Postural Tachycardia in Children and Adolescents: What is Abnormal?

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Objectives To evaluate whether the use of adult heart rate (HR) criteria is appropriate for diagnosing orthostatic intolerance (OI) and postural tachycardia syndrome (POTS) in children and adolescents, and to establish normative data and diagnostic criteria for pediatric OI and POTS.

Study design A total of 106 normal controls aged 8-19 years (mean age, 14.5 ± 3.3 years) underwent standardized autonomic testing, including 5 minutes of 70-degree head-up tilt. The orthostatic HR increment and absolute orthostatic HR were assessed and retrospectively compared with values in 654 pediatric patients of similar age (mean age, 15.5 ± 2.3 years) who were referred to our Clinical Autonomic Laboratory with symptoms of OI.

Results The HR increment was mildly higher in patients referred for OI/POTS, but there was considerable overlap between the patient and control groups. Some 42% of the normal controls had an HR increment of ≥30 beats per minute. The 95th percentile for the orthostatic HR increment in the normal controls was 42.9 beats per minute. There was a greater and more consistent difference in absolute orthostatic HR between the 2 groups, although there was still considerable overlap.

Conclusion The diagnostic criteria for OI and POTS in adults are unsuitable for children and adolescents. Based on our normative data, we propose new criteria for the diagnosis of OI and POTS in children and adolescents. *(J Pediatr 2012;160:222-6)*.

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The diagnosis of orthostatic intolerance (OI) and postural tachycardia syndrome (POTS) is based on a symptomatic, excessive orthostatic rise in heart rate (HR). Common symptoms of OI and POTS include lightheadedness, palpitations, presyncopal feelings, tremulousness, and leg weakness when assuming the upright position. These symptoms are considered related to a combination of reduced cerebral perfusion and increased sympathetic activation. OI and POTS occur predominately in females, with female:male of approximately 5:1.[1]

For a diagnosis of OI, current criteria postulate the presence of an orthostatic HR increment of at least 30 beats per minute (bpm) within 5 minutes of active standing or passive head-up tilt, associated with symptoms of lightheadedness or faintness.[1-4] For a diagnosis of POTS, most authors stipulate an absolute orthostatic HR of at least 120 bpm in addition to the criteria for OI.[1-4] Some authors use different criteria and definitions of OI and POTS, but the aforementioned criteria are the only published criteria based on normative data, which also demonstrate that the orthostatic HR increment is significantly influenced by age.[1]

The term "adolescent autonomic dysfunction" has been coined to describe the frequent association among chronic fatigue, headaches, abdominal pain, nausea, dizziness, and lightheadedness observed in adolescents.[5] Because of these recent observations and the frequency of these symptoms among pediatric patients, we have seen increasing numbers of children and adolescents referred to our Autonomic Laboratory with suspected OI.

Adult diagnostic criteria for OI and POTS have been adopted in studies of OI in the pediatric population, although little is known about the normal range of orthostatic HR and the HR increment in children and adolescents.[6-9] We and others have observed higher, asymptomatic orthostatic increases in HR in normal adolescents, an observation supported in a recently reported study of high school students in Rochester, Minnesota, which reported an HR increment with active standing as high as 48 bpm in normal high school students.[10-12]

Consequently, we raise the question of whether it is appropriate to use adult criteria for a diagnosis of OI and POTS in pediatric and adolescent populations. The goals of the present study were to assess orthostatic HR and HR increment with head-up tilt in a normal pediatric population in the controlled setting of an

BMI	Body mass index
BP	Blood pressure
bpm	Beats per minute
HR	Heart rate
OI	Orthostatic intolerance
POTS	Postural tachycardia syndrome

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autonomic laboratory, to establish normative data and criteria suitable for the diagnosis of pediatric/adolescent POTS and OI, and to compare these normative data with values from a large cohort of young patients referred to our laboratory for OI.

Methods

Normal control subjects aged <20 years (n = 106) were recruited from communities within southeastern Minnesota. All subjects were screened for conditions and medications that could affect autonomic testing and were required to have normal neurologic examination results. We searched our clinical database for patients aged <20 years referred to our laboratory with referral diagnoses of OI, lightheadedness, orthostatic tachycardia, and postural tachycardia.

Subjects were excluded from enrollment if there was evidence of failure of organ systems or of systemic illness that could affect study results, autonomic function, or the subject's ability to cooperate. Those receiving concomitant therapy with anticholinergic agents, adrenergic antagonists, vasoactive agents, or other medications that could interfere with testing of autonomic function also were excluded unless the drug was discontinued for at least 5 half-lives before the study. Among the 666 patients identified, 12 were found to have orthostatic hypotension, and those 12 patients were also excluded from further analysis.

The study was carried out with prospective normative data collection and retrospective analysis of patient data. The study protocol was approved by our Institutional Review Board and was carried out in accordance with the Declaration of Helsinki. Subjects whose charts were reviewed and data accessed gave written permission to allow the use of their medical records for research purposes. Normal subjects undergoing testing as part of this study and their legal guardians provided specific written informed consent before entering the study. The study was carried out at controlled ambient room temperature (23°C) in a quiet room dedicated to autonomic testing. All study subjects fasted for at least 4 hours before testing. No caffeine, nicotine, or alcohol was permitted on the day of testing before study completion.

All subjects underwent standardized autonomic testing, including a head-up tilt study. Tilt table testing consisted of supine resting for at least 30 minutes, followed by a 70-degree passive head-up tilt. We routinely tilt patients with a concern about OI for 10 minutes, so the majority of the patients underwent a 10-minute tilt study. Considering the criteria for a diagnosis of OI in adults noted earlier, the first 84 control subjects were tilted for 5 minutes. To provide additional data for a prolonged head-up tilt, the last 22 control subjects enrolled were tilted for 10 minutes. Orthostatic symptoms were recorded. Blood pressure (BP) responses were reviewed to exclude patients with orthostatic hypotension and to document the frequency of presyncope.

Primary endpoints were normative values of orthostatic HR and HR increment in a large cohort of normal controls aged <20 years, and comparison of orthostatic HR and HR increment in normal controls and a large cohort of pediatric patients with symptoms of OI. Secondary endpoints were normative values of supine HR and comparison with patients; influence of age, sex, and body mass index (BMI) on HR measurements; and frequency of tilt-induced symptoms and presyncope.

Beat-to-beat BP was continuously recorded using the photoplethysmographic volume clamp method (Finapres Model 2300; Ohmeda, Englewood, Colorado or Finometer Model 1.22; Finapres Medical Systems, Arnhem, The Netherlands). The analog BP signal was sampled at 250 Hz, and the maximal and minimal points occurring between heart beats were derived as beat-to-beat systolic and diastolic BP. Instantaneous HR was calculated from the R-R interval using continuous 3-lead electrocardiogram recordings. Respiratory excursions were measured using a nasal thermistor or a chest expansion bellows.

Data Analysis

HR was determined at supine rest (30 seconds before tilt) and during tilt (at 1 minute, 5 minutes and, when available, at 10 minutes) in 2 different ways: (1) as "spot HR" recorded by the technician during the study at the time points of interest using the HR calculation of the electrocardiogram (2-second average); and (2) as "average HR" using data averaging of 30-second time windows at the time points of interest to minimize the influence of spontaneous signal oscillations. The change in HR from baseline was calculated for each time point during tilt.

All data are expressed as mean ± SD. Linear regression analysis was performed to assess the influence of age and BMI on variables. The χ^2 test was performed to assess for the influence of sex. Normative ranges were determined using percentile calculations. Mann-Whitney Wilcoxon testing was performed to assess for differences in variables between patients and controls. Significance was accepted at the 5% level.

Results

This study included 106 normal control subjects (52 females and 55 males; mean age, 14.5 ± 3.3 years; age range, 8-19 years) and 654 patients (476 females and 178 males; mean age, 15.5 ± 2.3 years). The HR increment from baseline at 5 minutes of tilt was significantly higher in patients referred for OI/POTS compared with the control group (32 ± 14 bpm vs 27 ± 13 bpm; $P = .002$), although there was considerable overlap (**Figure 1**). The same was true for the 1-minute time point, but the HR increment was not different between the 2 groups at the 10-minute time point. However, given that most control subjects were tilted for 5 minutes only, the number of observations for that time point was small (n = 22 vs n = 106 for all other time points; **Figure 1**).

At 5 minutes of passive head-up tilt, 42% of the normal controls had an HR increment of ≥30 bpm using spot HR.

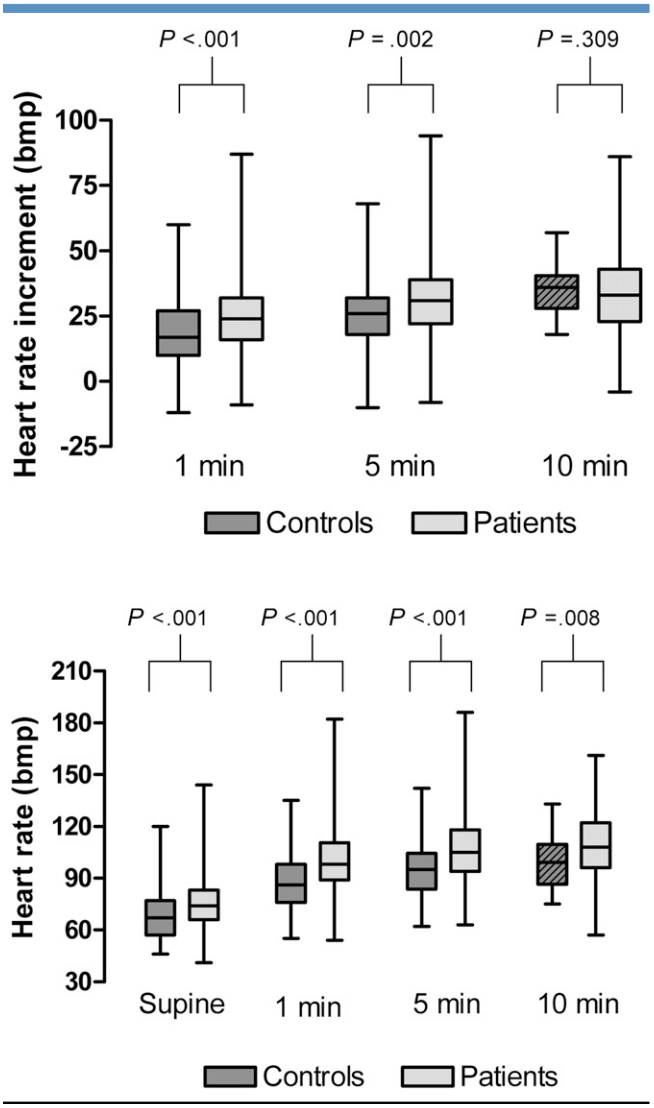

Figure 1. Orthostatic HR increment (*top*) and absolute HR at supine rest and during head-up tilt (*bottom*) in normal controls and patients with symptoms of OI. Note the considerable overlap between the patient and control groups. The box for controls at the 10-minute time point is shaded to emphasize the smaller number of observations at that time point (n = 22 vs n = 106).

Using averaged HR, the fraction of controls with an HR increment of ≥30 bpm was still 33%. In the patient group, 54.5% had an HR increment of ≥30 bpm at 5 minutes.

The 95th percentile for the 5-minute orthostatic HR increment among normal controls was 51 bpm using spot HR and 43 bpm using average HR (**Table**). Age, sex, and BMI had no influence on the orthostatic HR increment (**Figure 2**).

There was a greater and more consistent difference in the absolute orthostatic HR between the 2 groups, although there was still considerable overlap. This was true for all time points. The 5-minute orthostatic HR was 107 ± 18 bpm in patients versus 95 ± 16 bpm in controls ($P < .001$) (**Figure 1**). Although sex and BMI had no influence,

Table. HR increment and orthostatic HR at 5 minutes of head-up tilt

	Percentile (spot HR)			Percentile (average HR)		
	90th	95th	97.5th	90th	95th	97.5th
Orthostatic HR increment, bpm						
Age 8-19 years	44.0	51.3	55.6	39.0	42.9	52.7
Absolute orthostatic HR, bpm						
Age 8-13 years	130.0	131.2	142.0	127.6	136.9	139.1
Age 14-19 years	107.0	119.5	123.5	106.7	116.0	120.6

Within the age group studied, there was no significant influence of age, sex, or BMI on the HR increment. There was an influence of age on orthostatic HR, resulting in different values for different age groups.

absolute orthostatic HR decreased significantly with age (**Figure 2**). Therefore, for the purpose of calculating normative values, the control group was divided into children (age 8-13 years) and adolescents (age 14-19 years). For children, the 95th percentile for orthostatic HR at the 5-minute time point was 131 bpm using spot HR and 137 bpm using average HR. For adolescents, the 95th percentile was 120 bpm for spot HR and 116 bpm for average HR (**Table**).

Supine HR was also higher in patients compared with controls (75 ± 14 vs 68 ± 14; $P < .001$) (**Figure 1**). As for orthostatic HR, there was a significant influence of age (lower HR with increasing age; **Figure 2**), but no influence of sex or BMI.

Six control subjects (5.7%) developed signs of presyncope requiring early termination of the tilt test. Another 2 controls reported orthostatic symptoms during tilting that were not associated with presyncope. None of the controls had a previous history of syncope or of orthostatic symptoms. A total of 478 patients (74.2%) reported orthostatic symptoms during tilting; these symptoms were only rarely related to presyncope (n = 40; 6.2%).

Discussion

The concepts of adolescent autonomic dysfunction and pediatric/adolescent OI and POTS are gaining increasing acceptance, and these syndromes are increasingly being recognized as common disorders of youth.[5,6,13] Our pediatric referral clinic is seeing an overwhelming demand for evaluation and management of these disorders, which reportedly to affect millions of patients, can be quite disabling, and often have a significant impact on quality of life.[5,6,13] Given that these disorders are often chronic and refractory to treatment, their social and economic impact is considerable.[5,6,13]

This study was designed to fill an important gap in our knowledge of what is normal and abnormal when evaluating the HR and HR response with head-up tilt in children and adolescents in the autonomic laboratory. Despite suggestions that the criteria used to diagnose OI in adults might not be appropriate in the pediatric population, children and adolescents not only have been diagnosed with and treated for OI and POTS, but also have been enrolled in research studies

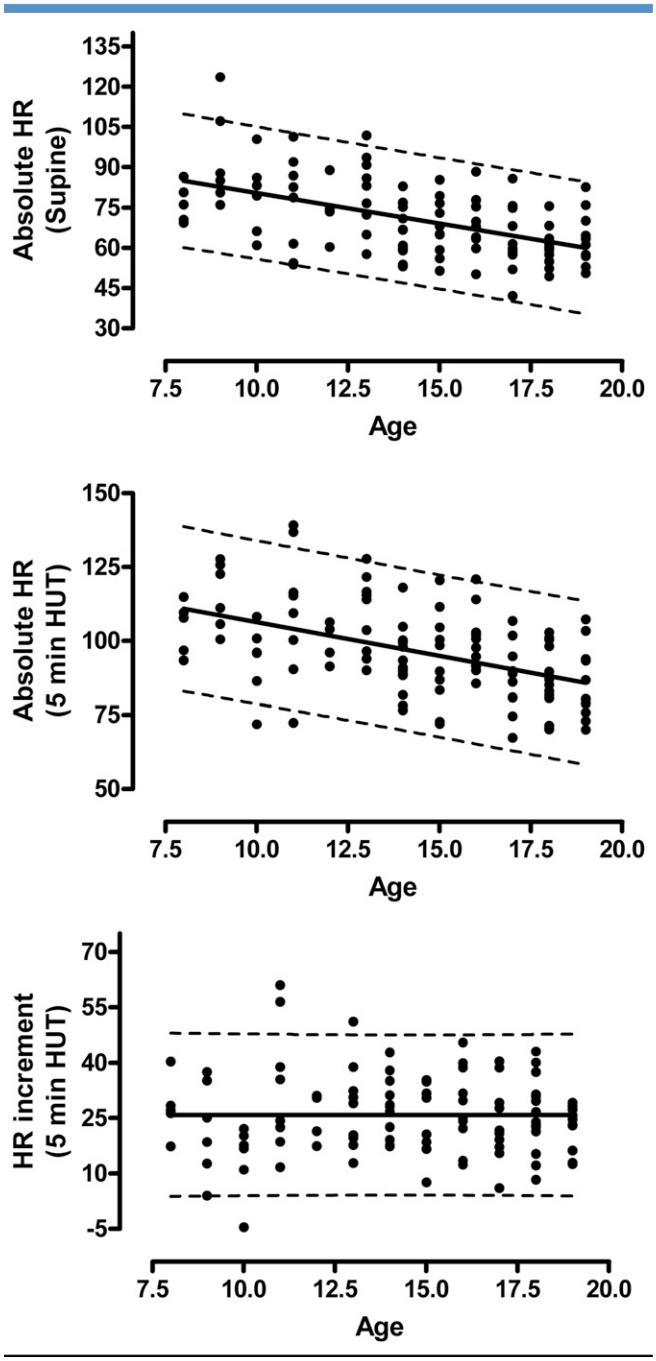

Figure 2. Linear regression analysis with prediction intervals for absolute supine (*top*) and orthostatic HR (*middle*), as well as orthostatic HR increment (*bottom*) by age. Averaged HR is shown; the findings for spot HR were similar except for wider prediction intervals. Note the significant influence of age on supine and orthostatic HR, but not on orthostatic HR increment.

on pediatric POTS based on those criteria, which could demonstrate to be inappropriate for this age group.[5-10,12,13]

Our study demonstrates that an orthostatic HR increment of 30 bpm—the main diagnostic criterion for OI in adults—is still well within the normal range for children and adolescents. The use of this increment as a cutoff for diagnosing OI in the pediatric population would result in very low specificity. This observation is supported by a recently published study on high school students in Rochester, Minnesota that found orthostatic HR changes as great as 48 bpm.[10]

Our data suggest that the HR increment in the age group studied is not significantly influenced by age, sex, or BMI. They also demonstrate the advantage of using data averages, because the range of normal could be narrowed considerably by eliminating the influence of oftentimes substantial spontaneous HR fluctuations. Using this approach, an orthostatic HR increment exceeding 40-45 bpm was shown to be excessive in this age group.

As expected, absolute HR was found to be influenced by age, and both supine and orthostatic HR decreased with age. Excessive orthostatic HR exceeded 130-140 bpm in children up to age 13 years and exceeded 120 bpm in adolescents aged 14 years and older. The latter value is close to what has been reported as excessive orthostatic HR in young adults.[1] Younger children, on the other hand, clearly can have a higher orthostatic HR without having OI, and 120 bpm is still a normal orthostatic HR at that age.

Our data raise many questions. Of note was the considerable overlap of the orthostatic rise in HR between control and patient group. Given that the diagnostic criteria for pediatric OI and POTS have not yet been established, we purposely avoided circular logic by including only patients with a final diagnosis of OI/POTS, which would have reflected diagnostic impressions based on adult HR criteria. Similarly, including only patients who fall outside of the now-established normative range would have had the predictable outcome of a large difference between patients and controls. Instead, we included all patients with clinically suspected OI and found that although a significantly higher orthostatic HR increase was seen, the difference was <5 bpm on average. This overlap is intriguing and raises the question whether HR increment alone can be relied on when diagnosing OI in a pediatric setting. Considering that the absolute orthostatic HR showed a greater and more consistent difference between patients and controls, one could argue that absolute orthostatic HR might be more important for the development of orthostatic symptoms and should be emphasized more in the diagnosis of pediatric OI. One could ask whether OI might not depend as much on HR in children and adolescents than it does in adults, or even whether the use of HR criteria might not be appropriate in general.

For the time being, HR criteria should be maintained in the diagnostic criteria for OI and POTS, because relying on symptoms alone cannot be satisfactory. However, clinicians should keep in mind not only that cardiovascular variables can fluctuate with the time of the day, from day to day, and depending on such factors as hydration status and medication intake, but also that a given HR increment may be associated with symptoms in some individuals but not in others.[14-16] As with other disorders, diagnostic criteria can guide, but cannot replace, a clinician's judgment. Diagnostic criteria are irreplaceable when scientific studies are being pursued, however.

Considering our normative data, and realizing that overly strict diagnostic guidelines are not desirable in these common but still poorly understood conditions, we suggest the following diagnostic criteria for pediatric OI/POTS: Pediatric OI: (1) Symptoms of OI, such as lightheadedness and palpitations, occurring frequently (>50% of the time) when assuming the upright position; and (2) orthostatic HR increment ≥40 bpm within 5 minutes of head-up tilt. Pediatric POTS: (1) Symptoms and HR increment fulfilling criteria for pediatric OI; and (2) absolute orthostatic HR ≥130 bpm (for age 13 years and younger), or ≥120 bpm (for age 14 years and older) within 5 minutes of head-up tilt.

A group of patients will have symptoms suggestive of OI but without evidence of orthostatic tachycardia and orthostatic hypotension. The etiology of symptoms in these patients is unclear, and further studies are needed to evaluate this likely heterogeneous patient group. Possible mechanisms include low baseline BP resulting in orthostatic symptoms despite relatively stable cardiovascular measures, hyperventilation resulting in reduced cerebral blood flow, body hypervigilance, anxiety disorders, migrainous phenomena, and vestibular disorders. Until this group of patients is better understood, we suggest using the label "orthostatic symptoms without tachycardia," which describes the phenomenon without implying knowledge of underlying pathophysiology.

These guidelines specifically refer to diagnoses of pediatric OI and POTS and are not meant to replace the complex clinical concept of adolescent autonomic dysfunction. Tilt-table testing alone cannot capture the full spectrum of symptoms that patients with this syndrome frequently experience, which range from orthostatic symptoms to chronic dizziness, fatigue, exercise intolerance, gastrointestinal dysmotility, and headaches. OI seems to be frequently associated with this syndrome but is a dominant feature only in part of the spectrum of adolescent autonomic dysfunction. Further research is needed to help develop better diagnostic criteria for this complex syndrome, to delineate specific categories, and to ultimately find more effective treatment strategies for the large number of affected adolescents. ■

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