Development of Hypertension in Adolescents with Pre-Hypertension

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Objective To evaluate the risk for developing incident hypertension (HTN) in adolescents with pre-hypertension.
Study design A secondary analysis of students participating in multiple school-based blood pressure (BP) screens from 2000 to 2007 was completed. At each screen, height, weight, and 2 to 4 BPs were measured on as many as 3 occasions when BP remained ≥95th percentile. Students with confirmed HTN at their initial screen were excluded, and incident HTN was defined as having a BP ≥95th percentile at all 3 visits of a later screen. Incidence rates (IR) and hazard ratios (HR) were calculated by using Cox Proportional models.
Results Of 1006 students, HTN developed in 11 (IR 0.5%/year) in a mean of 2.1 years of observation. IRs were higher in ''at-risk'' students (pre-hypertensive or hypertensive with follow-up BP <95th percentile), 1.4%/year (HR, 4.89; 1.48-16.19) and students with a BP ≥90th percentile at 3 baseline visits, 6.6%/year HR 24.33 (5.68-104.29)]. Although not significant, students with pre-hypertension by the 2004 Task Force definition also had an increased IR of 1.1%/year (HR, 2.98; 0.77-11.56)].
Conclusion Elevated BP increases the risk for the development of HTN during adolescence. Effective strategies for preventing HTN in at-risk adolescents are needed. *(J Pediatr 2012;160:98-103)*.

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Although its estimated prevalence was <1% approximately a decade ago,[1] recent reports indicate that hypertension (HTN) now affects between 3% and 5% of pediatric populations.[2-7] This increase, with the rise in other traditional cardiovascular risk factors such as obesity and diabetes mellitus, early in life has heightened concerns that premature cardiovascular disease and its associated sequelae may develop in a growing number of children and adolescents.

Recognizing these trends, in 2004 the National Blood Pressure (BP) Education Program Working Group on High Blood Pressure in Children and Adolescents published new guidelines for the classification of abnormal BP measurements in children.[8] Included in these recommendations was the designation of pre-hypertension (pre-HTN) to encourage early preventive interventions, such as diet and exercise, in children in whom HTN was most likely to develop.

The rate at which HTN actually develops in pediatric populations, however, remains poorly described, as does the level of risk associated with the designation of pre-HTN. This study, therefore, was designed to measure the incidence rate (IR) of HTN in a cohort of adolescents and to determine whether the current designation of pre-HTN increases the rate of development of HTN in these students.

Methods

Between 2000 and 2007, >18 000 children aged 10 to 19 years participated in a school-based BP screening program performed within 21 secondary schools of the Houston and Katy, Texas Independent School districts by the University of Texas–Houston Pediatric and Adolescent Hypertension Program. Schools were selected on the basis of willingness to participate and published demographic characteristics, with a goal of maintaining a roughly equal number of African-American, Caucasian, and Hispanic students screened. Students were

BP	Blood pressure
BMI	Body mass index
HR	Hazard ratio
HTN	Hypertension
IR	Incidence rate

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recruited primarily from physical education/athletics and health classes, although students from other electives were also included as allowed by school administration. All students provided informed verbal assent, and parental consent was obtained in accordance with school district policies and state law at the time of each screening.

Participating students reported basic demographic information including age, sex, and race/ethnicity (defined as African-American, Caucasian, Hispanic, Asian, or other). Height (cm), weight (kg), and mid-arm circumference (cm) were then measured by study personnel, followed by 3 or 4 BP measurements (depending on date of screening) after 5 minutes of rest. BP was measured with an appropriate-size cuff by using either the Space Labs 90207 or 90217 ambulatory monitor (Issaquah, Washington) or a Dinamap Pro/Critikon Compact T8 oscillometric monitor (Chalfont St. Giles, United Kingdom) depending on monitor availability and size of the child's arm. Both the Space Labs 90207[9] and Dinamap Pro[10] have undergone independent validation studies, receiving passing grades for systolic but not diastolic BP. Students with a mean systolic or diastolic BP ≥95th percentile for age, sex, and height had BP remeasured on as many as two subsequent occasions separated by 1 to 2 weeks when mean BP remained elevated.

A search of the screening database was performed to identify records of students who participated in the entire screening process on more than one occasion. A cohort of students who were non-hypertensive at initial screening encounter was generated from these records with these criteria: (1) systolic and diastolic BP at the first measurement session of the initial screening encounter was <95th percentile for age, sex, and height or follow-up measures within the initial screening encounter were in this range; and (2) weight, height, and at least 3 measured BP readings were recorded for each screening visit. A mean of the second and third BP measurements was used to determine hypertensive status at each BP session to minimize intrasession BP variability.

Baseline BP designation was determined by considering a student's BP at all visits of their initial screening encounter. As recommended by the 2004 Task Force,[8] students were considered normal when: (1) their BP at the first measurement session was <90th percentile (or 120/80 mm Hg) or (2) their BP at the first measurement session was ≥95th percentile, but their lowest follow-up BP during either the second or third measurements session was <90th percentile (or 120/80 mm Hg). Students were considered pre-hypertensive when: (1) their BP at the first measurement session was ≥90th (or 120/80) but <95th percentile or (2) their BP at the first measurement session was ≥95th percentile, but their lowest follow-up BP was ≥90th (or 120/80 mm Hg), but <95th percentile. Thus, pre-hypertensive status was ultimately based on a student's lowest BP obtained at one of potentially 3 measurement sessions. Alternatively, students were considered normal when their BP at the first measurement session was <90th percentile (or 120/80 mm Hg) and "at-risk" for HTN when their BP at the first measurement session was ≥90th percentile (or 120/80 mm Hg) regardless of any follow-up BP levels as long as students did not have confirmed HTN. Both systolic and diastolic BP were considered, and a student was classified as either pre-hypertensive or "at-risk" for HTN when either of the two met these definitions.

Incident HTN was defined when a student's systolic or diastolic BP was ≥95th percentile on all 3 measurement sessions of a subsequent encounter with the screening process. Because information on therapy was not collected, students were considered to have HTN at the first subsequent encounter in which they fulfilled criteria for HTN, even when BP was normal at a later screening date, because this may have been lowered with undocumented therapy. In addition, because the incidence of stage 2 HTN was low, HTN was not staged as recommended by the task force, and all students with either stage 1 or stage 2 HTN were evaluated together.

Statistical Analysis

All analysis was done with Intercooled Stata software version 9.2 (College Station, Texas), with a P value <.05 considered significant. Differences between groups were determined via two-sample Student t tests or Wilcoxon rank-sum tests for continuous variables and χ^2 contingency table analysis or Fisher exact test for categorical variables for normally and non-normally distributed data, respectively. Alternatively, ANOVA and the Kruskall-Wallis test were used to compare linear data in more than 2 groups. IR for the development of HTN are reported in person-years. Crude and adjusted hazard ratios (HR) were determined via Cox regression modeling considering baseline age, body mass index (BMI), BMI z score, obesity status, sex, and race/ethnicity as potential co-variates. Results are reported as HR (95% CI).

To control for the effect of obesity on the progression to HTN better, a secondary analysis of all incident cases and 15 randomly selected controls per case matched for age (± 1 year), sex, and BMI-z-tile (± 10%) was performed. Race/ethnicity was not included in the matching process as one of the incident HTN cases was classified as "other" and the number of matching controls was significantly limited when this variable was included. Logistic regression models were generated with this sample including time to follow-up as a co-variate in all models. Results are reported as OR (95% CI).

All research protocols were approved by the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston.

Results

A total of 1193 students were identified with repeated participation in the screening database. The final cohort included 1006 students, 926 of whom participated in the screening process twice, and 80 of whom participated on 3 or more occasions. Students excluded consisted of 129 with <3 valid BP readings per record, 30 with confirmed HTN at baseline, and 28 with a BP ≥95th percentile, but inadequate follow-up to determine baseline BP status. Demographic data at baseline by initial BP category are shown in **Table I**. Only 23 students were classified as underweight by Centers for