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SHORT COMMUNICATION

A new simple formula built on the American Academy of Pediatrics criteria for the screening of hypertension in overweight/obese children

Procolo Di Bonito[1] · Maria Rosaria Licenziati[2] · Anna Di Sessa[3] · Melania Manco[4] · Anita Morandi[5] · Claudio Maffeis[5] · Claudio Chiesa[6] · Lucia Pacifico[7] · Giuliana Valerio[8]

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Abstract

We evaluated the performance of a new simple formula (NSF) for the screening of hypertension by American Academy of Pediatrics Guidelines 2017 ($AAPG_{2017}$) in children with overweight/obesity (OW/OB). The performance of the NSF and the modified blood pressure to height ratio (MBPHR3) thresholds against $AAPG_{2017}$ was evaluated; both methods were also compared to assess the association with concentric left ventricular hypertrophy (cLVH). The study included 3259 OW/OB children (5–13 years). Two centers served as learning sample (LS) ($n = 1428$), four centers served as validation sample (VS) ($n = 1831$), and the echocardiographic evaluation was available in 409 children in VS. The NSF was [1.5 × systolic blood pressure (mmHg) + diastolic blood pressure (mmHg)] − [(26 × height (m)] − age (years). A cut-off of the NSF ≥ 193 mmHg showed sensitivity, specificity, positive, and negative predictive values of 0.92, 0.93, 0.83, and 0.97, respectively, versus the standard procedure. Against $AAPG_{2017}$, the NSF showed higher specificity and positive predictive values than the MBPHR3 thresholds. Among hypertensive children defined by $AAPG_{2017}$, NSF, or MBPHR3, the odds ratio (95%CI) for cLVH was respectively 1.73 (1.06–2.83), 1.69 (1.05–2.75), and 1.18 (0.75–1.85).

Conclusions: The NSF shows a very high performance for the screening of OW/OB children at risk of hypertension and cLVH.

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✉ Giuliana Valerio
giuliana.valerio@uniparthenope.it

Procolo Di Bonito
procolodibonito53@gmail.com

Maria Rosaria Licenziati
mrlicenziati@gmail.com

Anna Di Sessa
anna.disessa@libero.it

Melania Manco
melania.manco@opbg.net

Anita Morandi
anita.morandi@univr.it

Claudio Maffeis
claudio.maffeis@univr.it

Claudio Chiesa
claudio.chiesa@ift.cnr.it

Lucia Pacifico
lucia.pacifico@uniroma1.it

[1] Department of Internal Medicine, "S. Maria delle Grazie", Pozzuoli Hospital, Naples, Italy

[2] Obesity and Endocrine disease Unit, Department of Neuroscience, Santobono-Pausilipon Children's Hospital, Naples, Italy

[3] Department of Woman, Child and General and Specialized Surgery, University of Campania "Luigi Vanvitelli", Naples, Italy

[4] IRCCS, Bambino Gesù Children's Hospital, Rome, Italy

[5] Pediatric Diabetes and Metabolic Disorders Unit, University Hospital of Verona, Verona, Italy

[6] Institute of Translational Pharmacology, National Research Council, Rome, Italy

[7] Policlinico Umberto I Hospital, "Sapienza" University of Rome, Rome, Italy

[8] Department of Movement Sciences and Wellbeing, University of Naples Parthenope, Naples, Italy

What is Known:
- *The American Academy of Pediatrics released updated guidelines (AAPG 2017) to classify hypertension (HTN) in children.*
- *The process needs categorization of height percentiles and comparison of blood pressure* versus *gender and age-adjusted values.*

What is New:
- *A user-friendly formula built on the AAPG 2017 was validated for the categorization of HTN in children with overweight/obesity.*
- *The formula showed high performance in identifying children with HTN* versus *the standard procedure (sensitivity 0.92, specificity 0.93) and similar ability in identifying hypertensive children with concentric left ventricular hypertrophy* versus *the standard procedure (40% and 39% respectively).*

Keywords Children · Hypertension · Left ventricular hypertrophy · Pediatric obesity

Abbreviations

$AAPG_{2017}$	American Academy of Pediatrics Guidelines 2017
AUC	Area under curve
BMI	Body mass index
BP	Blood pressure
BPHR	Blood pressure/height ratio
cLVH	Concentric left ventricular hypertrophy
DBP	Diastolic blood pressure
HR_{HTN}	High risk of hypertension
HTN	Hypertension
IVST	Interventricular septum thickness
LS	Learning series
LVDD	Left ventricular diastolic diameter
LVMi	Left ventricular mass index
MBPHR3	Modified formula based on blood pressure/height ratio 3
NSF	New simple formula
OB	Obese
OW	Overweight
PWT	Posterior wall thickness
RWT	Relative wall thickness
SBP	Systolic blood pressure
SDS	Standard deviation score
VS	Validation series.

Introduction

The American Academy of Pediatrics Guidelines of 2017 ($AAPG_{2017}$) have changed the approach to the diagnosis of hypertension (HTN) in childhood [1]. New blood pressure (BP) cut-offs have been proposed in children < 13 years, while a fixed cut-off ≥ 130/80 mmHg has been proposed in adolescents ≥ 13 years. While the adoption of a single cut-off in adolescents simplifies the identification of youth at high risk of HTN (HR_{HTN}), the categorization of HR_{HTN} in children is still based on a complex process which entails the stratification both for systolic BP (SBP) and diastolic BP (DBP) on the basis of sex, height, and age. This burdensome procedure might discourage pediatricians from translating measurements of BP into stages of HTN and hinder the purpose of the screening.

In the past, several user-friendly screening tools for HTN were developed in children, such as those based on the BP/height ratio (BPHR) [2] and validated against the diagnostic criteria recommended by the 2004 Fourth Report. Also our group developed a simple formula, derived from the Fourth Report [3], to detect HR_{HTN} in overweight (OW) or obese (OB) youth.

Immediately after the publication of the $AAPG_{2017}$, the need to develop new simplified tables [4] or formulas [5, 6] emerged to replace the previous user-friendly screening tools.

Based on the above considerations, the aim of this study was to develop a new formula based on 95th BP percentile of the $AAPG_{2017}$ to simplify the screening of HTN in children with OW or OB. We compared the performance of our formula and another new modified formula based on BPHR (MBPHR3) [6] against the $AAPG_{2017}$ and their association with concentric left ventricular hypertrophy (cLVH).

Materials and methods

The study population was obtained from a database built from the CARITALY study. It includes clinical data of outpatient youth referred to secondary and tertiary pediatric care centers for the management of OW/OB in Italy in the period 2003–2016 [7]. The medical records of 3259 Caucasian OW/OB children (age 5.0–12.9 years) were considered. Children were divided into two groups: the learning series (LS) ($n = 1428$) and the validation series (VS) ($n = 1831$). The study was approved by the Ethics Committee of the University of Campania "Luigi Vanvitelli" (reference number 834/2016).

Body mass index (BMI) was calculated as weight (kg)/height (m^2) and converted into standard deviation scores (SDS). BP was measured by aneroid devices, calibrated periodically with a mercury sphygmomanometer according to standard procedures [8]. Three measurements were taken, 2 min apart, and the mean of the last two values was recorded [7]. BPHR was calculated as SBP or DBP divided by height (centimeters).

Echocardiographic data were available in 409 children in the VS, observed in the centers of Pozzuoli and Rome, as previously reported [7]. This subsample showed similar features to the overall sample. LV mass was calculated according

standard procedures and normalized for height$^{2.16}$ + 0.09 (LV mass index, LVMi) [9]. Relative wall thickness (RWT) was calculated from posterior wall thickness (PWT), interventricular septum thickness (IVST), and left ventricular diastolic diameter (LVDD) using the formula: (PWT + IVST)/LVDD and was normalized for age by the following equation: $RWT_a = RWT - 0.005 \times (age - 10)$ [10]. The International Obesity Task Force cut-offs were used to define OW or OB [11].

HR_{HTN} was defined according to the $AAPG_{2017}$, i.e., SBP and/or DBP ≥ 95th percentile for sex, age, and height [1]. The MBPHR3 was calculated as SBP/(height + 3 × (13 − age)) (MSBPHR3) and DBP/(height + 3 × (13 − age))(MDBPHR3). The cut-offs to define HR_{HTN} were as follows: MSBPHR3 ≥ 0.75 or MDBPHR3 ≥ 0.47 obtained in an American population [6]. cLVH was defined by LVMi ≥ 45 g/h$^{2.16}$ and $RWT_a > 0.375$, as recommended by the European Society of Hypertension Guidelines 2016 [8].

Continuous data were expressed as mean ± standard deviation. Means were compared by Student's *t* test. Chi-square and Fisher's exact tests, as appropriate, were used to compare proportions. The formula was obtained using a logistic regression analysis with enter procedure in the LS. The performance was analyzed by the area under curve (AUC) using the 95th percentile of BP by $AAPG_{2017}$ as variable of interest. The best cut-off from the formula was obtained by the Youden's index in the LS. AUC, sensitivity, specificity, positive (PPV), and negative predictive values (NPV); positive likelihood ratio (LR+); and the negative likelihood ratio (LR−) of the new formula or the MBPHR3 thresholds with respect to the 95th percentile of BP by $AAPG_{2017}$ were calculated using a 2 × 2 table. The odds ratio (95%CI) of cLVH associated with the 95th percentile of BP by $AAPG_{2017}$, the new formula, or the MBPHR3 thresholds was assessed by logistic regression analysis in the VS, adjusted for centers, age, and BMI. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0.

Results

The characteristics of children in the LS and VS are shown in Table 1. Groups differed for age, BMI, BMI-SDS, and SBP. The distribution of sex and DBP not was statistically different, as well as the prevalence of HR_{HTN}, as assessed by $AAPG_{2017}$. The new formula was obtained in the LS using HTN defined by the $AAPG_{2017}$ as dependent variable, and centers, SBP, DBP, age, sex, age, height, and weight as covariates. The following variables were significantly associated with HTN: SBP (beta 0.40, SE 0.03, $p < 0.0001$), DBP (beta 0.29, SE 0.02, $p < 0.0001$), height (beta − 7.1, SE 0.12, $p < 0.0001$), and age (beta − 0.27, SE 1.86, $p = 0.025$).

The new formula was obtained by multiplying each beta coefficient for the respective variable as elsewhere described [6], obtaining the following linear equation:

Table 1 Anthropometric and biochemical features of participants in the learning and validation series, and performance of the new simplified formula and the modified blood pressure/height ratio 3 thresholds versus standard criteria ($AAPG_{2017}$)

	Learning series	Validation series	
n	1428	1831	
Age (years)	9.5 ± 2.0	9.7 ± 1.9	
Boys, *n* (%)	774 (54)	936 (51)	
BMI, (kg/m^2)	28.0 ± 4.4	27.3 ± 4.7	
BMI-SDS	2.0 ± 0.5	1.9 ± 0.6	
Systolic BP (mmHg)	106.3 ± 14.0	108.2 ± 12.2	
Diastolic BP (mmHg)	65.1 ± 9.5	64.4 ± 9.3	
Performance	NSF	NSF	MBPH3
High risk of HTN, *n* (%)	389/1428 (27.2)	492/1831 (26.9)	710/1831 (39)
AUC (95% CI)	0.93 (0.91–0.94)	0.90 (0.88–0.92)	0.89 (0.87–0.91)
Sensitivity (95% CI)	0.92 (0.89–0.95)	0.86 (0.82–0.89)	0.93 (0.91–0.96)
Specificity (95% CI)	0.93 (0.91–0.94)	0.94 (0.93–0.95)	0.81 (0.79–0.83)
PPV (95% CI)	0.83 (0.79–0.86)	0.84 (0.81–0.87)	0.65 (0.61–0.68)
NPV (95% CI)	0.97 (0.96–0.98)	0.95 (0.93–0.96)	0.97 (0.96–0.98)
LR+ (95% CI)	13 (10–16)	15 (12–18)	5.0 (4.5–5.6)
LR− (95% CI)	0.09 (0.06–0.12)	0.15 (0.12–0.19)	0.08 (0.06–0.11)

Data are expressed as mean ± standard deviation or *n* (%)

AAPG American Academy of Pediatrics guidelines, *AUC* area under curve, *BMI* body mass index, *BMI-SDS* body mass index-standard deviation score, *BP* blood pressure, *HTN* hypertension, *LR−* negative likelihood ratio, *LR+* positive likelihood ratio, *MBPH3* modified formula based on blood pressure/height ratio 3, *NPV* negative predictive value, *NSF* new simplified formula, *PPV* positive predictive value

$$\text{New formula}: (0.40 \times \text{SBP} + 0.29 \times \text{DBP}) - (7.1 \times \text{height}) - (0.27 \times \text{age})$$

where SBP and DBP were expressed in millimeter of mercury, height in meters, and age in years. To obtain a simpler equation, we divided each coefficient by 0.27, i.e., the coefficient of age, obtaining the following new formula:

$$\text{New simplified formula (NSF)}: (1.5 \times \text{SBP} + \text{DBP}) - (26 \times \text{height})\ \text{age}$$

The accuracy of the two formulas was very high, showing an identical AUC (95%CI) of 0.982 (0.977–0.987), with respect to the standard procedures of classification of HTN by $AAPG_{2017}$. The best cut-off of the NSF to identify children at HR_{HTN} was ≥ 193 mmHg. Measures of accuracy of the NSF assessed in the LS and VS showed that the performance of NSF was quite similar (Table 1). In the VS, the NSF showed lower sensitivity and higher LR–, but higher specificity, PPV, and LR+ versus $AAPG_{2017}$, compared to the MBPHR3 thresholds. Furthermore, we assessed the association with cLVH in children who were categorized as HR_{HTN} by $AAPG_{2017}$, NSF, or MBPHR3 thresholds in the VS. The proportion of cLVH in children who were categorized as HR_{HTN} by $AAPG_{2017}$ was 44/112 (39%), 48/121 (40%) by NSF, and 56/180 (31%) with MBPHR3 thresholds. The odds ratio (95%CI) for cLVH was 1.73 (1.06–2.83, $p = 0.028$) with $AAPG_{2017}$, 1.69 (1.05–2.75, $p = 0.032$) with the NSF, and 1.18 (0.75–1.85, $p = 0.481$) with the MBPHR3.

Discussion

A simple formula built using the new $AAPG_{2017}$, and based on SBP, DBP, height, and age, showed high performance in identifying OW or OB children at HR_{HTN}. The ability in identifying cLVH in children at HR_{HTN} was similar using the standard procedures or NSF.

Although the new guidelines simplified the screening of HTN in adolescents [1], the process in children remains complex. The awareness that HTN could be underdiagnosed, as it occurred for the Fourth Report, led the extensors of $AAPG_{2017}$ to include simplified tables in order to facilitate the screening of the 90th percentile of BP [1]. Therefore, a tool simplifying also the screening of HTN is still needed. An alternative method has been proposed using the BP to height ratio. This method was previously built in the epoch of the Fourth Report using several formulas which provided different cut-offs [12]. Recently, new thresholds for SBP-to-height ratio and DBP-to-height ratio were proposed in children aged less than 13 years, built on the 95th percentile of BP of $AAPG_{2017}$, such as the MBPHR3 [6]. This method has been demonstrated to perform better than other tools, such as MBPHR7 or BPHR, for identifying HTN in a large population of Chinese and American children, in terms of sensitivity and NPV; on the contrary, it showed a low PPV as the other two methods. Similarly, we found that the MBPHR3 had higher sensitivity but lower specificity and PPV, as compared to the NSF. Therefore, our tool seems to better comply with the principle of screening in populations at HR_{HTN} such as children with OW/OB. In fact, when the attributable risk population is high, a test exhibiting a high specificity rather than sensitivity is favored. A high specificity allows excluding HTN that would require re-evaluation on at least two occasions.

Our formula shows several advantage: it may be easily memorized and applicable at bed-side without using an online calculator. In addition, it represents a simple tool to identify young people with OW or OB presenting both HT_{HTN} and high risk of cLVH.

In conclusion, we propose a NSF based on SBP, DBP, height, and age for the screening of OW/OB children with HR_{HTN} and associated cLVH.

Authors' contributions Study concept and design: Di Bonito, Valerio.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Di Bonito, Valerio.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Di Bonito.
Study supervision: All authors.

Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethics Committee of the University of Campania "Luigi Vanvitelli," reference number 834/2016) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the parents of all individual participants included in the study.

References

1. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, de Ferranti SD, Dionne JM, Falkner B, Flinn SK, Gidding SS, Goodwin C, Leu MG, Powers ME, Rea C, Samuels J, Simasek M, Thaker VV, Urbina EM (2017) Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 140(3):e20171904. https://doi.org/10.1542/peds.2017-1904
2. Ma C, Wang R, Liu Y, Lu Q, Lu N, Tian Y, Liu X, Yin F (2017) Performance of user-friendly screening tools for elevated blood pressure in children. Pediatrics 139:e20161986. https://doi.org/10.1542/peds.2016-1986

3. Di Bonito P, Valerio G, Pacifico L, Chiesa C, Invitti C, Morandi A, Maffeis C, Licenziati MR, Manco M, Miraglia Del Giudice E, Baroni MG, Loche S, Tornese G, Tomat M, de Simone G (2017) A new index to simplify the screening of hypertension in overweight or obese youth. Nutr Metab Cardiovasc Dis 27:830–835. https://doi.org/10.1016/j.numecd.2017.06.013
4. Yang L, Hou Y1, Zhao M, Bovet P, Xi B (2018) Simplified blood pressure tables based on different height percentiles for screening elevated blood pressure in children. J Hypertens Jul 30. https://doi.org/10.1097/HJH.0000000000001880
5. Mourato FA, Mourato MF, Mattos SDS, de Lima Filho JL, de Araújo Gueiros Lira GV, Nadruz W Jr. (2018) New modifications of the blood pressure-to-height ratio for the diagnosis of high blood pressure in children. J Clin Hypertens (Greenwich) 20:413–415. https://doi.org/10.1111/jch.13178
6. Zhang Y, Ma C, Yang L, Bovet P, Xi B (2018) Performance of modified blood pressure-to-height ratio for identifying hypertension in Chinese and American children. J Hum Hypertens 32:408–414. https://doi.org/10.1038/s41371-018-0056-z
7. Di Bonito P, Valerio G, Pacifico L, Chiesa C, Invitti C, Morandi A, Licenziati MR, Manco M, Giudice EMD, Baroni MG, Loche S, Tornese G, Franco F, Maffeis C, de Simone G (2019) Impact of the 2017 blood pressure guidelines by the American Academy of Pediatrics in overweight/obese youth. J Hypertens 37:732–738. https://doi.org/10.1097/HJH.0000000000001954
8. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, Invitti C, Litwin M, Mancia G, Pall D, Rascher W, Redon J, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wühl E, Zanchetti A (2016) 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens 34:1887–1920. https://doi.org/10.1097/HJH.0000000000001039
9. Chinali M, Emma F, Esposito C, Rinelli G, Franceschini A, Doyon A, Raimondi F, Pongiglione G, Schaefer F, Matteucci MC (2016) Left ventricular mass indexing in infants, children, and adolescents: a simplified approach for the identification of left ventricular hypertrophy in clinical practice. J Pediatr 170:193–198. https://doi.org/10.1016/j.jpeds.2015.10.085
10. de Simone G, Daniels SR, Kimball TR, Roman MJ, Romano C, Chinali M, Galderisi M, Devereux RB (2005) Evaluation of concentric left ventricular geometry in humans: evidence for age-related systematic underestimation. Hypertension 45:64–68. https://doi.org/10.1161/01.HYP.0000150108.37527.57
11. Cole TJ, Lobstein T (2012) Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes 7:284e94. https://doi.org/10.1111/j.2047-6310.2012.00064.x
12. Ma C, Kelishadi R, Hong YM, Bovet P, Khadilkar A, Nawarycz T, Krzywińska-Wiewiorowska M, Aounallah-Skhiri H, Zong X, Motlagh ME, Kim HS, Khadilkar V, Krzyżaniak A, Ben Romdhane H, Heshmat R, Chiplonkar S, Stawińska-Witoszyńska B, El Ati J, Qorbani M, Kajale N, Traissac P, Ostrowska-Nawarycz L, Ardalan G, Parthasarathy L, Zhao M, Xi B (2016) Performance of eleven simplified methods for the identification of elevated blood pressure in children and adolescents. Hypertension 68:614–620. https://doi.org/10.1161/HYPERTENSIONAHA.116.07659