Exercise Performance in Adolescents with Autonomic Dysfunction

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Objective To test the hypothesis that excessive postural tachycardia is associated with deconditioning rather than merely being an independent sign of autonomic dysfunction in patients with postural orthostatic tachycardia syndrome (POTS).

Study design We retrospectively analyzed records from 202 adolescents who underwent both head up-tilt and maximal exercise testing. Patients were classified as POTS if they had ≥30 min^{-1} rise in heart rate (HR) after tilt-table test; and deconditioned if peak O_2 uptake was <80% predicted. Changes in HR during exercise and recovery were compared between groups.

Results Two-thirds of patients were deconditioned, irrespective of whether they fulfilled diagnostic criteria for POTS, but peak O_2 uptake among patients with POTS was similar to patients without POTS. HR was higher at rest and during exercise; whereas stroke volume was lower during exercise, and HR recovery was slower in patients with POTS compared with patients without POTS.

Conclusions Most patients who presented with chronic symptoms of dizziness, fatigue, or pre-syncope, were deconditioned, but, because the proportion of deconditioned patients was similar in POTS vs non-POTS groups, we conclude that HR changes in POTS are not solely because of inactivity resulting in deconditioning. *(J Pediatr 2011;158:15-9)*.

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Nearly one-third of adolescents frequently experience bothersome fatigue, often accompanied by headache and abdominal discomfort.[1,2] Up to 1% of teenagers are debilitated with chronic fatigue.[3-5] Autonomic dysfunction is identified in as many as one half of patients who qualify for a diagnosis of chronic fatigue syndrome[6-9] and could potentially account for much of the persistent fatigue, headache, dizziness, and nausea that prompts adolescents to seek medical attention. Postural orthostatic tachycardia syndrome (POTS) was recognized in adults as a disease entity in 1993 and is characterized by fatigue, dizziness, abdominal discomfort, and excessive postural tachycardia.[10,11] POTS occurs in adolescents[12-14] and is increasingly recognized as an underlying mechanism contributing to a multiplicity of chronic symptoms. Perhaps as a result, many of these fatigued patients become inactive and deconditioned during the course of their debility.

Many adolescents present to the General Pediatric Diagnostic and Referral Service at Mayo Clinic with fatigue, dizziness, abdominal discomfort, and pain in various parts of the body (symptoms suggestive of autonomic dysfunction), and many of them qualify for a diagnosis of POTS.[15] On the basis of adult data,[10,11] the diagnostic criteria for POTS include a postural heart rate rise of at least 30 beats/min, although our data suggest that this criterion might not effectively differentiate between symptomatic and healthy adolescents.[16] This study was done to better define relationships between postural tachycardia and deconditioning in a population of adolescents with symptoms suggestive of autonomic dysfunction (chronic fatigue, dizziness, abdominal discomfort, and pain). We asked whether excessive postural tachycardia is associated with deconditioning rather than merely being an independent sign of autonomic dysfunction.

Methods

We conducted a retrospective medical record review of adolescents (10 to 18 years of age) seen in the Pediatric Diagnostic Referral Service or the Division of Pediatric Cardiology between May 1, 2003, and June 30, 2007, with symptoms suggesting autonomic dysfunction (chronic fatigue, dizziness, abdominal discomfort, and pain) and who had undergone autonomic testing and cardiopulmonary exercise

HR	Heart rate
HUT	Head-up tilt
POTS	Postural orthostatic tachycardia syndrome
SV	Stroke volume
SVI	Stroke volume index
Vo_2	Oxygen uptake

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testing. Patients with structural heart defects, significant cardiac arrhythmias, or seizure disorders were excluded. Medication use was not a reason for exclusion. The study was approved by the Mayo Clinic Institutional Review Board. Testing was conducted for clinical indications, although all subjects or their legal representatives consented to use of their medical records for research purposes. Our standard practice was to advise patients to discontinue vasoactive medications at least one day before exercise and head-up tilt testing.

Autonomic testing included a 10-minute head-up tilt test.[17] Subjects were identified as having postural orthostatic tachycardia syndrome if their highest heart rate during or after HUT was at least 30 beats per minute greater than their pre-tilt resting heart rate. Spirometry was performed before exercise, including measurement of maximum voluntary ventilation by the 12-second sprint method. Cardiopulmonary exercise testing was performed with a cycle ergometer according to the James protocol of 3-minute incremental steps of increasing work.[18] Oxygen saturation was monitored by pulse oximetry before and during exercise. Cardiac output (effective pulmonary blood flow) was measured with an acetylene-helium rebreathing technique.[19] Stroke volume (SV) was normalized for body surface area and expressed as stroke volume index (SVI). Patients were strongly encouraged to exercise to voluntary exhaustion, but, given their chronic fatigue state, a minority of patients failed to achieve the usual, accepted criteria (eg, HR >180 bpm and R-value >1.0) for a maximal test. Nevertheless, peak oxygen uptake (V_{O_2}) was determined as the highest achieved V_{O_2} sustained over 20 seconds and expressed as percent predicted.[20] James' normal values are computed based on sex, body surface area, and standing height, yielding values in $L \cdot min^{-1}$. Deconditioning was defined as peak V_{O_2} less than 80% predicted with no evidence of ventilatory limitation to exercise, conventionally defined as ratio of maximum exercise ventilation to maximum voluntary ventilation of <1 (one patient exceeded this cut-off, by 1%; and only 3 patients had a ratio >0.80, ie, breathing reserve <20%).

Statistical Analysis

Values are reported as mean ± standard deviation. All calculated P values were 2-sided, and P values < .05 were considered statistically significant. Comparisons between groups (POTS vs non-POTS; deconditioned vs conditioned; males vs females) were made with the 2-sample t test or χ^2 test, as appropriate. Regression models were fit to assess the relationship between cardiac output and V_{O_2}, and between HR and V_{O_2} per kg body mass [$ln(V_{O_2} \cdot kg^{-1})$] with data obtained with the patient seated upright on the ergometer and at 30 and 80 watts. Although workloads achieved at peak exercise varied between individual patients, 80 watts was the highest workload completed by all 202 patients. In the regression models, a compound symmetry correlation structure was specified to account for the correlation between multiple measurements from the same patient. Interaction terms were included to evaluate whether the relationship differed between POTS versus non-POTS, male versus female, and fit versus deconditioned, groups.

Results

Of the 202 patients who met the inclusion criteria (Table I), 148 (73%) were female. Complaints at the time of initial presentation included dizziness (84%), fatigue (71%), headache (63%), nausea (53%), abdominal pain (38%), and syncope (32%).

One-hundred forty-four (71%) met the criterion for POTS (postural heart rate increase of at least 30 bpm) on tilt-table testing. POTS and non-POTS groups did not differ by sex (P = .60), age (P = .65), height (P = .10), weight (P = .89), BMI (P = .20), or duration of symptoms before presentation (P = .55). Twenty-five patients (12 %) were ultimately prescribed β-blockers, 18 patients (9 %) were given the α-receptor agonist midodrine, and 25 patients (12%) received fludrocortisone. There was no difference in the usage of midodrine (P = .52) or fludrocortisone (P = .30), but patients with POTS were more likely to receive beta-blockers than patients without POTS: 22 (11%) versus 3 (1.5%) (P = .05).

Twenty-three patients had peak HR <170 beats/min, and 53 (26%) had peak HR <180 beats/min. There was great variability in individual peak oxygen uptake within both POTS and non-POTS groups. Mean peak V_{O_2} among all patients was low at 28 ± 8.5 $mL \cdot kg^{-1} \cdot min^{-1}$, or 73% ± 18% predicted (Figure 1). As expected, the average (mean ± SD) was significantly higher for males compared with females overall (P = .001): 32 ± 8 versus 27 ± 5 $mL \cdot kg^{-1} \cdot min^{-1}$, as well as within the POTS group (P = .006) and within the non-POTS group (P = .026). Two-thirds of patients (68%) were categorized as deconditioned based on peak V_{O_2} <80% predicted, but peak V_{O_2} among patients with POTS (28.6 ± 6.3 $mL \cdot kg^{-1} \cdot min^{-1}$) was similar to that among patients without POTS (29.1 ± 6.5 $mL \cdot kg^{-1} \cdot min^{-1}$; P = .63). Indeed, 99 of 144 patients with POTS (69%) and 38 of 58 patients without POTS (65%) were deconditioned (P = .66) (Table II).

The relationships between cardiac output and V_{O_2} were normal and similar between patients with and without POTS: $6.69 \cdot V_{O_2} + 3.71$ and $6.49 \cdot V_{O_2} + 4.00$ $L \cdot min^{-1}$ per $L \cdot min^{-1}$ V_{O_2}, respectively. Resting stroke volume indexes (SVI) were not significantly lower in patients with POTS compared with patients without POTS (mean ± SD): 33 ± 13 versus 36 ± 11 $mL \cdot m^2$ (P = .15); but the difference became significant during exercise at 30 watts (P = .023) and at 80 watts workload (P = .034). Graphical representation is shown in Figure 2 (available at www.jpeds.com). Patients

Table I. Patient characteristics, mean ± SD

	All patients	POTS group	Non-POTS group
Females, N (%)	148 (73%)	107 (53%)	41 (20%)
Males, N (%)	54 (27%)	37 (18%)	17 (9%)
Age at test, yr	15.7 ± 1.8	15.7 ± 1.8	15.6 ± 1.9
Height, cm	166 ± 10	167 ± 9	164 ± 10
Weight, kg	60.5 ± 13.4	60.4 ± 13.5	60.7 ± 13.4
BMI, kg/m^2	21.8 ± 3.9	21.5 ± 3.9	22.3 ± 3.9
Symptom duration, yr	2.5 ± 2.7	2.4 ± 2.4	2.9 ± 3.1