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ORIGINAL ARTICLE

Association of body composition and blood pressure categories with retinal vessel diameters in primary school children

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Alterations in retinal vessel diameters have been shown to be predictive of cardiovascular risk in adults and children. The aim of our study was to examine the association of body composition and blood pressure (BP) categories with retinal vessel diameters in school children. We examined anthropometric parameters, BP and retinal arteriolar (CRAE) and venular (CRVE) diameters as well as the arteriolar-to-venular diameter ratio (AVR) in 391 children (age: 7.3, s.d. 0.4). Differences between the lowest and highest BP quartiles indicated that higher systolic and diastolic BP were associated with narrower CRAE ($P<0.001$ for both). Children in the highest weight quartile had narrower CRAE compared with the lowest quartile ($P=0.05$). In the regression analysis, systolic and diastolic BP were associated with arteriolar narrowing (–0.4 measuring units (mu) per mm Hg, 95% confidence interval: [−0.6; −0.3] and −0.6 mu per mm Hg [−0.7; −0.4], respectively; $P<0.001$ for both). An independent association was found for diastolic BP only. Compared with normotensives (NT; 74.4% of cohort), arteriolar narrowing was already seen in children categorized as pre-hypertensive (PHT) (11.5% of cohort), which was similar to HT children (14.1% of cohort) (NT: mean 207.2 [205.6; 208.7] mu; PHT: 201.7 [197.8; 205.7] mu; HT: 199.7 [196.2; 203.3] mu; $P=0.01$ for PHT *vs.* NT and $P<0.001$ for HT *vs.* NT in systolic BP). Our results suggest that systolic and diastolic BP are main determinants of retinal arteriolar diameters; and therefore, microvascular health in young children. Pre-hypertension seems to be associated with retinal microvascular alterations early in life.
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Keywords: anthropometry; microcirculation; pre-hypertension; retinal vessels; youth

INTRODUCTION

It has been shown that alterations in retinal vessel diameters are related to a higher risk of obesity[1] and hypertension,[2] an increased risk of stroke[3] and a higher cardiovascular mortality rate in adults.[4] A graded association of narrower retinal arterioles with increasing blood pressure (BP) has been shown.[5–7] In children, a handful of studies on the association of retinal vessel diameters with body composition and BP have been conducted. Greater body mass index (BMI) has been found to correlate with narrower retinal arterial diameters, wider retinal venular diameters and a lower arteriolar-to-venular ratio (AVR).[8–11] Height, weight and waist circumference also seem to influence retinal vessel diameters in children.[8,11] Most of these studies have examined the association of either body composition or BP with retinal vessel diameters in an Asian or mixed race population. A study in an Australian and Singapore cohort of primary school children found an association of higher systolic and diastolic BP with retinal arteriolar narrowing.[12] In preschool-aged children as young as 3–6 years, BMI and systolic BP had an inverse association with retinal arterioles and BMI was positively associated with retinal venular diameters.[13] In a recently published large-scale survey in the Netherlands examining 4000 school children with a median age of 6, higher systolic as well as diastolic BP were associated with retinal arteriolar narrowing.[14] A German study in 10- to 12-year-old school children reported an association between retinal vessel alterations, BP as well as BMI.[11] Higher BMI was associated with wider venular diameters and systolic BP with arteriolar narrowing. In a recent survey of over 700 children and adolescents in China, the Guangzhou Twin Eye Study, body composition was only found to be associated with retinal vessel diameters in older children and adolescents aged 12–19 years and not in younger children.[15] Therefore, the available data are scarce and seem inconsistent, with findings depending on age-group and ethnic population. Retinal arteriolar narrowing has been shown to be associated with large artery stiffness, an indicator of (pre-)atherosclerosis in the macrocirculation.[16] Other potential markers of preterm atherosclerosis include fetal aortic wall thickness, which has been shown to be a very early marker of hypertension.[17]

Few studies have analyzed the association of body composition and BP in a single study to compare their impact on retinal microvascular health in the same population. In addition, waist-to-height ratio is more strongly associated with cardiovascular risk factors than the BMI

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in children and has not yet been related to retinal microvascular health.[18–23] Moreover, BP levels categorizing normotensive (NT), pre-hypertensive (PHT) and hypertensive (HT) children have not been associated with retinal vessel diameters before. In our sample of healthy primary school children, we therefore aimed to investigate the association of retinal vessel diameters with BMI, waist circumference, percentage body fat, waist-to-height ratio and BP categories in 6- to 8-year-old primary school children.

METHODS

Study design and participants

The study was designed as a large-scale, cross-sectional study. In 2014, the Sportcheck study investigated all first-grade pupils of primary schools in the canton Basel-Stadt. From the 1255 children that took part in measurements of weight and height, 540 (43%) were allowed by their parents to join additional tests on anthropometric parameters, BP and static retinal vessel diameters. Due to illness at one of the two test dates or relocation, 149 children dropped out. From the full cohort, 391 children took part in the anthropometric and retinal microvascular measurements (Figure 1). The study was approved by the ethics committee of the University of Basel (EKBB, Basel, No. 258/12). Written informed consent was obtained from all study participants and their families.

Static retinal vessel analysis

Measurements of retinal vessel diameters were performed using a Static Retinal Vessel Analyzer (SVA-T, Imedos Systems UG, Jena, Germany). The system allows non-invasive and non-mydriatic measurements of retinal vessel diameters. It consists of a Topcon fundus camera and an advanced image processing unit (Vesselmap 2, Visualis, Imedos Systems UG).[5] The method and procedures have been described in detail elsewhere.[11] Briefly, four valid digital images were taken from the retina of the left and the right eye, with an angle of 30° and the optic disc in the center.[24] Using the Parr-Hubbard formula, diameters were calculated to central retinal arteriolar (CRAE) and venular (CRVE) equivalents.[5] The AVR was calculated using CRAE and CRVE. Retinal vessel diameters are presented in measuring units (mu). One measuring unit relates to 1 μm in the model of Gullstrand's normal eye. The assessment of the retinal vessels was performed by a single experienced examiner. Reproducibility for all three parameters was high with a correlation coefficient for CRAE of $r=0.94$ and a coefficient of variation (CV) of 2.1%. For CRVE, the correlation coefficient was $r=0.95$ and the CV was 2.0% (AVR: $r=0.94$ and CV = 2.3%) ($P<0.001$ each).

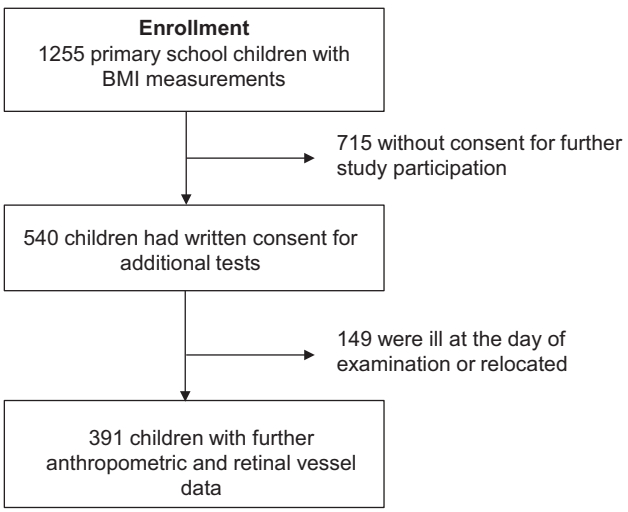

Figure 1 Study flow diagram.

Body composition and BP

Body height was measured without shoes to the nearest 0.2 cm using a wall-mounted stadiometer (Seca 206, Seca, Basel, Switzerland). Body weight was determined in light clothing and without shoes to the nearest 50 g using an electronic scale (Seca 899, Seca). BMI was calculated by dividing body weight by height in meters squared. Waist circumference was measured using a flexible tape at the natural waist (half way between the ribcage and the iliac crest). Skinfold thickness was measured in triplicate to the nearest 0.5 mm with Harpenden Calipers (HSK-BI, British Indicators, West Sussex, UK), calibrated to exert a pressure of 10 g cm^{-2} at two sites (triceps and subscapular) based on standard procedures.[25] The two skinfolds were taken to calculate percent body fat. The waist-to-height ratio was calculated by dividing the waist circumference by height (in cm).[20]

On the basis of the recommendations of the American Heart Association, BP (mm Hg) was measured after a rest period of 5 min at the bare right arm.[26] Children were seated in a comfortable position in a quiet room. To reduce inter-observer variability, an automated oszillograph (Oscillomate, CAS Medical Systems, Branford, CT, USA) was used. The standard cuff-size for children of 12–19 cm fitted all children. BP measurements were taken five times. The mean of the three measurements with the smallest variation was used for further analysis.[27] Systolic and diastolic BP were categorized in NT, PHT and HT based on the reference values by age, sex and height measured in the German Health Interview and Examination Survey for Children and Adolescents (KiGGS 2003–2006), including a large German cohort of over 17 500 children aged 3–17 years.[28] According to the reference of this large German cohort, children were classified as PHT with a BP over the 90th percentile and as HT with a BP over the 95th percentile, which is considered as a widespread convention.[27–29] The KiGGS BP reference values are not influenced by the prevalence of overweight children in the reference population and they are based on validated oscillometric devices.

Statistical analysis

Sample size was estimated based on previous findings in BP and retinal vessels in children.[11] On the basis of this study, the estimated effect size (Cohen's d) was considered as moderate ($d=0.6$). Calculated with the software G-Power using F-tests ($f=0.25$, power = 0.90 and 5% level of significance), we estimated the sample size to be approximately 290 children in total. To describe baseline characteristics, descriptive statistics were performed. Mean (95% CI) CRAE, CRVE and AVR were compared across anthropometric parameters' 1st and 4th quartiles by use of univariate analysis of covariance with age and sex as a covariate, and BP was additionally adjusted for BMI. BMI was also analyzed as z scores calculated for sex and age. To analyze retinal vessel diameters in different categories of systolic and diastolic BP, univariate analysis of variance was performed. To estimate absolute changes in retinal arteriolar and venular diameters for one unit change of anthropometric parameters, multiple linear regression analysis was applied. Pearson's correlation coefficient and coefficient of variation were estimated to evaluate the reproducibility of retinal photographs. We used Stata version 12.1 (StataCorp LP, College Station, TX, USA) for our analyses. 95% confidence intervals were presented for measures of effect to indicate the amount of uncertainty.

RESULTS

Baseline characteristics of the study population with and without retinal photographs are shown in Table 1. BP values for all children with retinal images according to age, sex and height are shown in Table 2. Comparing the 1st with the 4th quartile of children's BMI, a tendency for wider retinal arterioles in children with lower BMI was found (3.9 mu, $P=0.06$). Looking at the interquartile differences, taller children had narrower retinal arterioles (−4.7 mu, $P=0.03$) and a lower AVR (−0.02; $P=0.02$). Likewise, heavier children showed narrower arterioles (−4.8 mu, $P=0.05$) and a lower AVR (−0.02, $P=0.05$). However, after adjusting for BP, no significant differences were found for any parameter of body composition (data not shown). No differences were found between waist-to-height ratio and the interquartiles of retinal vessel parameters ($0.3<P<0.7$). On

Table 1 Baseline characteristics of the study population

	Children with gradable retinal photographs			*Children without gradable retinal photographs*		
Parameter	N	*Mean*	*s.d.*	N	*Mean*	*s.d.*
Age	391	7.3	0.4	864	7.5	0.4
Sex						
Female	200			389		
Male	191			475		
Height (cm)	391	126.3	5.3	862	126.7	5.8
Weight (kg)	391	26.1	4.5	862	26.9	5.6
BMI (kg m^{-2})	391	16.3	2.1	862	16.6	2.6
Waist circumference (in cm)	391	58.1	6.0			
Percentage body fat (%)	391	16.8	5.0			
Waist-to-height ratio	391	0.46	0.04			
Systolic blood pressure (mm Hg)	391	104.7	7.9			
Diastolic blood pressure (mm Hg)	391	65.7	6.7			
CRAE (mu)	391	205.5	13.7			
CRVE (mu)	391	231.6	13.6			
AVR	391	0.89	0.05			

Abbreviations: AVR, arteriolar-to-venular ratio; BMI, body mass index; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent.

the basis of interquartile differences between the lowest and the highest BP quartiles, higher systolic BP was associated with arteriolar narrowing (−9.0 mu, $P<0.001$) and a smaller AVR (−0.03, $P<0.001$). Higher diastolic BP correlated with narrower retinal arterioles (−10.1 mu, $P<0.001$), narrower venules (−3.5 mu, $P=0.05$) and a smaller AVR (−0.03, $P<0.001$) across the quartiles (Table 3).

In the regression analysis, CRAE correlated negatively with height and weight but failed to do so after adjustment for systolic and diastolic BP (Table 3). For every mm Hg increase in systolic BP, CRAE decreased by 0.4 mu ($P<0.001$) and AVR decreased by 0.001 ($P<0.001$). However, the association was dependent on diastolic BP. Associations of diastolic BP with retinal arteriolar narrowing were independent of age, sex, BMI and systolic BP. For every mm Hg increase in diastolic BP, CRAE decreased by 0.4 mu ($P=0.003$) after adjustment for confounders (Table 4).

In our cohort, 74.4% of children were categorized as NT ($n=291$), 11.5% as PHT ($n=45$) and 14.1% ($n=55$) as being HT on the basis of systolic BP levels according to the above KiGGS criteria.[28] Children with systolic PHT had narrower retinal arterioles compared with children with NT (−5.5 mu, $P=0.01$), which was similar to findings in children with HT (−7.5 mu, $P<0.001$). Similar results were found for diastolic BP categories and CRAE (Table 5). No differences between the BP categories were found for CRVE. Children in the systolic (−0.02, $P<0.001$) and the diastolic HT category showed a lower AVR compared with NT (−0.03, $P<0.001$). No differences between the NT and PHT categories were found for AVR (Table 5).

DISCUSSION

Our results demonstrate that BP is associated with retinal microvascular alterations in children aged 6–8 years of age. In children with PHT, categorized according to one of the largest childhood surveys in Europe (KiGGS 2003–2006), retinal arteriolar narrowing can already be detected. In adults, high normal BP seems to be linked with a lower AVR and retinal arteriolar narrowing.[30] This is the first study demonstrating the adverse effects of PHT on retinal microvascular health in children as young as 6–8 years. In adults, arteriolar narrowing is associated with incidence of hypertension and risk of coronary artery disease, and it predicts cardiovascular morbidity and mortality.[2,4,31,32] Therefore, retinal arteriolar narrowing is a preclinical marker of cardiovascular risk and disease manifestation in adults. Whether retinal arteriolar narrowing in young children represents adverse microvascular impairments and predicts future cardiovascular risk remains to be investigated. However, previous studies have shown that childhood BP is associated with future hypertension and cardiovascular mortality.[33,34] A recent Chinese study found that children aged 6 with elevated BP have accelerated cardiac remodelling and vascular dysfunction in adulthood.[35] In our study, retinal arteriolar narrowing is associated with higher systolic and diastolic BP but only diastolic BP was independently associated with retinal arteriolar narrowing. This indicates the importance of diastolic BP as a determinant of microvascular health in children. Previous studies in adults have shown that both systolic and diastolic BP are primarily associated with retinal arteriolar narrowing. Our findings in children are in line with the available data. The autoregulation of the retinal vascular bed ensures that retinal perfusion remains the same over a wide range of BP increases. To normalize retinal perfusion pressure when exposed to higher BP, retinal arteries contract (myogenic response) and, therefore, protect the sensitive capillary bed behind it from increased pressures. Longer term, the vascular wall of retinal arterioles thickens and the lumen diameter decreases (remodelling) leading to arteriolar narrowing. We also found correlations of body composition with retinal vessel diameters in our cohort. Although our findings for BMI and retinal vessel diameters are similar to previous findings, our associations of BMI with retinal vessel diameters were not independent of BP. In a recent Chinese study, associations of body composition and retinal vessels were only found in older children (12–19 years) and not in younger children (7–11 years).[15] In a previous study in pre-adolescent children, BMI was adjusted for mean arterial pressure and was independently associated with narrower arterioles and wider venules.[10] Our study was the first to analyze the association of waist-to-height ratio, as a marker of central obesity, and retinal microcirculation. We found no relationship between the waist-to-height ratio and retinal vessel diameters. Compared with BMI measurements, the waist-to-height ratio is independent of age and includes the fat mass of the body.[18]

Our findings are of high clinical relevance for cardiovascular health promotion in school children. Our results demonstrate that BP and, to a lesser extent, body composition are main determinants of retinal microvascular health in young children. Body composition and BP are often interdependent in adulthood and childhood. Most strikingly, PHT in healthy children is already associated with retinal arteriolar narrowing. This may prove to be indicative of an increased future cardiovascular risk in young children with PHT. In our study, about 25% of children were found to be either PHT or HT. Similar adverse associations with retinal vessel diameters were seen in both BP categories. These children are likely to benefit most from future school and family-based lifestyle intervention strategies.

Our results go in line with the results of the previous German study, which used the same equipment, software and analyzing routine for retinal vessel analysis.[11] Compared with the German cohort, the mean CRAE was 3 mu and the mean CRVE 5 mu smaller in our cohort. This is likely because of the age difference with a mean age of 7.3 years (SD: 0.4) in our study and a mean age of 11.1 years (SD: 0.6) in the German cohort. The sex differences are also similar to the German study. Girls are more likely to have wider retinal arteriolar and venular

Table 2 Mean blood pressure of our cohort by gender, age and height classified in blood pressure categories according to the KiGGS study (2003–2006)

			Systolic blood pressure						*Diastolic blood pressure*					
			Normotensive		*Pre-hypertensive*		*Hypertensive*		*Normotensive*		*Pre-hypertensive*		*Hypertensive*	
Sex	*Age (years)*	*Height (cm)*	N	*Mean mm Hg (s.d.)*	N	*Mean mm Hg (s.d.)*	N	*Mean mm Hg (s.d.)*	N	*Mean mm Hg (s.d.)*	N	*Mean mm Hg (s.d.)*	N	*Mean mm Hg (s.d.)*
Male	6	113	1	94.6 (—)	0	—	0	—	1	54.0 (—)	0	—	0	—
		115	3	102.3 (3.9)	0	—	0	—	3	60.7 (1.9)	0	—	0	
		118	3	96.7 (4.1)	0	—	0	—	3	58.4 (4.9)	0	—	0	
		121	8	103.0 (3.5)	2	109.2 (0.2)	1	111.3 (—)	8	61.3 (4.9)	2	69.5 (0.7)	1	71.0 (—)
		125	4	105.3 (1.9)	2	110.0 (1.4)	0	—	3	66.0 (1.8)	0	—	3	79.9 (1.3)
		128	4	95.7 (8.1)	1	111.7 (—)	1	118.7 (—)	6	61.6 (8.0)	0	—	0	—
		130	4	104.8 (3.4)	0	—	0	—	4	58.3 (6.3)	0	—	0	—
	7	116	4	101.3 (3.1)	1	108.0 (—)	0	—	5	63.1 (0.9)	0	—	0	—
		119	9	98.4 (4.8)	0	—	1	114.7 (—)	6	59.6 (5.6)	3	69.4 (0.5)	1	72.7 (—)
		121	18	100.5 (4.0)	2	110.3 (0.5)	4	118.8 (7.2)	14	61.0 (4.2)	4	70.2 (0.6)	6	74.5 (3.2)
		124	27	99.4 (5.4)	4	110.7 (1.0)	10	115.0 (2.6)	28	62.2 (4.2)	3	70.4 (0.4)	10	73.9 (2.6)
		128	28	102.4 (5.8)	5	111.5 (0.9)	4	115.3 (1.5)	29	63.5 (4.5)	3	70.2 (0.2)	5	74.3 (1.7)
		131	15	101.4 (6.2)	2	111.2 (0.2)	9	120.1 (4.1)	18	61.6 (7.0)	0	—	8	77.3 (3.7)
		135	4	106.6 (2.9)	1	113.7 (—)	1	120.7 (—)	4	65.8 (1.5)	0	—	2	80.2 (3.5)
		137	2	98.7 (1.4)	0	—	3	120.9 (8.0)	3	62.1 (4.0)	0	—	2	75.2 (0.7)
	8	118	1	90.7 (—)	0	—	0	—	1	59.0 (—)	0	—	0	—
		124	0	—	0	—	0	—	0	—	0	—	0	—
		126	1	105.7 (—)	0	—	0	—	0	—	1	71.0 (—)	0	—
		130	0	—	0	—	0	—	0	—	0	—	0	—
		134	0	—	0	—	0	—	0	—	0	—	0	—
		138	0	104.7 (—)	0	—	0	—	1	59.7 (—)	0	—	0	—
Female	6	112	1	106 (—)	0	—	0	—	1	65.6 (—)	0	—	0	—
		114	2	99.2 (8.7)	0	—	0	—	1	61.0 (—)	0	—	1	72.3(—)
		117	14	99.1 (6.1)	0	—	0	—	12	60.9 (4.6)	3	69.6 (1.0)	0	—
		121	13	100 (5.7)	1	111.3 (—)	1	122.3 (—)	12	61.4 (4.4)	2	70.7 (1.4)	1	75.0 (—)
		124	8	102.6 (5.0)	0	—	3	119.6 (0.7)	6	64.6 (4.0)	0	—	5	74.7 (4.0)
		127	3	103.8 (2.9)	0	—	0	—	2	65.8 (0.2)	1	71.0 (—)	0	—
		129	7	104.9 (3.9)	1	113.3 (—)	0	—	6	64.1 (3.3)	1	72.7 (—)	1	73.0 (—)
	7	115	6	99.2 (1.7)	1	108.7 (—)	1	124.0 (—)	7	62.2 (2.9)	0	—	1	79.3 (—)
		118	4	100.8 (5.6)	0	—	2	114.5 (2.1)	4	62.8 (3.5)	1	69.0 (—)	1	76.3 (—)
		120	20	99.2 (6.0)	3	110.8 (0.8)	0	—	19	61.8 (5.6)	1	70.3 (—)	3	75.4 (3.9)
		123	26	101.8 (4.3)	8	110.5 (1.2)	6	115.7 (3.1)	29	64.3 (3.4)	5	71.2 (0.4)	6	74.1 (1.6)
		127	21	103.0 (4.7)	7	111.3 (1.2)	4	118.5 (4.3)	18	63.1 (4.1)	4	71.1 (0.6)	10	76.2 (3.6)
		130	13	102.8 (4.8)	1	114.3 (—)	0	—	9	65.1 (4.2)	3	71.4 (1.2)	2	76.3 (3.3)
		133	8	104.5 (3.0)	2	115.7 (0)	1	125.3 (—)	8	64.1 (3.0)	2	71.5 (0.2)	1	82.3 (—)
		135	5	99.4 (6.4)	1	113 (—)	2	123.2 (9.2)	6	62.0 (6.6)	0	—	2	79.7 (6.6)
	8	117	1	103.3 (—)	0	—	0	—	1	63.0 (—)	0	—	0	—
		123	0	—	0	—	0	—	0	—	0	—	0	—
		125	1	108.6 (—)	0	—	0	—	1	66.0 (—)	0	—	0	—
		128	1	100.9 (—)	0	—	0	—	1	67.0 (—)	0	—	0	—

Normotensive <90th percentile; pre-hypertensive >90th–<95th percentile; hypertensive >95th percentile.

diameters than boys, while there are no sex differences in AVR.[11] Previous data have shown that parental hypertension,[36] low birthweight[37] as well as physical inactivity[11,38] are also associated with retinal vessel alterations. These factors are involved in the pathogenesis and development of high BP and should be considered in future research approaches.

One of the strength of the study is the extensive imaging regime. By taking two retinal image of each eye per child, a high degree of accuracy in the measurement of retinal vessel diameters is achieved. A limitation of the study is its relatively small sample size. Although the sample size was estimated to be approximately 290 children, a larger sample would better represent the population and would further limit the influence of outliers. Another limit to our and previous studies is the fact that the cross-sectional design does not examine temporal information. Prospective long-term follow-up studies are necessary to differentiate independent and clinically relevant effects of body composition and BP on retinal microvascular health. Future studies need to clarify whether retinal arteriolar narrowing in young children really predicts cardiovascular outcome and permanent structural alterations in adolescence and adulthood or if it simply reflects

Table 3 Retinal vessel diameter and AVR in relation to 1st and 4th quartile analysis of anthropometric parameters adjusted for age and sex

		CRAE (mu)		*CRVE (mu)*		*AVR*	
Quartile	*N*	*Mean (95% CI)*	P	*Mean (95% CI)*	P	*Mean (95% CI)*	P
BMI (kg m^{-2})							
1st, <15.03	98	207.2 (204.4; 209.8)	0.06	232.3 (229.7; 235.0)	0.4	0.89 (0.88; 0.90)	0.2
2nd, 15.03–15.90	98	204.7 (201.9; 207.3)		231.3 (228.7; 234.0)		0.89 (0.88; 0.90)	
3rd, 15.91–17.23	98	207.0 (204.3; 209.6)		232.2 (229.5; 234.9)		0.89 (0.88; 0.90)	
4th, >17.23	97	203.3 (200.6; 206.0)		230.4 (227.7; 233.0)		0.88 (0.87; 0.89)	
BMI z-score							
1st, < −1	43	207.1 (203.1; 211.1)	0.2	233.8 (229.8; 237.8)	0.2	0.89 (0.87; 0.90)	0.9
2nd, −1–1	301	205.5 (204.0; 207.1)		231.5 (229.9; 233.0)		0.89 (0.88; 0.89)	
3rd, >+1	47	203.9 (200.0; 207.7)		230.2 (226.3; 234.0)		0.89 (0.87; 0.90)	
Height (cm)							
1st, <122.7	102	208.1 (205.4; 210.7)	0.03	231.3 (228.7; 234.0)	0.9	0.90 (0.89; 0.91)	0.02
2nd, 122.7–126.1	96	204.7 (202.1; 207.4)		231.4 (228.7; 234.1)		0.89 (0.88; 0.90)	
3rd, 126.2–129.9	96	205.6 (202.9; 208.3)		232.2 (229.5; 234.9)		0.89 (0.88; 0.90)	
4th, >129.9	97	203.4 (200.7; 206.1)		231.3 (228.6; 234.0)		0.88 (0.87; 0.89)	
Weight (kg)							
1st, <23.1	101	207.9 (205.3; 210.6)	0.05	231.2 (228.5; 233.8)	0.8	0.90 (0.89; 0.91)	0.05
2nd, 23.1–25.4	96	206.1 (203.4; 208.7)		234.0 (231.3; 236.7)		0.88 (0.87; 0.89)	
3rd, 25.5–28.1	99	204.8 (202.1; 207.4)		231.0 (228.4; 233.6)		0.89 (0.88; 0.90)	
4th, >28.1	95	203.1 (200.4; 205.9)		230.1 (227.4; 232.9)		0.88 (0.87; 0.89)	
Waist circumference (cm)							
1st, <54.10	98	206.2 (203.6; 208.9)	0.2	232.6 (229.9; 235.3)	0.5	0.89 (0.88; 0.90)	0.5
2nd, 54.10–56.60	98	206.0 (203.3; 208.6)		231.5 (228.8; 234.1)		0.89 (0.88; 0.90)	
3rd, 56.65–60.40	98	206.4 (203.7; 209.0)		231.1 (228.5; 233.8)		0.89 (0.88; 0.90)	
4th, >60.40	97	203.4 (200.7; 206.1)		231.1 (228.4; 233.8)		0.88 (0.87; 0.89)	
Percentage body fat (%)							
1st, <13.11	98	203.9 (201.2; 206.7)	0.7	229.9 (227.2; 232.6)	0.9	0.89 (0.88; 0.90)	0.7
2nd, 13.11–15.76	99	207.1 (204.5; 209.8)		231.1 (228.5; 233.8)		0.90 (0.89; 0.91)	
3rd, 15.77–19.28	97	205.9 (203.2; 208.6)		234.5 (231.9; 237.2)		0.88 (0.87; 0.89)	
4th, >19.28	97	205.0 (202.3; 207.7)		230.7 (228.0; 233.4)		0.89 (0.88; 0.90)	
Waist-to-height ratio							
1st, <0.4324	98	205.5 (202.9; 208.2)	0.7	232.6 (230.0; 235.3)	0.3	0.88 (0.87; 0.90)	0.6
2nd, 0.4325–0.4504	98	205.2 (202.6; 207.9)		231.8 (229.2; 234.5)		0.89 (0.88; 0.90)	
3rd, 0.4505–0.4779	98	206.4 (203.8; 209.1)		230.8 (228.2; 233.5)		0.90 (0.89; 0.91)	
4th, >0.4780	97	204.8 (202.1; 207.5)		231.0 (228.3; 233.7)		0.89 (0.88; 0.90)	
Systolic blood pressure (mm Hg)[a]							
1st, <100.3	102	210.6 (208.0; 213.1)	<0.001	232.7 (230.1; 235.4)	0.2	0.91 (0.90; 0.92)	<0.001
2nd, 100.3–104.3	100	206.4 (203.9; 209.0)		232.0 (229.3; 234.6)		0.89 (0.88; 0.90)	
3rd, 104.4–109.7	92	203.0 (200.3; 205.6)		231.2 (228.4; 233.9)		0.88 (0.87; 0.89)	
4th, >109.7	97	201.6 (198.9; 204.3)		230.3 (227.5; 233.0)		0.88 (0.87; 0.89)	
Diastolic blood pressure (mm Hg)[a]							
1st, <61.3	103	210.0 (207.5; 212.5)	<0.001	232.9 (230.3; 235.5)	0.05	0.90 (0.89; 0.91)	<0.001
2nd, 61.3–65.7	96	206.8 (204.2; 209.4)		230.8 (228.1; 233.5)		0.90 (0.89; 0.91)	
3rd, 65.8–70.4	99	204.8 (202.3, 207.4)		233.0 (230.3; 235.6)		0.88 (0.87; 0.89)	
4th, >70.4	93	199.9 (197.2; 202.5)		229.4 (226.6; 232.1)		0.87 (0.86; 0.88)	

Abbreviations: AVR, arteriolar-to-venular ratio; BMI, body mass index; CI, confidence interval; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent.
[a]Additionally adjusted for BMI.

Table 4 Regression analysis of retinal vessel diameter and AVR in relation to anthropometric parameters

		CRAE (mu change per unit)		*CRVE (mu change per unit)*		*AVR (per unit change)*	
Parameter	*Model*	B *(95% CI)*	P	B *(95% CI)*	P	B *(95% CI)*	P
BMI (kg m^{-2})	1	−0.6 (–1.2; 0.09)	0.09	−0.4 (–1.0; 0.3)	0.3	< −0.001 (–0.003; 0.001)	0.4
	2	−0.2 (–0.8; 0.5)	0.6	−0.2 (–0.9; 0.5)	0.5	<0.001 (–0.002; 0.003)	0.9
Height (cm)	1	−0.3 (–0.6; −0.05)	0.02	−0.02 (–0.3; 0.2)	0.9	−0.001 (–0.002; <0.001)	0.01
	2	−0.2 (–0.4; 0.1)	0.2	0.05 (–0.2; 0.3)	0.7	< −0.001 (–0.002; <0.001)	0.1
Weight (kg)	1	−0.4 (–0.7; −0.06)	0.02	−0.2 (–0.5; 0.1)	0.3	< −0.001 (–0.002; <0.001)	0.09
	2	−0.2 (–0.5; 0.2)	0.3	−0.06 (–0.4; 0.3)	0.7	< −0.001 (–0.002; <0.001)	0.5
Waist circumference (cm)	1	−0.2 (–0.4; 0.07)	0.2	−0.07 (–0.3; 0.2)	0.5	< −0.001 (–0.001; <0.001)	0.3
	2	−0.03 (–0.3; 0.2)	0.8	−0.1 (–0.2; 0.2)	0.9	< −0.001 (< −0.001; <0.001)	0.8
Percentage body fat (%)	1	< −0.001 (–0.3; 0.3)	0.9	0.1 (–0.2; 0.4)	0.5	< −0.001 (–0.001; <0.001)	0.4
	2	0.1 (–0.1; 0.4)	0.4	0.2 (–0.1; 0.4)	0.3	< −0.001 (–0.001; <0.001)	0.9
Waist-to-height ratio	1	−7.3 (–39.3; 24.6)	0.7	−9.6 (–41.6; 22.2)	0.6	0.001 (–0.1; 0.1)	0.9
	2	3.5 (–28.4; 35.4)	0.8	−3.9 (–37.0; 29.1)	0.8	0.03 (–0.09; 0.2)	0.7
Systolic blood pressure (mm Hg)	1	−0.4 (–0.6; −0.3)	<0.001	−0.2 (–0.3; 0.005)	0.06	−0.001 (–0.002; < −0.001)	<0.001
	3	−0.2 (–0.4; 0.07)	0.2	−0.1 (–0.4; 0.1)	0.4	< −0.001 (–0.001; <0.001)	0.5
Diastolic blood pressure (mm Hg)	1	−0.6 (–0.7; −0.4)	<0.001	−0.2 (–0.4; 0.04)	0.1	< −0.002 (–0.003; −0.001)	<0.001
	3	−0.4 (–0.7; −0.1)	0.003	−0.06 (–0.3; 0.2)	0.7	< −0.002 (–0.003; < −0.001)	0.003

Abbreviations: AVR, arteriolar-to-venular ratio; BMI, body mass index; CI, confidence interval; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent.
Model 1 = adjusted for age and sex; Model 2 = Model 1 plus adjustment for systolic and diastolic blood pressure, Model 3 = Model 1 plus adjustment for BMI, systolic and diastolic blood pressure, respectively.

Table 5 Mean retinal vessel diameters and blood pressure categories

	CRAE (mu)	*CRVE (mu)*	*AVR*
	Mean (CI 95%)	*Mean (CI 95%)*	*Mean (CI 95%)*
Systolic blood pressure			
Normotensive (*N* = 291)	207.2 (205.6; 208.7)	232.2 (230.6; 233.8)	0.89 (0.89; 0.90)
Pre-hypertensive (*N* = 45)	201.7 (197.8; 205.7)	229.2 (225.2; 233.2)	0.88 (0.87; 0.90)
Hypertensive (*N* = 55)	199.7 (196.2; 203.3)	230.1 (226.5; 233.7)	0.87 (0.86; 0.88)
P-value[a]	0.01	0.2	0.1
P-value[b]	<0.001	0.3	<0.001
Cohen's *d*[c]	0.4	0.2	0.3
Cohen's *d*[d]	0.6	0.2	0.5
Diastolic blood pressure			
Normotensive (*N* = 280)	207.5 (205.9; 209.0)	232.1 (230.5; 233.7)	0.90 (0.89; 0.90)
Pre-hypertensive (*N* = 39)	201.7 (197.5; 205.9)	228.8 (224.6; 233.1)	0.88 (0.87; 0.90)
Hypertensive (*N* = 72)	200.0 (196.9; 203.1)	230.8 (227.7; 234.0)	0.87 (0.86; 0.88)
P-value[a]	0.01	0.2	0.1
P-value[b]	<0.001	0.5	<0.001
Cohen's *d*[c]	0.4	0.2	0.3
Cohen's *d*[d]	0.6	0.1	0.6

Abbreviations: AVR, arteriolar-to-venular ratio; CI, confidence interval; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; mu, measuring units.
[a]*P*-value between normotensive and pre-hypertensive groups.
[b]*P*-value between normotensive and hypertensive groups.
[c]Cohen's *d* between normotensive and pre-hypertensive groups.
[d]Cohen's *d* between normotensive and hypertensive groups.

autoregulatory mechanisms in response to higher BP in children. We aim to perform longitudinal studies into adolescence and beyond in the future. Finally, the prevalence of pre-hypertension and hypertension in our study was relatively high. Therefore, we cannot rule out the possibility of a study bias.

On the basis of our results, we would like to conclude that higher BP, even at the level of PHT, seems to be the driving force for microvascular target organ alterations in young school children. Childhood health programs may have to focus more on BP lowering interventions to prevent development of atherosclerosis and manifestation of cardiovascular disease later in life.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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