Hypertension Research (2018) 41:193–197
https://doi.org/10.1038/s41440-017-0006-0

ARTICLE

Wrist circumference is associated with increased systolic blood pressure in children with overweight/obesity

Simona Zampetti[1] · Giuseppe Campagna[1] · Federica Lucantoni[1] · Lidia Marandola[1] · Luca D'Onofrio[1] · Claudio Chiesa[2] · Lucia Pacifico[3] · Andrea Vania[4] · Raffaella Buzzetti[1] · Gaetano Leto[1]

Received: 26 June 2017 / Revised: 10 August 2017 / Accepted: 29 August 2017 / Published online: 15 January 2018

Abstract

Wrist circumference is a clinical marker for insulin-resistance in overweight/obese children and adolescents. Insulin resistance is considered a major determinant of increased vascular resistance and hypertension. The aim of the study was to investigate the association between wrist circumference and systolic (S) and diastolic (D) blood pressure (BP) in a population of overweight/obese children and adolescents. A population of 1133 overweight/obese children and adolescents ($n = 1133$) were consecutively enrolled. Multivariate regression analyses were used to investigate the influence of independent variables on the variance of BP. The prevalence of hypertension was 21.74% in males and 28.95% in females ($p = 0.048$). The results showed that SBP was significantly associated with wrist circumference in both genders ($p < 0.0001$ for both comparisons). We found no association between DBP and wrist circumference in either gender. Wrist circumference accounted for 17% of the total variance of SBP in males and 14% in females. Wrist circumference, a marker of insulin resistance, is associated with increased SBP in overweight/obese children and adolescents, suggesting a role of insulin resistance in the pathogenesis and development of hypertension.

Introduction

Cardiovascular diseases (CVD) are the leading causes of death in Western countries [1] and are generally present in adulthood; however, the process of atherosclerosis that underlies CVD can begin early in childhood [2]. Insulin resistance, according to several pathophysiological models, is one of the most important risk factors for atherosclerosis and CVD [3].

Hypertension, another relevant risk factor for the development of CVD in adulthood, is associated with insulin resistance more often than expected, and prospective studies have demonstrated that insulin resistance may precede the development of hypertension [4]. This evidence has led some authors, since the 1980s, to speculate that essential hypertension could be an insulin-resistant state [4]. To date, many epidemiological and clinical studies have demonstrated a close linkage between insulin resistance and hypertension [5, 6].

Potential mechanisms by which insulin resistance and associated hyperinsulinemia may alter blood pressure (BP) have been proposed, and they include insulin-mediated effects on the sympathetic nervous system and renal sodium reabsorption [7].

The association of obesity and hypertension establishes a double burden on the heart during adulthood [8, 9]; in particular, in children with obesity, hypertension has already been associated with end-organ damage, such as left ventricular hypertrophy and endothelial dysfunction [10]. Therefore, early management of hypertension in children is now considered to be of major clinical relevance for the effective prevention of associated morbidity.

Simona Zampetti and Giuseppe Campagna contributed equally to this work

✉ Raffaella Buzzetti
raffaella.buzzetti@uniroma1.it

1 Department of Experimental Medicine, Sapienza University, Rome, Italy

2 Institute of Translational Pharmacology, National Research Council, Rome, Italy

3 Policlinico Umberto I Hospital, Sapienza University, Rome, Italy

4 Department of Paediatrics and Paediatric Neuropsychiatry, Centre for Pediatric Dietetics and Nutrition, Sapienza University, Rome, Italy

In an attempt to identify an easy-to-detect clinical marker of insulin resistance in children with overweight and obesity, we have previously demonstrated, by nuclear magnetic resonance imaging, an association between wrist circumference, particularly its bone component, insulin levels and homeostasis model assessment of insulin resistance (HOMA-IR) [11]. Furthermore, wrist circumference has been observed as a useful marker for the early identification of hypertension in a population of healthy Indian children [12].

Considering that wrist circumference is a well-established marker of insulin resistance and that insulin resistance one of the promoting factors for the onset of hypertension, we hypothesize the existence of a strict linkage between wrist circumference and BP. Therefore, we investigated the association between wrist circumference and BP in a pediatric population affected by overweight/obesity.

Methods

Sample

A total of $N = 1133$ children and adolescents with overweight/obesity (580 boys and 553 girls) (age range: 5–16 years) were consecutively enrolled at the outpatient clinics of the Department of Pediatrics, "Sapienza" University of Rome. The exclusion criteria were the presence of renal disease, previous diagnosis of diabetes mellitus and/or endocrine diseases, any condition known to influence blood pressure (e.g., glucocorticoid therapy or antihypertensive drug), and history of pre-existing heart disease.

The study protocol was approved by the ethical committee of "Sapienza" University, and parents gave written consent for their children to participate to the study.

In all subjects, body weight, height, wrist circumference, body mass index (BMI), fasting glucose, insulin levels and lipid profiles were evaluated at entry. The BMI of each individual was converted by smooth age-specific curves to an standard deviation score (BMI-SDS) for the child's age [13].

Dominant wrist circumference was measured with subjects in a seated position using a tension-gated tape measure positioned over the Lister tubercle of the distal radius and over the distal ulna [11]. Degree of obesity was quantified using Cole's method [13].

BP measurement followed the recommendation of the "Fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents" [14].

Systolic and diastolic BP were measured twice on the right arm after a 10-min rest period in the supine position using an automated oscillatory system (Dinamap Vital Signs Monitor, Model 1846 SX; Criticon Incorporated, Tampa, FL, USA).

All children with increased BP (BP ≥ 95 percentile according to BP charts for age, gender, and height) during the first visit underwent two additional visits on different occasions within 2–3 weeks. Hypertension was defined as an average SBP or DBP that was ≥95 percentile on three separate visits.

Serum total cholesterol, HDL-cholesterol and triglyceride levels were determined by a Technicon RA-1000 Autoanalyzer, and glucose levels were determined by the glucose oxidase method. Serum insulin was measured by radioimmunoassay. Insulin resistance was estimated according to HOMA-IR. Subjects were evaluated by a doctor for pubertal stages. Tanner stage I was defined as prepuberty, Tanner stage II to IV as midpuberty, and Tanner stage V as postpuberty.

Statistical analysis

A Shapiro–Wilk test was used to verify the normality of the distribution of continuous variables. For continuous variables, median values among two groups were compared by a Mann-Whitney U test when the data were not normally distributed. Multivariate regression analyses (backward method) were used to investigate the influence of independent variables on the variance of BP. Before performing multivariate regression analysis, we tested the presence of collinearity using BP as a dependent variable and wrist circumference, age and height as independent variables.

A probability level of $p < 0.05$ was considered to be statistically significant. All analyses were performed using Statistical Analysis Software v.9.4.

Results

The clinical and biochemical characteristics of 1133 overweight/obese children and adolescents divided according to gender are reported in Table 1. Males were older and showed higher values of BMI-SDS, wrist circumference and fasting glucose levels compared to females ($p < 0.002$ for all comparisons). We observed that there was no statistically significant difference according to gender for SBP, DBP, HOMA-IR or lipid profile. As anticipated in the statistical analysis section before performing multivariate regression analysis, we demonstrated the presence of high collinearity (eigenvalue = 0.0015, condition index = 51 and proportion of variance = 0.87 (wrist circumference) vs 0.80 (height)) [15, 16] and medium correlation ($\rho = 0.68$, $p < 0.0001$) between wrist circumference and height in males by using BP as the dependent variable and wrist circumference, age and height as independent variables. In

Table 1 Clinical and biochemical characteristics of 1133 overweight/obese children and adolescents divided according to gender

	Males (n = 580)	Females (n = 553)	P-value
Age (years)	10.5 ± 2.22	10.0 ± 2.97	0.002
Hight (m)	1.48 ± 0.14	1.43 ± 0.16	<0.0001
BMI-SDS	2.06 ± 0.41	1.96 ± 0.44	0.001
Wrist Circumference (cm)	16.0 ± 1.41	15.3 ± 1.14	<0.0001
Systolic blood pressure (mmHg)	110.0 ± 14.86	110.0 ± 14.83	ns
Diastolic blood pressure (mmHg)	70.0 ± 14.81	70.0 ± 14.83	ns
Fasting glucose (mg/dL)	86.0 ± 8.15	85.0 ± 8.18	0.007
HOMA-IR	2.84 ± 1.65	2.84 ± 1.75	ns
Total cholesterol (mg/dL)	165.0 ± 31.88	162.0 ± 28.17	ns
HDL-cholesterol (mg/dL)	48.0 ± 11.12	48.0 ± 11.86	ns
Triglycerides (mg/dL)	75.0 ± 44.48	75.0 ± 38.85	ns
Hypertension (%)	109 (22.6)	133 (28.2)	0.048

Data are expressed as median (±SD *q* range)

Table 2 Multivariate regression analysis for explaining the independent contribution of wrist circumference to blood pressure according to gender

Variables	β ± SE	IC95%	P-value	R^2
MALES				
Systolic blood pressure				
Wrist circumference	2.60 ± 0.64	(1.35–3.85)	< 0.0001	0.17
Diastolic blood pressure				
Wrist circumference	0.47 ± 0.59	(−0.69–1.63)	ns	
FEMALES				
Systolic blood pressure				
Wrist circumference	2.90 ± 0.74	(1.44–4.37)	< 0.0001	0.14
Diastolic blood pressure				
Wrist circumference	0.40 ± /0.68	(−0.95–1.74)	ns	

All data were adjusted for age, Tanner stage, and BMI-SDS

females, we also demonstrated the presence of high collinearity (eigenvalue = 0.002, condition index = 46 and proportion of variance = 0.91 (wrist circumference) vs 0.76 (height)) [15, 16] and medium correlation ($\rho = 0.64$, $p < 0.0001$) between wrist circumference and height. The presence of high collinearity between wrist circumference and height prevents any attempt to compare the effect to variables in the same regression model.

The prevalence of hypertension was 21.74% in males and 28.95% in females ($p = 0.01$). The results of the multivariate regression analysis performed on the 1133 children and adolescents stratified according to gender and adjusted for age, Tanner stage and BMI-SDS using wrist circumference as the independent variable and SBP and DBP as dependent variables are reported in Table 2.

We found no association between DBP and wrist circumference in either gender. Wrist circumference explained 21% of the variance of SBP in males and 18% in females. To evaluate the contribution of wrist circumference to explained variance (R^2) of SBP, we used the backward method (Table 2). Wrist circumference accounted for 17% of the total variance of SBP in males and 14% in females.

Discussion

The findings of our study provide the first evidence that wrist circumference is positively associated with SBP in a population of children and adolescents with overweight/obesity.

Our results showing a high prevalence of hypertension among overweight/obese children and adolescents of both genders are in line with some previous reports [17, 18]. A study performed in children affected by obesity reported that 33% were hypertensive [19]. On the other hand, some Authors found a lower prevalence of hypertension in children with overweight/obesity at the age of 11–15 years with 13.9% in boys and 12.3% in girls [20].

The wide variability of the prevalence of hypertension among studies performed in children with obesity may be due to methodological differences in the selection criteria: age range, sample size, and degree of obesity. Previous studies have demonstrated a positive association between other anthropometric parameters, such as waist circumference, waist-to height ratio, neck circumference and elevated BP, in children and adolescents [21]. Recently, we demonstrated that wrist circumference measurements have excellent intra- and inter-operator reproducibility and unlike other anthropometric parameters, it does not require multiple repeated measurements for precision and reliability [22]. Wrist circumference could be advantageous in clinical practice compared classical anthropometrical measurements, such as waist circumference or waist-height ratio, to identify subjects with insulin resistance. Even though waist circumference is a good marker of cardiovascular risk in obese adults [23], waist circumference is affected by clothing and respiration and its values differed significantly according to the anatomical site of measurement, since to date there is no agreement on the optimal site at which to measure it in children [24].

Insulin has a central role in bone metabolism, enhancing osteoblast proliferation and differentiation and promoting bone formation rates through action on the insulin receptor [25]. Impairment of insulin signaling leads to a reduction of bone mass as reported in patients affected by type 1 diabetes mellitus [25]. On the other hand, hyperinsulinaemia and insulin resistance lead to increased bone mineral density [25]. Furthermore, during growth, bone is responsive to the anabolic action of insulin [26], and it is possible to avoid the deleterious effects of hyperglycemia due to a prolonged insulin resistance state.

Considering all this evidence, we previously demonstrated that wrist circumference is a reliable marker of insulin resistance for the first time [11].

Based on our previous findings and the well-known relationship that binds insulin resistance and the development of hypertension during metabolic syndrome [4], the newly found association of this anthropometric marker with SBP confirms the relevant role that insulin resistance has in the pathogenesis and development of hypertension in overweight/obese children and adolescents.

A striking finding of our results is that wrist circumference was associated only with SBP and not DBP in children and adolescents with overweight/obesity.

The Framingham study reported that elevation of SBP predicts the risk of CVD better than increases in DBP [27]. A reduction in coronary vascular disease and mortality was demonstrated when treating patients with isolated systolic hypertension. One of the main mechanisms of isolated systolic hypertension in adults is the increasing arterial stiffness caused by atherosclerotic vascular disease [28]. Atherosclerosis is not sufficiently advanced to cause increased arterial stiffness in children, thus a different mechanism must be involved [18]. Some studies suggest that the root cause of high SBP in subjects with obesity is primarily due to a combination of factors that raise systemic vascular resistance [29]. The coordinated appearance of insulin resistance and high BP in obese individuals led several authors to hypothesize that insulin resistance is one of the major determinants of increased systemic vascular resistance in obesity [29]. In support of this theory, several studies found a relationship between fasting insulin and SBP [30]. Insulin could cause hypertension through stimulation of the sympathetic nervous system, an increase in renal sodium retention, modulation of calcium transport, and consequent induction of hypertrophy of vascular smooth muscle [7]. Sinaiko et al. found that fasting insulin levels were significantly associated with SBP in a population of children [30].

Our findings are supported by other evidence observed in an Asian adult population. In a West Asian cohort of women, wrist circumference was associated with incident hypertension and incident CVD after 10 years of follow-up [31].

The same authors developed an algorithm to estimate the risk of predicted hypertension incidence using data mining approaches, and they found that wrist circumference was a predictor of hypertension in a model with six variables in Middle Eastern women [32]. These data support the observation that in adulthood, wrist circumference is also associated with BP values. Moreover, wrist circumference was significantly related to the visceral adiposity index, and higher gender-specific tertiles of wrist circumference were associated with an increased risk of Metabolic Syndrome; these evidence suggest wrist circumference as a reliable candidate marker for cardiovascular and metabolic risk [33].

A limitation of the current study could be to have examined only a sample of children and adolescents with overweight/obesity; for this reason, it would be beneficial to extend our findings in further studies with children and adolescents of normal BMI. Furthermore, studies conducted on a larger sample size are needed to determine a cut-off value of wrist circumference.

In conclusion, given the established relationship between insulin resistance and hypertension and our previous findings of wrist circumference as a marker of insulin resistance, in this study, we found that wrist circumference is positively associated with SBP in a child and adolescent population with overweight/obesity, confirming the relevant role that insulin resistance has in the pathogenesis and development of hypertension.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. WHO Global status report on noncommunicable diseases 2014. WHO (e-pub ahead of print ISBN 978 92 4 156485 4, 2015).
2. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011;128:S213–56. https://doi.org/10.1542/peds.2009-2107C.
3. McLaughlin T, Allison G, Abbasi F, Lamendola C, Reaven G. Prevalence of insulin resistance and associated cardiovascular disease risk factors among normal weight, overweight, and obese individuals. Metabolism. 2004;53:495–9. http://www.ncbi.nlm.nih.gov/pubmed/15045698. Accessed 8 May 2017
4. Ferrannini E, Buzzigoli G, Bonadonna R, Giorico MA, Oleggini M, Graziadei L, Pedrinelli R, Brandi L, Bevilacqua S. Insulin resistance in essential hypertension. N Engl J Med. 1987;317:350–7. https://doi.org/10.1056/NEJM198708063170605.
5. Hu FB, Stampfer MJ. Insulin resistance and hypertension: the chicken-egg question revisited. Circulation. 2005;112:1678–80. https://doi.org/10.1161/CIRCULATIONAHA.105.568055.
6. Zhou M-S, Wang A, Yu H. Link between insulin resistance and hypertension: What is the evidence from evolutionary biology? Diabetol Metab Syndr. 2014;6:12. https://doi.org/10.1186/1758-5996-6-12.
7. Cruz ML, Huang TT-K, Johnson MS, Gower BA, Goran MI. Insulin sensitivity and blood pressure in black and white children. Hypertens. 2002;40:18–22. http://www.ncbi.nlm.nih.gov/pubmed/12105132. Accessed 8 May 2017

8. Krzesiński P, Stańczyk A, Piotrowicz K, Gielerak G, Uziębło-Zyczkowska B, Skrobowski A. Abdominal obesity and hypertension: a double burden to the heart. Hypertens Res. 2016;39:349–55. https://doi.org/10.1038/hr.2015.145.
9. Middlemiss JE, McEniery CM. Feeling the pressure: (patho) physiological mechanisms of weight gain and weight loss in humans. Hypertens Res. 2017;40:226–36. https://doi.org/10.1038/hr.2016.142.
10. Feber J, Ahmed M. Hypertension in children: new trends and challenges. Clin Sci. 2010;119:151–61. https://doi.org/10.1042/CS20090544.
11. Capizzi M, Leto G, Petrone A, Zampetti S, Papa RE, Osimani M, Spoletini M, Lenzi A, Osborn J, Mastantuono M, Vania A, Buzzetti R. Wrist circumference is a clinical marker of insulin resistance in overweight and obese children and adolescents. Circulation. 2011;123:1757–62. https://doi.org/10.1161/CIRCULATIONAHA.110.012898.
12. Kajale NA, Khadilkar AV, Chiplonkar SA, Khadilkar VV. Body fat indices for identifying risk of hypertension in Indian children. Indian Pediatr. 2014;51:555–60. http://www.ncbi.nlm.nih.gov/pubmed/25031134. Accessed 8 May 2017
13. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000;320:1240–3. http://www.ncbi.nlm.nih.gov/pubmed/10797032. Accessed 8 May 2017
14. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004;114:555–76. http://www.ncbi.nlm.nih.gov/pubmed/15286277. Accessed 8 May 2017
15. Belsley DA. A Guide to using the collinearity diagnostics. Comput Sci Econ Manag. 4: 33–50 1991
16. Freund RJ, Littell RC. SAS System for regression. SAS Institute Inc., Cary, NC, 1991.
17. Moore WE, Eichner JE, Cohn EM, Thompson DM, Kobza CE, Abbott KE. Blood pressure screening of school children in a multiracial school district: the Healthy Kids Project. Am J Hypertens. 2009;22:351–6. https://doi.org/10.1038/ajh.2009.13.
18. Bar Dayan Y, Elishkevits K, Grotto I, Goldstein L, Goldberg A, Shvarts S, Levin A, Ohana N, Onn E, Levi Y, Bar Dayan Y. The prevalence of obesity and associated morbidity among 17-year-old Israeli conscripts. Public Health. 2005;119:385–9. https://doi.org/10.1016/j.puhe.2004.05.021.
19. Sorof JM, Poffenbarger T, Franco K, Bernard L, Portman RJ. Isolated systolic hypertension, obesity, and hyperkinetic hemodynamic states in children. J Pediatr. 2002;140:660–6. https://doi.org/10.1067/mpd.2002.125228.
20. Antoniades O, Douda HT, Papazoglou D, Tokmakidis SP. Prevalence of hypertension and determinants of cardiac function in overweight and obese children and adolescents. PANR Journal 2016. https://www.panr.com.cy/?p=1366.
21. Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, Georgiou C, Kafatos A. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord. 2000;24:1453–8. http://www.ncbi.nlm.nih.gov/pubmed/11126342. Accessed 8 May 2017.
22. Campagna G, Zampetti S, Gallozzi A, Giansanti S, Chiesa C, Pacifico L, Buzzetti R. Excellent intra and inter-observer reproducibility of wrist circumference measurements in obese children and adolescents. PLoS ONE. 2016;11:e0156646 https://doi.org/10.1371/journal.pone.0156646.
23. Dimitriadis K, Tsioufis C, Mazaraki A, Liatakis I, Koutra E, Kordalis A, Kasiakogias A, Flessas D, Tentolouris N, Tousoulis D. Waist circumference compared with other obesity parameters as determinants of coronary artery disease in essential hypertension: a 6-year follow-up study. Hypertens Res. 2016;39:475–9. https://doi.org/10.1038/hr.2016.8.
24. Hirschler V, Aranda C, Calcagno M de L, Maccalini G, Jadzinsky M. Can waist circumference identify children with the metabolic syndrome? Arch Pediatr Adolesc Med. 2005;159:740–4. https://doi.org/10.1001/archpedi.159.8.740.
25. Palermo A, D'Onofrio L, Buzzetti R, Manfrini S, Napoli N. Pathophysiology of bone fragility in patients with diabetes. Calcif Tissue Int. 2017;100:122–32. https://doi.org/10.1007/s00223-016-0226-3.
26. Fulop T, Larbi A, Douziech N. Insulin receptor and ageing. Pathol Biol. 2003;51:574–80. http://www.ncbi.nlm.nih.gov/pubmed/14622948. Accessed 12 June 2017.
27. Kannel WB, Schwartz MJ, McNamara PM. Blood pressure and risk of coronary heart disease: the Framingham study. Dis Chest. 1969;56:43–52. http://www.ncbi.nlm.nih.gov/pubmed/5789839. Accessed 8 May 2017.
28. Franklin SS. Arterial stiffness and hypertension: a two-way street? Hypertens. 2005;45:349–51. https://doi.org/10.1161/01.HYP.0000157819.31611.87.
29. Torrance B, McGuire KA, Lewanczuk R, McGavock J. Overweight, physical activity and high blood pressure in children: a review of the literature. Vasc Health Risk Manag. 2007;3:139–49. http://www.ncbi.nlm.nih.gov/pubmed/17583184. Accessed 8 May 2017
30. Sinaiko AR, Donahue RP, Jacobs DR, Prineas RJ. Relation of weight and rate of increase in weight during childhood and adolescence to body size, blood pressure, fasting insulin, and lipids in young adults. The Minneapolis Children's Blood Pressure Study. Circulation. 1999;99:1471–6. http://www.ncbi.nlm.nih.gov/pubmed/10086972. Accessed 8 May 2017
31. Mohebi R, Mohebi A, Sheikholeslami F, Azizi F, Hadaegh F. Wrist circumference as a novel predictor of hypertension and cardiovascular disease: results of a decade follow up in a West Asian cohort. J Am Soc Hypertens. 2014;8:800–7. https://doi.org/10.1016/j.jash.2014.08.010.
32. Ramezankhani A, Kabir A, Pournik O, Azizi F, Hadaegh F. Classification-based data mining for identification of risk patterns associated with hypertension in Middle Eastern population. Medicine. 2016;95:e4143. https://doi.org/10.1097/MD.0000000000004143.
33. Maddaloni E, Cavallari I, De Pascalis M, Keenan H, Park K, Manfrini S, Buzzetti R, Patti G, Di Sciascio G, Pozzilli P. Relation of body circumferences to cardiometabolic disease in overweight-obese subjects. Am J Cardiol. 2016;118:822–7. https://doi.org/10.1016/j.amjcard.2016.06.044.