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Autonomic symptom burden in adults with tilt-table test-confirmed postural orthostatic tachycardia syndrome and migraine versus tension-type headache: a cross-sectional pilot study

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Abstract

Postural orthostatic tachycardia syndrome (POTS) is characterized by orthostatic symptoms and excessive heart rate increases in the absence of orthostatic hypotension [1,2]. Its pathophysiology is heterogeneous, involving potentially overlapping mechanisms such as partial autonomic neuropathy, hypovolemia, and hyperadrenergic physiology [2]. Headache is a frequent comorbidity, with a systematic review reporting a pooled migraine prevalence of 36.8% among patients with POTS [3]. Autonomic alterations have been described in migraine [4], and central networks implicated in migraine, including hypothalamic and locus-coeruleus pathways, also contribute to autonomic regulation [5]. However, whether patient-reported autonomic symptom burden differs according to headache phenotype in patients with established POTS remains unclear. We therefore compared autonomic symptom burden in adults with tilt-table-confirmed POTS and concomitant migraine versus tension-type headache (TTH), using the weighted COMPASS-31 total score as the primary outcome.

Introduction

To the Editor,

Postural orthostatic tachycardia syndrome (POTS) is characterized by orthostatic symptoms and excessive heart rate increases in the absence of orthostatic hypotension [1, 2]. Its pathophysiology is heterogeneous, involving potentially overlapping mechanisms such as partial autonomic neuropathy, hypovolemia, and hyperadrenergic physiology [2]. Headache is a frequent comorbidity, with a systematic review reporting a pooled migraine prevalence of 36.8% among patients with POTS [3]. Autonomic alterations have been described in migraine [4], and central networks implicated in migraine, including hypothalamic and locus-coeruleus pathways, also contribute to autonomic regulation [5]. However, whether patient-reported autonomic symptom burden differs according to headache phenotype in patients with established POTS remains unclear. We therefore compared autonomic symptom burden in adults with tilt-table-confirmed POTS and concomitant migraine versus tension-type headache (TTH), using the weighted COMPASS-31 total score as the primary outcome.

Methods and Results

This cross-sectional analysis of a prospectively recruited cohort was conducted at a tertiary neurology center between October 2022 and July 2024. The local ethics committee approved the study (EK No. 1133/2022), and all participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and is reported in accordance with the STROBE statement [6].

Adults aged 18–50 years referred to tilt-table testing because of orthostatic symptoms were prospectively screened. Of 40 individuals assessed for eligibility, one withdrew because of pregnancy, and one withdrew consent. The resulting study cohort comprised 38 participants. POTS was diagnosed by head-up tilt-table testing performed prior to study inclusion, in accordance with established

diagnostic criteria [1, 2]. Primary headache disorders were classified according to the *International Classification of Headache Disorders*, third edition (ICHD-3) [7]. Of the 38 participants, 24 fulfilled the diagnostic criteria for POTS and had concomitant migraine (n = 17) or TTH (n = 7). These 24 participants constituted the final analytic sample. The remaining 14 participants did not meet the diagnostic criteria for POTS and were therefore not included in the present analysis. Autonomic symptom burden was assessed using the weighted Composite Autonomic Symptom Score-31 (COMPASS-31) total score [8], the primary outcome. Sex was abstracted from the clinical record as part of routine care.

Continuous variables are reported as median (interquartile range [IQR]) and categorical variables as n/N (%). Between-group comparisons used two-sided Mann–Whitney U tests with exact p-values for continuous variables and Fisher's exact tests for categorical variables. For the primary COMPASS-31 comparison, the Hodges-Lehmann location shift (migraine minus TTH) and its 95% confidence interval (CI) were calculated. Because of the sex imbalance between groups, an exploratory female-only sensitivity analysis used the same methods. No formal sample-size calculation was performed. There were no missing data for the variables reported here. Analyses were conducted using IBM SPSS Statistics, version 28.

Twenty-four participants with POTS and a primary headache disorder were included: 17 (71%) with migraine and seven (29%) with TTH. Among participants with migraine, two had episodic migraine with aura, nine episodic migraine without aura, and six chronic migraine. Sixteen of 17 participants with migraine and four of seven participants with TTH were female (Fisher's exact p = 0.059). Median age was 34 years (IQR, 25–41) in the migraine group and 29 years (22–34) in the TTH group. Two participants with migraine were receiving preventive treatment: one was receiving amitriptyline and the other fremanezumab plus metoprolol.

Participants with POTS and migraine reported higher autonomic symptom burden than those with POTS and TTH, as reflected by higher weighted COMPASS-31 total scores (median [IQR], 42.14 [39.79–53.01] vs. 34.36 [30.60–38.72]; Mann–Whitney U = 18.0, exact two-sided p = 0.007; Fig. 1). The Hodges–Lehmann estimate of the between-group difference was 10.74 points (95% CI, 3.48–18.41).

In an exploratory sensitivity analysis restricted to female participants, COMPASS-31 scores were also higher in the migraine group (median [IQR], 41.89 [39.70–53.05] vs. 30.60 [26.60–34.52]; Mann–Whitney U = 2.0, exact two-sided p = 0.002; Hodges–Lehmann location shift, 14.48 points; 95% CI, 4.92–25.61). This analysis included only four women with TTH.

Discussion

In this single-center cross-sectional pilot cohort, adults with tilt-table-confirmed POTS and migraine reported higher COMPASS-31 total scores than adults with POTS and TTH. Although the COMPASS-31 comparison was the primary analysis of the current study, the finding is hypothesis-generating and does not establish the direction or underlying mechanism of the observed association.

Migraine is commonly reported in POTS, although the available prevalence literature is heterogeneous and does not provide a precise estimate across clinical settings [3]. Our findings suggest that, among patients with POTS and a primary headache disorder, patient-reported autonomic symptom burden may differ according to headache phenotype. Autonomic alterations have been described in migraine [4], and central networks relevant to migraine, including hypothalamic and locus-coeruleus pathways, also contribute to autonomic regulation [5]. In a separate study, patients with POTS and patients with chronic migraine showed sensory abnormalities relative to healthy controls, but their patterns differed, suggesting partially overlapping rather than interchangeable mechanisms [9]. These observations provide biological context for the association but do not establish its mechanism in the present cohort.

Two explanations remain plausible. Migraine-related symptoms may contribute to greater self-reported autonomic symptom burden, or greater autonomic symptom burden and migraine may reflect shared or correlated clinical characteristics. The cross-sectional design cannot distinguish these possibilities. The exploratory female-only sensitivity analysis should also be interpreted cautiously because it included only four women with TTH.

Several limitations constrain interpretation. The sample size was small, particularly the TTH group, and the headache groups were imbalanced by sex. Recruitment from a tertiary neurology center may limit generalizability. We did not include a POTS-without-headache comparator and therefore cannot estimate the contribution of a primary headache disorder itself to autonomic symptom burden. Headache frequency differed between groups, and the analysis cannot separate the association of headache phenotype from that of headache frequency or other correlated clinical characteristics. Potential medication-related influences were not accounted for. Hypermobility spectrum disorders and Ehlers–Danlos syndrome were not systematically assessed, although hypermobility disorders are clinically relevant in POTS populations [10]. Prior SARS-CoV-2 infection and Long COVID were not systematically assessed and may represent additional unmeasured clinical factors [11].

Larger prospective studies with balanced headache groups, a POTS-without-headache comparator, and systematic assessment of relevant clinical factors and objective autonomic measures are needed to determine whether this association is reproducible. Until then, the present findings support careful headache phenotyping in POTS but require replication before clinical or mechanistic conclusions can be drawn.

Declarations

Consent for publication:

Not applicable.

Ethics approval and consent to participate:

The study was approved by the Ethics Committee of the Medical University of Innsbruck (EK No. 1133/2022). All participants provided written informed consent before participation. The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amendments.

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Author contributions:

C.E. and L.A.B. contributed to the conception and design of the study, data analysis and interpretation, and drafting of the manuscript. L.A.B., F.L., K.K., F.F., A.S., and R.G. contributed to data acquisition. G.B. and A.F. contributed to the conception and supervision of the study and interpretation of the findings. All authors critically revised the manuscript for important intellectual content, approved the final version, and agreed to be accountable for the work.

Data availability:

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and data-protection requirements.

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Figures

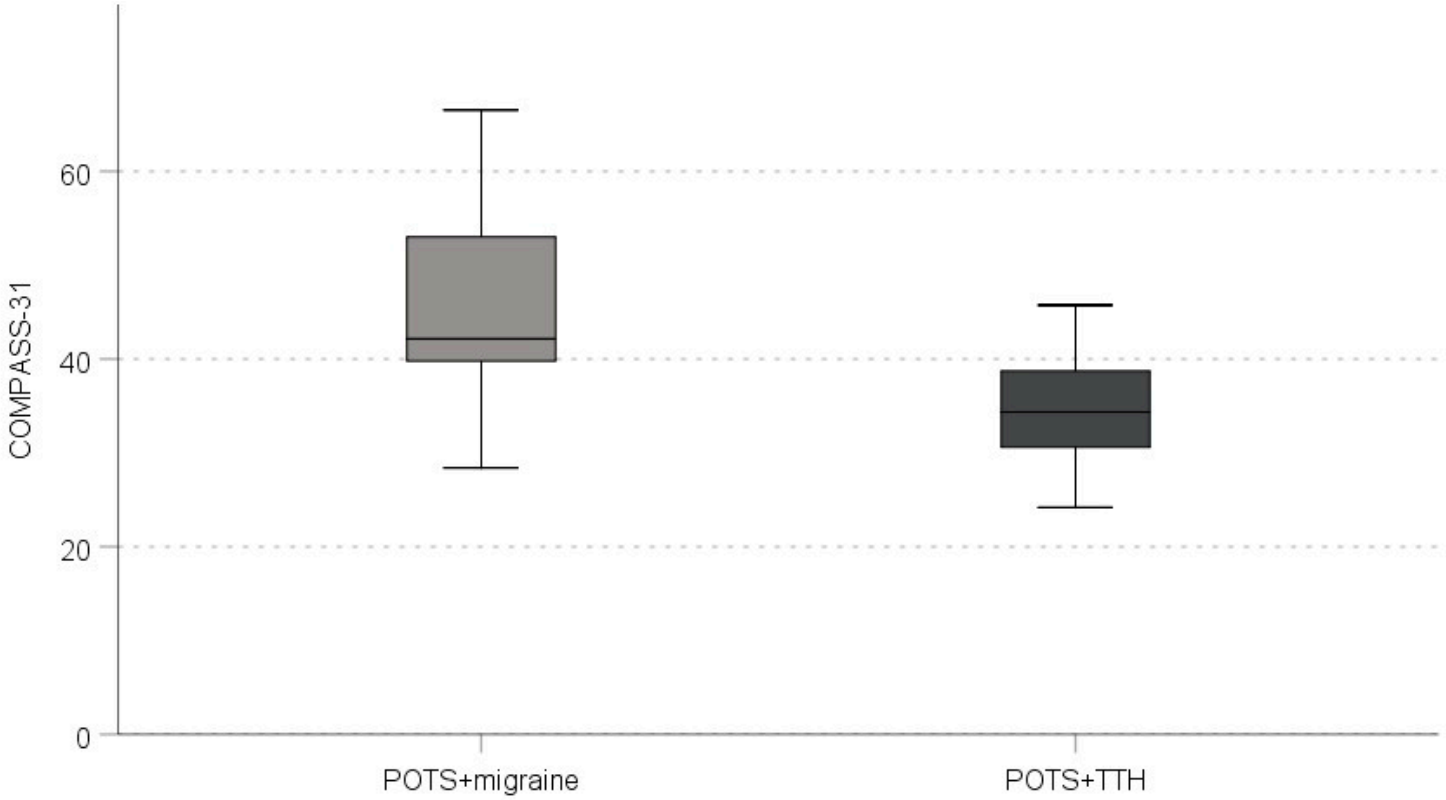


Figure 1

Weighted COMPASS-31 total scores in adults with postural orthostatic tachycardia syndrome (POTS) and migraine versus tension-type headache (TTH). Boxplots show the distribution of COMPASS-31 total scores in participants with POTS and migraine (n = 17) and POTS and TTH (n = 7). Boxes represent the interquartile range, horizontal lines represent medians, and whiskers extend to the most extreme observations within 1.5 interquartile ranges. Median COMPASS-31 total score was 42.1 (IQR, 39.8–53.0) in the migraine group and 34.4 (IQR, 30.6–38.7) in the TTH group (exact two-sided p = 0.007).