.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

- 1. Sheldon RS, Grubb BP II, Olshansky B, et al. 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. *Heart Rhythm*. 2015;12(6):e41-e63.
- Vernino S, Bourne KM, Stiles LE, et al. Postural orthostatic tachycardia syndrome (POTS): state of the science and clinical care from a 2019 National Institutes of Health expert consensus meeting part 1. Auton Neurosci. 2021;235:102828.
- Arnold AC, Ng J, Raj SR. Postural tachycardia syndrome—diagnosis, physiology, and prognosis. *Auton Neurosci*. 2018;215:3-11.
- Mathias CJ, Low DA, Iodice V, Owens AP, Kirbis M, Grahame R. Postural tachycardia syndrome-current experience and concepts. *Nat Rev Neurol.* 2011;8(1):22-34.
- Fanciulli A, Leys F, Krbot Skorić M, et al. Impact of the COVID-19 pandemic on clinical autonomic practice in Europe a survey of the European academy of neurology (EAN) and the European Federation of Autonomic Societies (EFAS). *Eur J Neurol*. 2023;30(6):1712-1726. doi:10.1111/ene.15787
- Igharo D, Thiel JC, Rolke R, et al. Skin biopsy reveals generalized small fibre neuropathy in hypermobile Ehlers-Danlos syndromes. *Eur J Neurol*. 2023;30(3):719-728.
- Haensch CA, Tosch M, Katona I, Weis J, Isenmann S. Small-fiber neuropathy with cardiac denervation in postural tachycardia syndrome. *Muscle Nerve*. 2014;50(6):956-961.
- 8. Mar PL, Raj SR. Postural orthostatic tachycardia syndrome: mechanisms and new therapies. *Annu Rev Med.* 2020;71:235-248.
- Li H, Yu X, Liles C, et al. Autoimmune basis for postural tachycardia syndrome. J Am Heart Assoc. 2014;3(1):e000755.
- Stewart JM, Montgomery LD. Regional blood volume and peripheral blood flow in postural tachycardia syndrome. *Am J Physiol Heart Circ Physiol*. 2004;287(3):H1319-H1327.
- 11. Reilly CC, Floyd SV, Lee K, et al. Breathlessness and dysfunctional breathing in patients with postural orthostatic tachycardia

syndrome (POTS): the impact of a physiotherapy intervention. *Auton Neurosci.* 2020;223:102601.

- Boulding R, Stacey R, Niven R, Fowler SJ. Dysfunctional breathing: a review of the literature and proposal for classification. *Eur Respir Rev.* 2016;25(141):287-294.
- Noble DJ, Hochman S. Hypothesis: pulmonary afferent activity patterns during slow, deep breathing contribute to the neural induction of physiological relaxation. *Front Physiol.* 2019;10:1176.
- 14. PubMed. Search for "breathing techniques". 2022.
- Pramanik T, Sharma HO, Mishra S, Mishra A, Prajapati R, Singh S. Immediate effect of slow pace bhastrika pranayama on blood pressure and heart rate. J Altern Complement Med. 2009;15(3):293-295.
- 16. Kavi L, Nuttall M, Low DA, et al. A profile of patients with postural tachycardia syndrome and their experience of healthcare in the UK. *Br J Cardiol.* 2016;23:33.
- 17. Beck AT. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561-571.
- Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893-897.
- Sletten DM, Suarez GA, Low PA, Mandrekar J, Singer W. COMPASS 31: a refined and abbreviated composite autonomic symptom score. *Mayo Clin Proc.* 2012;87(12):1196-1201.
- Spahic JM, Hamrefors V, Johansson M, et al. Malmö POTS symptom score: assessing symptom burden in postural orthostatic tachycardia syndrome. J Intern Med. 2023;293(1):91-99.
- Tesfaye S, Boulton AJM, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care*. 2010;33(10):2285-2293.
- Raj SR, Biaggioni I, Yamhure PC, et al. Renin-aldosterone paradox and perturbed blood volume regulation underlying postural tachycardia syndrome. *Circulation*. 2005;111(13):1574-1582.
- Kuppusamy M, Kamaldeen D, Pitani R, Amaldas J. Immediate effects of Bhramari pranayama on resting cardiovascular parameters in healthy adolescents. *J Clin Diagn Res.* 2016;10(5):Cc17-9.
- 24. Shaw BH, Stiles LE, Bourne K, et al. The face of postural tachycardia syndrome insights from a large cross-sectional online community-based survey. *J Intern Med.* 2019;286(4):438-448.

- 25. Thieben MJ, Sandroni P, Sletten DM, et al. Postural orthostatic tachycardia syndrome: the Mayo clinic experience. *Mayo Clin Proc.* 2007;82(3):308-313.
- 26. Jerath R, Edry JW, Barnes VA, Jerath V. Physiology of long pranayamic breathing: neural respiratory elements may provide a mechanism that explains how slow deep breathing shifts the autonomic nervous system. *Med Hypotheses*. 2006;67(3):566-571.
- 27. Stuesse SL, Fish SE. Projections to the cardioinhibitory region of the nucleus ambiguus of rat. *J Comp Neurol*. 1984;229(2):271-278.
- Malpas SC. Neural influences on cardiovascular variability: possibilities and pitfalls. *Am J Physiol Heart Circ Physiol.* 2002;282(1): H6-H20.
- 29. Balban MY, Neri E, Kogon MM, et al. Brief structured respiration practices enhance mood and reduce physiological arousal. *Cell Rep Med*. 2023;4(1):100895.
- Cappo BM, Holmes DS. The utility of prolonged respiratory exhalation for reducing physiological and psychological arousal in non-threatening and threatening situations. J Psychosom Res. 1984;28(4):265-273.
- 31. Szulczewski MT, Rynkiewicz A. The effects of breathing at a frequency of 0.1 Hz on affective state, the cardiovascular system, and adequacy of ventilation. *Psychophysiology*. 2018;55(12):e13221.
- Thijs RD, Wieling W, van den Aardweg JG, van Dijk JG. Respiratory countermaneuvers in autonomic failure. *Neurology*. 2007;69(6): 582-585.

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