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Distinct hemodynamic phenotypes during passive head-up tilt table testing in women with chronic primary headache

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Introduction
Chronic primary headache (CPH) is associated with orthostatic intolerance, but whether this reflects uniform dysautonomia or distinct hemodynamic phenotypes is unclear.

Objective
To identify hemodynamic phenotypes in women with CPH and characterize tilt responses using linear mixed-effects models (LMM).

Method
Sixty-one women with CPH and 18 controls underwent passive head-up tilt testing (70°, 20 minutes). Stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR), and heart rate were measured by thoracic bioimpedance at six time points. K-means clustering (K=2), based on Random Forest–selected variables (SV and TPR at 5 minutes), defined phenotypes across 79 participants. LMM (Group×Time, adjusted for covariates) assessed trajectories.

Results
Cluster 1 (n=31 cases, 50.8%; 83.3% of controls; χ^2=4.78, p=0.029) showed preserved hemodynamics (SV=79.3 mL; TPR=1,201 dyn·s·cm^{-5}). Cluster 2 (n=30 cases, 49.2%) exhibited a dysautonomic profile (SV=55.4 mL; TPR=1,761 dyn·s·cm^{-5}) and was older (40.6±11.6 vs. 30.3±9.1 vs. 29.7±6.8 years; p<0.001). LMM confirmed reduced SV (β=−24.2 mL), exaggerated vasoconstriction at 5 minutes (β=+214 dyn·s·cm^{-5}), and vasomotor decompensation at recovery (β=−279) in Cluster 2 (all p≤0.006). Cluster 1 was indistinguishable from controls. Vasovagal syncope was more frequent in Cluster 1 (32.3% vs. 13.3%; p=0.012). Women ≥45 years were predominantly in Cluster 2 (84.6% vs. 39.6%; p=0.010).

Conclusion
CPH is hemodynamically heterogeneous. A dysautonomic phenotype—impaired venous return, compensatory vasoconstriction, and vasomotor decompensation—affects ~50% of patients and is strongly associated with age ≥45 years. Tilt-based hemodynamic profiling may help identify clinically relevant subgroups and support more targeted diagnostic and therapeutic strategies. Prospective validation is warranted.

Keywords:
Chronic primary headache
Orthostatic intolerance
Tilt table test
Hemodynamic phenotyping
Autonomic nervous system

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