Original Research Article

Modeling Longitudinal Changes in Hypertensive and Waist Phenotype: The Oporto Growth, Health, and Performance Study

MICHELE SOUZA,[1,2] JOEY EISENMANN,[3] FERNANDA SANTOS,[1,4] THAYSE GOMES,[1] SARA PEREIRA,[1] CLAUDIA FORJAZ,[5] AND JOSÉ MAIA[1]*
[1]*CIFI²D, Faculty of Sport, University of Porto, Porto, Portugal*
[2]*Department of Physical Education, Center of Sports, Federal University of Santa Catarina, Florianópolis, SC, Brazil*
[3]*Department of Radiology, Michigan State University, East Lansing, MI, USA*
[4]*Department of Physical Education and Sports Science, CAV, Federal University of Pernambuco, Vitória de Santo Antão, PE, Brazil*
[5]*Exercise Hemodynamic Laboratory, School of Physical Education and Sport, University of S. Paulo, S. Paulo, Brazil*

Objectives: This study aimed to: (1) model changes in the hypertensive and waist phenotype (HWP) in youth, and (2) investigate the effects of sex, biological maturation, total physical activity (TPA), and physical fitness (PF) in HWP trajectories.

Methods: Data were obtained annually for 3 years from the Oporto Growth, Health, and Performance Study, and comprised 5,549 adolescents (2,732 girls) divided into four age cohorts (10, 12, 14, and 16 years). The HWP was computed as the sum of the standardized score of waist circumference and mean arterial pressure. Biological maturation was indirectly assessed by the maturity offset procedure; TPA was estimated with the Baecke questionnaire; PF measures included 1-mile run/walk, 50-yard dash (50YD), standing long jump (SLJ), handgrip strength (HGr), and agility shuttle run. Longitudinal changes in HWP were analyzed using multilevel modelling.

Results: HWP increased across time with a nonlinear trend in girls and boys. However, when adjusted for a set of predictors, the trend was reversed: girls and boys had a significant annual decrease on HWP of -0.202 ± 0.032 and -0.147 ± 0.032, respectively. Maturity offset was positively associated with HWP changes ($\beta = 0.913 \pm 0.023$); TPA had a negative association ($\beta = -0.027 \pm 0.011$); and improved PF tests were associated with a significant reduction in HWP across time ($\beta_{1mile} = -0.081 \pm 0.009$; $\beta_{SLJ} = -0.003 \pm 0.00$; $\beta_{50YD} = 0.106 \pm 0.020$; and $\beta_{HGr} = -3.335 \pm 0.196$).

Conclusions: Boys showed higher HWP values compared to girls from 10 to 18 years of age. Adolescents who were more biologically mature had a more adverse HWP. Longitudinal increases in TPA and PF predicted annual decreases in HWP across the adolescence years. Am. J. Hum. Biol. 28:387–393, 2016.

INTRODUCTION

The contemporary lifestyle behaviors of youth, including poor diet, high amounts of screen time, and low levels of physical activity (PA) and physical fitness (PF), are important factors contributing to the current epidemic of child and adolescent overweight and obesity worldwide (Weiss et al., 2013). This phenomenon is of utmost clinical interest due to its association with the development of cardiometabolic risk factors in youth that may increase the risk for adult cardiovascular disease (Weiss et al., 2013).

In addition to the overall total body adiposity level, it has been shown that abdominal obesity, and its proxy—waist circumference (WC), has increased at a higher rate than total body obesity in children over the last two decades (Garnett et al., 2011; McCarthy et al., 2003), and WC tends to track into adolescence (Chrzanowska et al., 2012) and adulthood (Eisenmann et al., 2004). Furthermore, it is well recognized that increasing abdominal adipose tissue has a unique role in the pathogenesis of cardiometabolic diseases (Zimmet et al., 2007), such as elevated blood pressure (BP), independent of weight status (Schroder et al., 2014). Thus, it is not surprising that the prevalence of high BP has also increased in youth (Sorof and Daniels, 2002). Indeed, children and adolescents with elevated WC have fivefold to sixfold increased odds of having high BP (Choy et al., 2011), which also persists into adulthood (Chen and Wang, 2008).

WC is considered one of the best anthropometric measures in clinical and large-scale screening of cardiometabolic risk factors in children and adults (Choy et al., 2011; Schroder et al., 2014), and its combined use with mean arterial pressure (MAP) (Bouchard and Shepard, 1994) is highly useful and feasible to evaluate and prevent future cardio-metabolic health problems (Choy et al., 2011; Schroder et al., 2014). However, the dichotomous classification of BP and WC may be restrictive because their original values are continuously distributed and positively correlated with other cardio-metabolic risks across a wide range of values (Eisenmann, 2008; Sorof and Daniels, 2002). Additionally, as MAP and WC are correlated with each other, both in terms of their level and rate of change over time, it may be of interest to represent this combined phenotype by a continuous score (Eisenmann, 2008), i.e., a hypertensive and waist phenotype (HWP). The HWP represents a feasible cardio-metabolic proxy that can be assessed more easily in the school setting, in terms of staff training and access to the equipment, compared to blood chemistry markers. Therefore, the HWP may be an effective primary prevention measure.

The growth-related changes in WC and BP during childhood and adolescence are manifested by biological, environmental, genetic, and lifestyle factors (Weiss et al., 2013).

*Correspondence to: José Maia, CIFI²D, Faculty of Sport, University of Porto-Porto, Rua Dr. Plácido Costa, 91, 4200-450 - Porto-Porto, Portugal. E-mail: jmaia@fade.up.pt

Received 27 March 2015; Revision received 8 July 2015; Accepted 4 October 2015

DOI: 10.1002/ajhb.22799
Published online 30 October 2015 in Wiley Online Library (wileyonlinelibrary.com).

TABLE 1. Sample size by age, sex, and cohort

Cohort	Ages (years)	Girls	Boys	Total
C1	10–12	1,008	1,042	2,050
C2	12–14	795	890	1,685
C3	14–16	648	619	1,267
C4	16–18	281	266	547
Total		2,732	2,817	5,549

Regarding biological factors, puberty has an impact on fat distribution, generally with an android pattern for boys and gynoid for girls (Ekelund et al., 2009). Systolic BP increases during pubertal growth with greater increments for boys due to the effect of gonadal hormones (testosterone) (Shankar et al., 2005). Furthermore, puberty is associated with a temporary decrease in insulin sensitivity, which can have a transitory effect on appetite regulation and obesity-related hypertension (Sorof and Daniels, 2002; Weiss et al., 2013).

Compared to lifestyle factors, the physical and built environment and genetic effects are less modifiable. However, PA and PF are examples of modifiable factors that have been inversely associated with the clustering of cardio-metabolic risk factors in youth (Froberg and Andersen, 2005; Steele et al., 2008), i.e., moderate-to-high levels of PA and PF are protective factors of cardio-metabolic risk (Bailey et al., 2012; Froberg and Andersen, 2005; Janz et al., 2002; Steele et al., 2008). Despite previous research examining these associations, there are some issues that are not well elucidated. For example, (i) almost all previous studies are cross-sectional, which limits the ability to provide a robust understanding about the dynamic of change in cardio-metabolic risk through the effect of time- invariant and variant correlates; (ii) the inverse association between PA and cardio-metabolic risk still needs to be investigated in longitudinal studies, since cross-sectional studies are inconclusive (Froberg and Andersen, 2005; Steele et al., 2008); and (iii) typically, when studies report the association between PF and cardio-metabolic risk, the term "fitness" almost exclusively refers to cardiorespiratory fitness (CRF) and does not address other PF components, namely muscular, morphological, motor, and metabolic fitness (Bouchard and Shepard, 1994) in the analysis. Indeed, PF is not a unitary, but rather a multifactorial, construct.

Given the aforementioned gaps and limitations in the literature, especially the observation that no recent longitudinal studies have described the dynamics of change in cardio-metabolic risk factors, this study aims to: (1) longitudinally model changes of the HWP in adolescents, and (2) investigate the effects of time-invariant (sex) and time-varying correlates (biological maturation, PA, and PF) on HWP trajectories across time.

METHODS

Sample

Data are from the Oporto Growth, Health, and Performance Study (OGHPS), which has an overall aim to investigate the interaction among individual characteristics, environmental, and lifestyle factors that affect the growth, development and health of Portuguese adolescents. The OGHPS has a mixed-longitudinal design involving randomly selected adolescents from 10 to 18 years of age divided into four cohorts: 10, 12, 14, 16 years at baseline. For the present study, we considered data obtained from a total of 5,549 subjects (Table 1). All measurements were conducted annually during the same months (November to April) to avoid seasonal variations. The OGHPS protocols were approved by the Ethics Committee of the University of Porto; legal authorization was obtained from school directors, and parents gave their informed consent.

Biological maturation

Biological maturation was indirectly assessed by the maturity offset regression procedure proposed by Mirwald et al. (2002), which estimates how many years a subject is from peak height velocity (PHV). A positive (+) maturity offset represents the number of years the participant is beyond PHV, whereas a negative (–) maturity offset represents the number of years the subject is before PHV.

Physical activity

Total physical activity (TPA) was estimated with the Baecke questionnaire (Baecke et al., 1982), a reliable and valid instrument (Philippaerts et al., 1999) that describes three basic domains of PA (school PA, leisure time PA, and sport participation PA). It comprises a total of 16 questions divided into these three domains and each is scored from 1 to 5. The TPA score was obtained from the unweighted sum of the three domains, and scores ranged from 3 (lowest) to 15 (highest). All adolescents answered the questionnaires during their physical education classes under the supervision of teachers who were trained by the research team.

Physical fitness

Five measures were considered to represent overall PF. CRF was estimated from the 1-mile run/walk test of Fitnessgram (1994) battery, where all subjects ran/walked a distance of 1609m in the shortest time possible. The other fitness components were assessed with several items from the 1988 AAHPERD youth fitness test (1976): (a) speed—50 yard dash: run this distance in the shortest time possible; (b) explosive leg power—standing long jump: jump as far as possible from a standing position; (c) agility—shuttle run: run as fast as possible from the starting line to a line 9 m away where two small wooden blocks were placed, pick-up one of the blocks, return to the starting line, place the block on the line, and then repeat the route; and (d) static strength—handgrip strength: grip the dynamometer (Takei Physical Fitness Test GRIP-D, Japan) with maximum force during 5 to 10 s. Static strength (kg) was expressed relative to body mass (kg) given the high dependency of hang grip strength to body size (Malina et al., 2004) (i.e., weight).

Hypertensive and waist phenotype

WC was anatomically identified as the smallest circumference between the lowest rib and the superior border of the iliac crest and measured to the nearest 1 cm with non-elastic tape (Sanny, American Medical of Brazil, São Paulo, Brazil). BP was measured with an automated device (Omrom M6 hem-7001-E, Omron Healthcare) previously validated by The International Protocol of the European Society of Hypertension (Topouchian et al., 2006). Three different cuff sizes were available and appropriate cuff size was determined according to the best fit to the participant's arm circumference. All adolescents rested 5 min prior to

the first BP measurement. They remained seated with the back relaxed against the chair, legs uncrossed, and feet flat on the floor. The right upper limb was positioned with support at the heart level and palm of the hand turned upward. Three consecutive measures with at least 2 min interval were obtained. For the present study, the average values of systolic and diastolic BP were used to compute MAP. Subjects' MAP values were calculated using the following formula: MAP (mm Hg) = Diastolic BP + 1/3 (Systolic BP − Diastolic BP). To compute the HWP, MAP, and WC results were transformed into *z*-scores and then summed; increasing positive *z*-values are indicative of less-favorable cardio-metabolic score.

Data quality control

Data quality control was assured in three different steps: (1) training of all team members by experienced researchers of the Kinanthropometry Laboratory of the Sports Faculty, University of Porto, Portugal; (2) conducting random retests (intrarater reliability) on each assessment day; (3) reliability calculations using the Analysis of variance (ANOVA)-based intraclass correlation coefficient (R), as well as the technical error of the measurement (TEM): TEM = 0.1 cm for WC; for PF tests, R values ranged from 0.93 (1-mile run/walk) to 0.97 (handgrip); and for PA, $R = 0.80$.

Statistical analysis

Exploratory and descriptive data analyses were conducted with SPSS 20.0 software. Modelling changes in HWP were done in HLM 6.0 software within the framework of the multilevel approach (Bryk and Raudenbush, 1987) using maximum likelihood estimation procedures. In HLM analysis, the numbers and spacing of measurement observations may vary across subjects, and it can also accommodate data from mixed-longitudinal designs with missing data, under the assumption that missing is at random (Raudenbush, 1995). In order to best describe individual longitudinal trajectories, average trajectories and respective predictors, a series of hierarchical nested models were fitted by using a stepwise approach. To facilitate interpretation of model parameters describing change, the time metric was centered at baseline, i.e., the first measurement of cohort 1. Thus the time 0 corresponds to 10 years of age, and the temporal metric of *X*-axis has become 0, 1, 2, 3, 4, 5, 6, 7, and 8, which corresponds to 10, 11, 12, 13, 14, 15, 16, 17, and 18 years of age. In the first step, a null model (M_0) was run to define the level-1 submodel using up to a second-degree polynomial of time. A series of hierarchically nested level-1 models were fitted, with increasing patterns of HWP change (linear and quadratic).The effect of gender was also tested (level-2 variable). The next step was to run a model (M_1) that used time-varying covariates—maturity offset and TPA (level 1). On the subsequent model (M_2), PF-tests were also included. To facilitate the interpretation, all predictors but sex (female = 0 and males = 1) were centered on the grand mean. Deviance statistics were used as a measure of global fit. Differences in deviances are distributed as an approximate Chi-square (χ^2) distribution with degrees of freedom determined by the difference in the number of estimated parameters between the models. It is expected that as model increases in complexity (i.e., adding parameters) a statistically significant decrease in deviance is expected.

RESULTS

Descriptive statistics for girls and boys at each annual time point (T0–T8) are in Table 2. Both sexes had an average increase in the HWP from 10 to 18 years of age. On average, girls' estimated age at PHV occurred at about 12 years of age, while in boys, it was at about 13 years of age. Girls' and boys' TPA mean values increased until age 13 years, and then declined. Boys showed systematic mean improvements in all PF tests over time, except for CRF. Girls showed considerable variation in their mean values for CRF, explosive leg power, agility, and speed tests; a slight mean improvement in static strength over time.

Multilevel modelling results are presented in Table 3. A nonlinear trend was the best fitting trajectory for HWP across time. On average, 10-year-old girls had a low HWP at baseline ($\beta = -1.012 \pm 0.051$), and no significant differences were found compared to boys ($\beta = 0.026 \pm 0.066$) as shown in Figure 1. However, sex differences emerged with increasing age, a sign of a cross-level interaction. Specifically, in girls, their instantaneous HWP growth rate at baseline is $\beta = 0.364$ *z*-scores followed by negative curvature, i.e., a mean negative aceleration ($\beta = -0.022 \pm 0.003$); boys instantaneous HWP growth rate at baseline is higher than girls ($\beta = 0.497$ *z*-scores) with a similar mean negative accelaration. This suggests that, on average, boys increase their HWP at a faster rate than girls. Additionally, there seems to be a tendency for a stabilization in metabolic risk. There is noteworthy interindividual variation at baseline, and the trend is expressed by the statistically significant variances.

In model 1, maturity offset andTPA were included as time-varying predictors for HWP trajectories. Sex differences were present at baseline. On average, the HWP of a random 10-year-old girl was now 0.437 (± 0.063) holding all other predictor variables at their respective means, i.e., for a girl at her estimated peak height velocity and with a mean TPA of 7.69 units, a mean velocity and acceleration trend is now evident for HWP. The more mature youth have higher HWP values ($\beta = 0.883 \pm 0.022$), whereas the higher the TPA the lower the HWP ($\beta = -0.053 \pm 0.010$). Although interindividual differences are less pronounced given the reductions of baseline and slope variances, they are still statistically significant.

In the final and best fitting model (M_2), a series of PF components were added. Sex differences are evident at baseline, more favorable for girls ($\beta_{girls} = -0.025 \pm 0.063$; $\beta_{boys} = 0.979 \pm 0.067$). Conditional on the new set of predictors, girls and boys instaneous velocity at baseline is −0.202 and −0.147, respectively. The mean negative acceleration is still present ($\beta = -0.023 \pm 0.004$) in both sexes. Consistent with M_1, maturity offset has a positive longitudinal association with HWP changes ($\beta = 0.913 \pm 0.023$) and TPA has a negative association ($\beta = -0.027 \pm 0.011$). With the exception of the shuttle run, improvements in PF significantly reduces HWP values across time ($\beta_{1mile} = 0.081 \pm 0.009$; $\beta_{SLJ} = -0.003 \pm 0.001$; $\beta_{50YD} = 0.106 \pm 0.020$; and $\beta_{HGr} = -3.335 \pm 0.196$).

Discussion

This study shows a series of multilevel nested models that were sequentially fitted in order to provide a better understanding of the longitudinal changes in the HWP of Portuguese youth, as well as to investigate the effects of

TABLE 2. Descriptive statistics for girls and boys in each annual time point (T0–T8)

		T0 (10 years) Mean (SD)	T1 (11 years) Mean (SD)	T2 (12 years) Mean (SD)	T3 (13 years) Mean (SD)	T4 (14 years) Mean (SD)	T5 (15 years) Mean (SD)	T6 (16 years) Mean (SD)	T7 (17 years) Mean (SD)	T8 (18 years) Mean (SD)
WC (cm)	♀	63.83 (7.65)	64.51 (7.94)	66.23 (8.09)	67.78 (7.33)	68.63 (7.32)	69.41 (7.18)	70.41 (7.28)	70.57 (7.56)	70.18 (6.56)
	♂	66.11 (8.55)	67.34 (8.65)	68.65 (8.71)	70.66 (8.11)	72.16 (7.90)	73.85 (7.43)	75.25 (7.73)	75.93 (7.44)	75.86 (7.79)
MAP (mm Hg)	♀	78.73 (8.17)	77.73 (7.69)	80.60 (7.75)	80.23 (7.73)	82.17 (7.60)	81.76 (7.55)	83.33 (7.66)	84.33 (5.78)	83.30 (6.67)
	♂	77.87 (8.08)	76.74 (7.04)	79.53 (7.60)	80.47 (7.80)	83.68 (7.79)	84.25 (7.76)	86.02 (7.97)	86.57 (8.43)	84.31 (7.22)
SBP	♀	109.52 (11.38)	108.53 (10.34)	112.27 (10.43)	111.85 (10.02)	114.28 (10.00)	113.63 (10.24)	115.40 (10.22)	115.84 (8.58)	114.05 (8.63)
	♂	108.67 (10.92)	108.23 (9.32)	113.07 (11.11)	116.05 (11.28)	121.10 (11.31)	122.85 (10.79)	125.86 (11.99)	127.17 (12.77)	120.51 (9.34)
DPB	♀	63.34 (7.67)	62.33 (7.35)	64.76 (7.38)	64.42 (7.52)	66.11 (7.43)	65.82 (7.33)	67.30 (7.40)	68.57 (5.61)	67.92 (6.94)
	♂	62.47 (7.79)	61.00 (7.01)	62.75 (7.22)	62.69 (7.43)	64.98 (7.54)	64.95 (7.94)	66.10 (7.87)	66.28 (7.66)	66.21 (7.39)
HWP	♀	−0.85 (1.56)	−0.90 (1.54)	−0.34 (1.57)	−0.20 (1.48)	0.14 (1.45)	0.18 (1.44)	0.50 (1.46)	0.64 (1.31)	0.46 (1.25)
	♂	−0.69 (1.69)	−0.68 (1.58)	−0.18 (1.65)	0.17 (1.59)	0.74 (1.54)	1.02 (1.49)	1.40 (1.56)	1.55 (1.55)	1.26 (1.51)
Maturity offset	♀	−1.50 (0.62)	−1.08 (0.75)	−0.34 (0.88)	0.70 (0.61)	1.27 (0.51)	1.85 (0.51)	2.43 (0.54)	2.83 (0.50)	3.33 (0.52)
(years)	♂	−2.18 (0.61)	−1.69 (0.76)	−0.89 (1.03)	0.25 (0.72)	1.31 (0.88)	2.29 (0.72)	3.15 (0.85)	3.69 (0.78)	4.26 (0.82)
TPA (units)	♀	7.69 (1.21)	7.75 (1.32)	7.70 (1.30)	7.83 (1.23)	7.67 (1.33)	7.71 (1.38)	7.48 (1.25)	7.25 (1.32)	7.25 (1.17)
	♂	8.29 (1.32)	8.51 (1.35)	8.55 (1.35)	8.59 (1.37)	8.45 (1.34)	8.27 (1.38)	8.16 (1.36)	8.21 (1.54)	7.93 (1.21)
Physical Fitness										
One-mile run	♀	11.19 (1.84)	10.47 (1.83)	10.92 (1.99)	10.01 (1.92)	10.96 (2.25)	10.48 (2.22)	11.98 (2.66)	12.00 (1.99)	13.21 (3.32)
(min)	♂	9.86 (2.02)	9.39 (2.04)	9.40 (2.09)	8.29 (1.80)	8.56 (1.84)	8.00 (2.05)	9.08 (2.43)	8.42 (1.32)	9.40 (4.38)
SLJ (cm)	♀	127.59 (21.40)	130.28 (21.76)	134.39 (22.65)	142.2 (25.35)	140.71 (25.05)	139.39 (24.78)	138.16 (23.24)	140.55 (27.36)	138.75 (18.22)
	♂	137.15 (23.41)	142.50 (22.97)	152.34 (25.89)	170.09 (28.20)	178.20 (28.72)	189.00 (28.50)	189.72 (31.03)	202.77 (22.74)	202.00 (34.39)
SHR (s)	♀	12.76 (1.40)	12.24 (1.58)	12.10 (1.33)	11.75 (1.33)	11.88 (1.28)	11.91 (1.33)	12.26 (1.23)	12.09 (1.41)	12.40 (1.34)
	♂	12.02 (1.61)	11.69 (1.47)	11.35 (1.31)	10.69 (1.36)	10.69 (1.18)	10.22 (1.02)	10.64 (1.23)	10.00 (0.90)	10.27 (0.13)
50YD (s)	♀	9.29 (0.85)	9.05 (0.99)	8.78 (1.03)	8.45 (0.90)	8.40 (0.99)	8.34 (0.79)	8.50 (0.95)	8.44 (1.22)	9.15 (0.92)
	♂	8.90 (0.91)	8.73 (1.03)	8.32 (1.05)	7.71 (0.99)	7.43 (0.94)	7.10 (0.92)	7.06 (0.87)	6.59 (0.47)	7.00 (0.25)
HGr ($kg \cdot kg^{-1}$	♀	0.44 (0.09)	0.46 (0.09)	0.46 (0.09)	0.48 (0.09)	0.47 (0.09)	0.48 (0.08)	0.46 (0.09)	0.48 (0.09)	0.50 (0.08)
body mass)	♂	0.46 (0.10)	0.47 (0.10)	0.50 (0.10)	0.54 (0.10)	0.56 (0.10)	0.59 (0.11)	0.59 (0.12)	0.61 (0.11)	0.62 (0.11)

T, time; WC, waist circumference; MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HWP, hypertensive waist phenotype; TPA, total physical activity; SLJ, standing long jump; SHR, shuttle run; 50YD, 50 yard dash; HGr, relative handgrip.

TABLE 3. Results summary for the three nested models

	Null Model (M_0)	Model I (M_1)	Model II (M_2)
Regression coefficients (fixed effects)			
Baseline (10 years)	−1.012 (0.051)*	0.437 (0.063)*	−0.025 (0.063)§
Sex	0.026 (0.066)§	0.820 (0.067)*	0.979 (0.067)*
Linear slope	0.364 (0.022)*	−0.284 (0.029)*	−0.202 (0.032)*
Sex	0.133 (0.016)*	−0.068 (0.019)*	0.055 (0.020)*
Quadratic slope	−0.022 (0.003)*	−0.015 (0.003)*	−0.023 (0.004)*
Maturity Offset		0.883 (0.022)*	0.913 (0.023)*
TPA (units)		−0.053 (0.010)*	−0.027 (0.011)**
One-mile run (min)			0.081 (0.009)*
SLJ (cm)			−0.003 (0.001)*
SHR (s)			0.007 (0.012)§
50YD (s)			0.106 (0.020)*
HGr ($kg \cdot kg^{-1}$ body mass)			−3.335 (0.196)*
Variance components (random effects)			
Baseline	2.540*	1.470*	0.916*
Slope	0.027*	0.004*	0.003**
Covariance	−0.146*	−0.030	−0.005
Residual	0.459	0.480	0.489
Model summary			
Deviance	33,839.333	24,122.208	17,648.352
Number of estimated parameters	9	11	16

Parameter estimate standard errors listed in parentheses.
TPA, total physical activity; SLJ, standing long jump; SHR, shuttle run; 50YD, 50 yard dash; HGr, relative handgrip strength.
*$P < 0.01$; **$P < 0.05$; §Nonsignificant.

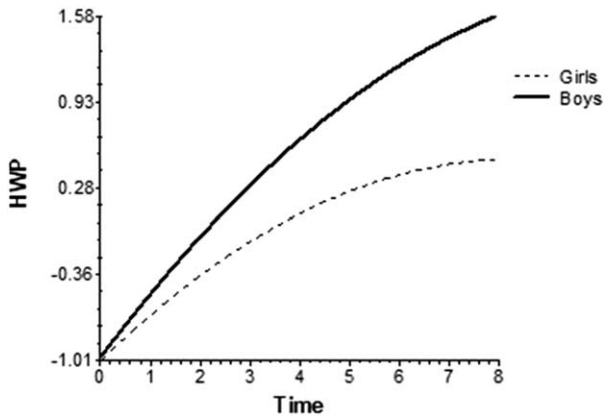

Fig. 1. Average trajectories of HWP as function of time (time 0 = 10 years, time 1 = 11 years, …, time 8 = 18 years) and sex (no other covariates are included in the model that produced these mean trajectories). HWP, hypertensive and waist phenotype.

sex, biological maturation, TPA, and PF in HWP trajectories. As such, we will discuss each model in a stepwise approach from M_0 (predictors: time and sex) to M_2 (best fitting model, predictors: time, sex, biological maturation, TPA, and PF).

Overall, M_0 findings showed that HWP values increased across time with a non-linear trend in both girls and boys. Furthermore, boys showed a more unfavorable HWP trend. In the present study, HWP included only two key markers of metabolic syndrome, namely WC and BP, compared to other studies that incorporate blood chemistry markers such as glucose or insulin and blood lipid parameters (total cholesterol, high-density lipoprotein cholesterol, triglycerides). During adolescence and puberty, these two indicators present distinct developmental changes in both sexes, although comparable in pattern. Until the adolescent growth spurt, both boys and girls tend to accumulate more adiposity in the trunk than in the limbs (Malina et al., 2004). However, it is well recognized that boys accumulate a centralized fat deposition after the pubertal period (Ekelund et al., 2009; Malina et al., 2004). Similarly, systolic BP increases from childhood to adolescence, but boys tend to have greater mean values than girls, especially after the pubertal period (Shankar et al., 2005). These general growth-related trends were confirmed in M_0. Furthermore, previous data showed that males tend to have a higher prevalence on a wide range of cardio-metabolic risk factors including hyperglycemia and dyslipidemia (Moran et al., 2008; Steele et al., 2008). Although boys tend to show a decrease in total body fat percent when contrasted to girls during adolescence, longitudinal data (Moran et al., 2008) showed that adverse changes in insulin resistance, systolic BP, and abdominal fat may possibly play a role in the greater cardio-metabolic risk in post-pubertal boys.

The best fitting model (M_2) showed that boys have higher risk already at the onset of adolescence as compared to girls. This result may be counterintuitive since the timing and tempo of the adolescent growth spurt generally occurs earlier in girls. As such, at 10 years of age, it would be reasonable to find that boys would be more "protected" than girls. Although we do not have a clear explanation for why this higher risk appears earlier in males, it is possible that female sex hormones (estrogen), via multiple mechanisms, reduces the cardio-metabolic risk in girls, and this effect first becomes apparent at the beginning of the adolescent growth spurt (Moran et al., 2008).

There was a positive relationship between maturity offset and HWP suggesting that those ahead in their biological maturation have a more adverse HWP. This unfavorable effect was anticipated due to weight gain (Ekelund et al., 2009) and obesity-related hypertension (Sorof et al., 2002; Weiss et al., 2013), as well as other adverse health outcomes such as elevated concentrations of triglycerides, low high-density lipoprotein cholesterol concentrations and temporary decreases in insulin sensitivity (Ekelund et al., 2009). Indeed, pubertal timing is an independent predictor of adult cardio-metabolic risk as shown in a large prospective birth cohort study (Widen et al., 2012), where earlier puberty was related with

higher adult body mass index, waist and hip circumference, fasting insulin, diastolic BP, and decreased HDL cholesterol in both males and females.

Both PA and PF were longitudinally associated with HWP suggesting that positive changes in TPA and PF (with the exception of the shuttle run) predicted an annual decrease in HWP. There is a wealth of cross-sectional data (Bailey et al., 2012; Ekelund et al., 2007; Moreira et al., 2011; Rizzo et al., 2007) showing the association between PA and cardio-metabolic risk factors in youth, but the results are inconsistent (Froberg and Andersen, 2005; Steele et al., 2008). For example, Bailey et al. (2012) found no significant correlations between objectively measured PA (accelerometer) with cardio-metabolic risk score (WC, diastolic BP, fasting blood glucose and triglycerides, and total cholesterol/HDL cholesterol ratio) in 100 adolescents aged from 10 to 14 years. On the other hand, a study (Moreira et al., 2011) of 417 Azorean adolescents aged 15 to 18 years indicated that those who were more active (measured by pedometers; steps per day) had lower odds for having one or more adverse cardio-metabolic risk factors. Some authors suggest that the inconsistent results can be linked to the method used to assess PA (Steele et al., 2008) (objective versus self-reported), and also to the sample used in terms of diversity and sample size (Froberg and Andersen, 2005). Compared to cross-sectional studies, very few longitudinal investigations have been conducted on this topic. The Muscatine Study (Janz et al., 2002) did not find any significant association between self-reported PA changes from 10 to 13 years of age and cardio-metabolic health outcomes at 14 years of age. In contrast, results from the Amsterdam Growth and Health Study (Twisk et al., 2001) spanning adolescence to young adulthood (12–27 years) demonstrated that the relationship between PA (assessed with a structured interview) and a clustering score of metabolic risk was present during the entire longitudinal period. Despite the difference in age, our results substantiate the longitudinal protective effect of higher TPA levels on cardio-metabolic risk factors.

With regard to PF, several cross-sectional reports (Bailey et al., 2012; Ekelund et al., 2007; Ogunleye et al., 2013; Rizzo et al., 2007) have shown an inverse association with cardio-metabolic risk factors; however, direct comparison between studies is difficult due to methodological differences and because most studies mostly focus solely on CRF as the indicator of PF. More recently, studies have recognized the role of muscular fitness in the prevention of cardio-metabolic risk factors among children and adolescents (Magnussen et al., 2012; Moreira et al., 2011; Steene-Johannessen et al., 2009) concluding that those who have greater muscular fitness have lower cardio-metabolic scores (including WC, BP, triglycerides, HDL cholesterol, and insulin resistance) independent of CRF. To our knowledge, the Muscatine Study (Janz et al., 2002) was the only longitudinal report that examined the association between PF (marked by CRF and static strength) and cardio-metabolic health outcomes. Similarly to the present study, their results indicated that maintaining high levels of CRF and muscular strength from 10 to 13 years of age was associated with lower levels of WC and systolic BP at 14 years of age. Since no recent longitudinal study has investigated the influence of other PF components on cardio-metabolic risk factors trajectories, the current study provides relevant information indicating that being physically fit and consistently improving the muscular fitness components of speed, explosive leg power, and static handgrip strength during adolescence may confer additional benefits to cardio-metabolic health beyond those attributed to CRF.

There are at least three limitations that should be recognized in the present study. First, compared to previous studies of the metabolic syndrome, the HWP is limited to BP and WC due to feasibility and financial restrictions. However, it is important to note that the WC-BP phenotype has great potential and utility for school-based screenings given its feasibility. Second, PA was estimated via questionnaire. However, the Baecke questionnaire is widely used in large-scale studies (Matton et al., 2007; Wijnstok et al., 2013). There is also consistent evidence that the Baecke questionnaire is reliable with Portuguese children and adolescents (Ferreira et al., 2002; Vasconcelos and Maia, 2001). Third, we had difficulty comparing our results to previous research due to the absence of longitudinal studies concerning cardio-metabolic risk factors changes during childhood and adolescence. Fourth, although we did not explicitly model cohort and age effects in the analysis of our mixed-longitudinal data, Duncan and Duncan (2012) confirmed the capability of such a design to adequately approximate parameters estimated with a true longitudinal design. Further, Yun (2011) showed not only the efficiency of the model we used, when compared to other models that accommodate more complex random components with cohort and age effects, but also revealed that the parameter estimates of the fixed part are very similar.

Despite these limitations, the study has strengths that should be considered. First, the mixed-longitudinal approach provides a better understanding of the dynamics of changes in all variables. Second, we used a highly flexible statistical procedure to fit the complexities of HWP trajectories. Third, the sample size was large ($n = 5{,}500$) and spanned ages 10 to 18 years. Fourth, the age cohorts represent an important life period in terms of acquisition and development of lifestyle behaviors that are linked to health outcomes in adulthood.

In conclusion, the major finding of this study was that longitudinal improvements in TPA and PF provided a consistent protective effect in the development of the HWP across the adolescence years. From a public health perspective, these results support the importance of early recognition and treatment of cardio-metabolic risk factors. In this sense, school-based health examinations should incorporate WC and BP as simple and effective primary prevention measures, since they are two important predictors in the large-scale screening of cardio-metabolic disorders in children and adolescents. Furthermore, it is important to address the relevance of school context and youth sports programs to promote and encourage children and adolescents in the regular engagement in moderate-to-vigorous physical activities/physical exercises that ensure improvements in all PF components. In turn, such strategies will have the potential to prevent cardio-metabolic disorders associated with obesity and sedentary lifestyle later in life.

ACKNOWLEDGMENTS

We would like to thank the study participants along with their parents, teachers, and school principals for their involvement in the study.

LITERATURE CITED

(AAHPER) AAfHPEaR. 1976. Youth fitness test manual. Washington, DC: AAHPER.

Baecke J, Burema J, Frijters J. 1982. A short questionnaire for the measurenment of habitual physical activity in epidemiological studies. Am J Clin Nutr 36:936–942.

Bailey DP, Boddy LM, Savory LA, Denton SJ, Kerr CJ. 2012. Associations between cardiorespiratory fitness, physical activity and clustered cardiometabolic risk in children and adolescents: the HAPPY study. Eur J Pediatr 171:1317–1323.

Bouchard C, Shepard K. 1994. Physical activity, fitness and health. The model and the key concepts. In: Bouchard C, Shepard K, Stephens T, editors. Physical activity, fitness and health- International proceedings and consensus statement. Champain, IL: Human Kinetics. p 77–78.

Bryk A, Raudenbush S. 1987. Application of Hierarchical Linear Models to Assessing Change. Psychological Bulletin 101(1):147–158.

Chen X, Wang Y. 2008. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. Circulation 117:3171–3180.

Choy CS, Chan WY, Chen TL, Shih CC, Wu LC, Liao CC. 2011. Waist circumference and risk of elevated blood pressure in children: a cross-sectional study. BMC Public Health 11:613.

Chrzanowska M, Suder A, Kruszelnicki P. 2012. Tracking and risk of abdominal obesity in the adolescence period in children aged 7-15. The Cracow Longitudinal Growth Study. Am J Hum Biol 24:62–67.

Duncan S, Duncan T. 2012. Accelerated longitudinal designs. In: Laursen B, Litlle T, Card N, editors. Handbook of developmental research methods. New YorK: The Guilford Press.

Eisenmann JC. 2008. On the use of a continuous metabolic syndrome score in pediatric research. Cardiovasc Diabetol 7:17.

Eisenmann JC, Welk GJ, Wickel EE, Blair SN. 2004. Stability of variables associated with the metabolic syndrome from adolescence to adulthood: the Aerobics Center Longitudinal Study. Am J Hum Biol 16:690–696.

Ekelund U, Anderssen S, Andersen LB, Riddoch CJ, Sardinha LB, Luan J, Froberg K, Brage S. 2009. Prevalence and correlates of the metabolic syndrome in a population-based sample of European youth. Am J Clin Nutr 89:90–96.

Ekelund U, Anderssen SA, Froberg K, Sardinha LB, Andersen LB, Brage S. 2007. Independent associations of physical activity and cardiorespiratory fitness with metabolic risk factors in children: the European youth heart study. Diabetologia 50:1832–1840.

Ferreira J, Marques A, Maia J. 2002. Physical fitness, physical activity and health in young population from Viseu—a study in children and youngsters of both gender from 10 to 18 years old. Viseu: Departamento Cultural - Instituto Superior Politécnico de Viseu.

Fitnessgram. 1994. The prudencial fitnessgram test administration manual. Dallas, TX: The Cooper Institute for Aerobics Research.

Froberg K, Andersen LB. 2005. Mini review: physical activity and fitness and its relations to cardiovascular disease risk factors in children. International journal of obesity 29Suppl2:S34–39.

Garnett SP, Baur LA, Cowell CT. 2011. The prevalence of increased central adiposity in Australian school children 1985 to 2007. Obes Rev 12:887–896.

Janz KF, Dawson JD, Mahoney LT. 2002. Increases in physical fitness during childhood improve cardiovascular health during adolescence: the muscatine study. Int J Sports Med 23 (Suppl 1):S15–S21.

Magnussen CG, Schmidt MD, Dwyer T, Venn A. 2012. Muscular fitness and clustered cardiovascular disease risk in Australian youth. Eur J Appl Physiol 112:3167–3171.

Malina R, Bouchard C, Bar-Or C. 2004. Growth, maturation and physical activity, 2nd ed. Champaign, IL: Human Kinetics.

Matton L, Duvigneaud N, Wijndaele K, Philippaerts R, Duquet W, Beunen G, Claessens AL, Thomis M, Lefevre J. 2007. Secular trends in anthropometric characteristics, physical fitness, physical activity, and biological maturation in Flemish adolescents between 1969 and 2005. Am J Hum Biol 19:345–357.

McCarthy HD, Ellis SM, Cole TJ. 2003. Central overweight and obesity in British youth aged 11-16 years: cross sectional surveys of waist circumference. BMJ 326:624.

Mirwald RL, Baxter-Jones AD, Bailey DA, Beunen GP. 2002. An assessment of maturity from anthropometric measurements. Med Sci Sports Exerc 34:689–694.

Moran A, Jacobs DR, Jr., Steinberger J, Steffen LM, Pankow JS, Hong CP, Sinaiko AR. 2008. Changes in insulin resistance and cardiovascular risk during adolescence: establishment of differential risk in males and females. Circulation 117:2361–2368.

Moreira C, Santos R, de Farias Junior JC, Vale S, Santos PC, Soares-Miranda L, Marques AI, Mota J. 2011. Metabolic risk factors, physical activity and physical fitness in Azorean adolescents: a cross-sectional study. BMC Public Health 11:214.

Ogunleye AA, Sandercock GR, Voss C, Eisenmann JC, Reed K. 2013. Prevalence of elevated mean arterial pressure and how fitness moderates its association with BMI in youth. Public Health Nutr 16:2046–2054.

Philippaerts RM, Westerterp KR, Lefevre J. 1999. Doubly labelled water validation of three physical activity questionnaires. Int J Sports Med 20: 284–289.

Raudenbush S. 1995. Hierarchical linear models to study the effects of social context on development. In: Gottman J, editor. The analysis of change. Mahwah, NJ: Lawrence Erlbaum Associates, Publishers. p 165–202.

Rizzo NS, Ruiz JR, Hurtig-Wennlof A, Ortega FB, Sjostrom M. 2007. Relationship of physical activity, fitness, and fatness with clustered metabolic risk in children and adolescents: the European youth heart study. J Pediatr 150:388–394.

Schroder H, Ribas L, Koebnick C, Funtikova A, Gomez SF, Fito M, Perez-Rodrigo C, Serra-Majem L. 2014. Prevalence of abdominal obesity in spanish children and adolescents. Do we need waist circumference measurements in pediatric practice? PloS One 9:e87549.

Shankar RR, Eckert GJ, Saha C, Tu W, Pratt JH. 2005. The change in blood pressure during pubertal growth. J Clin Endocrinol Metab 90: 163–167.

Sorof J, Daniels S. 2002. Obesity hypertension in children: a problem of epidemic proportions. Hypertension 40:441–447.

Steele RM, Brage S, Corder K, Wareham NJ, Ekelund U. 2008. Physical activity, cardiorespiratory fitness, and the metabolic syndrome in youth. J Appl Physiol 105:342–351.

Steene-Johannessen J, Anderssen SA, Kolle E, Andersen LB. 2009. Low muscle fitness is associated with metabolic risk in youth. Med Sci Sports Exerc 41:1361–1367.

Topouchian JA, El Assaad MA, Orobinskaia LV, El Feghali RN, Asmar RG. 2006. Validation of two automatic devices for self-measurement of blood pressure according to the International Protocol of the European Society of Hypertension: the Omron M6 (HEM-7001-E) and the Omron R7 (HEM 637-IT). Blood Press Monit 11:165–171.

Twisk JW, Kemper HC, Van Mechelen W, Post GB. 2001. Clustering of risk factors for coronary heart disease. the longitudinal relationship with lifestyle. Ann Epidemiol 11:157–165.

Vasconcelos M, Maia J. 2001. Is there a decline in physical activity? A cross-sectional study in children and youngsters of both gender from 10 to 19 years old. Portuguese J Sports Sci 1:44–52.

Weiss R, Bremer AA, Lustig RH. 2013. What is metabolic syndrome, and why are children getting it? Ann N Y Acad Sci 1281:123–140.

Widen E, Silventoinen K, Sovio U, Ripatti S, Cousminer DL, Hartikainen AL, Laitinen J, Pouta A, Kaprio J, Järvelin MR, Peltonen L, Palotie A. 2012. Pubertal timing and growth influences cardiometabolic risk factors in adult males and females. Diabetes Care 35:850–856.

Wijnstok NJ, Hoekstra T, van Mechelen W, Kemper HC, Twisk JW. 2013. Cohort profile: the Amsterdam Growth and Health Longitudinal Study. Int J Epidemiol 42:422–429.

Yun J. 2011. Statistical issues on studies of mixed longitudinal designs. PhD dissertation. University of Texas, School of Public Health. United States of America.

Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S, IDF Consensus Group. 2007. The metabolic syndrome in children and adolescents - an IDF consensus report. Pediatr Diabetes 8:299–306.