U.PORTO

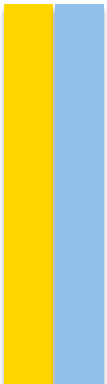
MESTRADO INTEGRADO
MEDICINA

Comparison between direct and ambulatory brachial cuff-based oscillometric pulse wave velocity in overweight adolescents

Ana Rita Bastos Pereira

M

2022



Comparison between direct and ambulatory brachial cuff-based oscillometric pulse wave velocity in overweight adolescents

MESTRADO INTEGRADO EM MEDICINA

Ana Rita Bastos Pereira

(anarita1188@gmail.com)

Orientador: Liane Maria Correia Rodrigues da Costa Nogueira Silva

Coorientador: Sara Maria Mosca Ferreira da Silva

EPIUnit – Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal;
Unidade de Nefrologia Pediátrica, Serviço de Pediatria, Centro Materno-Infantil do Norte, Centro Hospitalar Universitário do Porto, Porto, Portugal;
Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal.

Junho 2022

Comparison between direct and ambulatory brachial cuff-based oscillometric pulse wave velocity in overweight adolescents

DISSERTAÇÃO DE CANDIDATURA AO GRAU DE MESTRE EM MEDICINA, SUBMETIDA AO INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR – UNIVERSIDADE DO PORTO

Autora: Ana Rita Bastos Pereira

Orientadora: Prof. Dra. Liane Correia Costa

Coorientadora: Dra. Sara Mosca

Porto, Junho 2022

AGRADECIMENTOS

Em primeiro lugar, deixo um agradecimento especial à Prof.ª Doutora Liane Costa por ter aceite a coordenação da minha tese de mestrado, assim como pela sua orientação em todas as fases da dissertação, disponibilidade, motivação e aconselhamento, todas as apreciações e sugestões. Considero que, para além da ajuda na tese, também contribuiu para o meu interesse pela vertente da investigação na medicina, bem como para o meu conhecimento acerca dos procedimentos e ferramentas a usar neste contexto, o que será muito útil na minha vida futura enquanto médica de qualquer especialidade.

À Dr.ª Sara Mosca, coorientadora, agradeço também a disponibilidade e acompanhamento ao longo da realização do artigo, bem como na sua revisão final.

Por fim, agradecer ainda às famílias participantes no estudo Geração XXI, particularmente, às incluídas no projeto ObiKid 2.0 e a toda a restante equipa envolvida.

RESUMO

Introdução e objetivos: A obesidade infantil, como se sabe contribui para o desenvolvimento da aterosclerose e para um maior risco de morbidade e mortalidade cardiovascular na vida adulta. A rigidez arterial é considerada um marcador de dano vascular com valor preditivo para a ocorrência de eventos cardiovasculares e mortalidade por todas as causas. Esta pode ser avaliada por vários métodos, sendo a velocidade de onda de pulso carotídeo-femoral (VOP-cf) de longe o mais utilizado. Mais recentemente, para avaliar a rigidez arterial, foram desenvolvidos dispositivos que estimam a análise da onda de pulso ambulatória pelo método oscilométrico com braçadeira braquial (AOP), sendo cada vez mais utilizados como um método não invasivo e de mais fácil aplicação. O nosso objetivo foi caracterizar a rigidez arterial em adolescentes sem sobrepeso e com sobrepeso/obesidade, avaliada por VOP-cf e AOP, e comparar a estimativa deste parâmetro obtida pelos dois métodos.

Métodos: Foi feita uma análise transversal, incluindo 118 adolescentes entre os 12-14 anos de idade acompanhados numa coorte previamente estabelecida desde o nascimento (Geração XXI). Foram avaliados em todos os participantes a antropometria, a VOP-cf e a pressão arterial ambulatória de 24 h baseada no método oscilométrico com braçadeira braquial, sendo estimada a AOP. A classificação dos adolescentes consoante o índice de massa corporal foi feita de acordo com as referências de crescimento da Organização Mundial da Saúde.

Resultados: Um total de 118 adolescentes (54,2% do sexo masculino) com 14 anos (sem sobrepeso, n=77; sobrepeso/obesidade, n=41) foram incluídos no presente estudo. Os adolescentes com sobrepeso/obesidade apresentaram níveis significativamente maiores de VOP-cf (6,71 ± 1,22 vs. 6,07 ± 0,89, p=0,005), AOP total (4,61 ± 0,199 vs. 4,53 ± 0,22, p=0,038) e AOP diurna (4,67 ± 0,196 vs. 4,57 ± 0,21, p=0,008). Para além disso, reportamos correlações positivas significativas entre VOP-cf e AOP, apenas no grupo com sobrepeso/obesidade, no período noturno ($r=0,336$; $p<0,05$).

Conclusões: Os maiores valores de rigidez arterial encontrados em adolescentes com sobrepeso/obesidade, por ambos os métodos utilizados, reforçam a contribuição do excesso de peso para a lesão vascular no início da vida. A comparação desses dois métodos, pouco relatados na literatura até ao momento, contribui com dados muito necessários para auxiliar no estabelecimento de métodos de fácil utilização para avaliação da rigidez arterial e identificação de indivíduos de maior risco.

Palavras-chave: Velocidade de onda de pulso; rigidez arterial; análise da onda de pulso ambulatória (método oscilométrico com braçadeira braquial); obesidade infantil; risco cardiovascular

ABSTRACT

Background and objectives: Childhood obesity is known to contribute to the development of atherosclerosis and a higher risk of cardiovascular morbidity and mortality later in life. Arterial stiffness is considered a marker of vascular damage with predictive value for the occurrence of cardiovascular events and all-cause mortality. It can be evaluated by several methods, with carotid-femoral pulse wave velocity (cf-PWV) being by far the most used. More recently, devices estimating pulse wave analysis by ambulatory brachial cuff-based oscillometry (PWA) were developed and are being increasingly used as an easier-to-use, non-invasive method for assessing arterial stiffness. We aimed to characterize arterial stiffness in nonoverweight and overweight/obese adolescents, evaluated by cf-PWV and PWA, and to compare the estimation of this parameter obtained by these two methods.

Methods: Cross-sectional analysis, including 118 adolescents aged 12–14 years old, followed in previously established birth-cohort (Generation XXI). Anthropometrics, cf-PWV and 24-h ambulatory blood pressure with brachial cuff-based oscillometry estimated PWA were evaluated in all participants. The body mass index classification was made according to World Health Organization growth references.

Results: A total of 118 adolescents (54.2% male) aged 14 years old (nonoverweight, n=77; overweight/obesity, n=41) were included in the present study. The overweight/obese adolescents presented significantly higher levels of cf-PWV (6.71 ± 1.22 vs. 6.07 ± 0.89, p=0.005), total PWA (4.61 ± 0.199 vs. 4.53 ± 0.22, p=0.038) and daytime PWA (4.67 ± 0.196 vs. 4.57 ± 0.21, p=0.008). Significant positive correlations between cf-PWV and PWA were only found in the overweight/obese group, during the nighttime period (r=0.336; p<0.05).

Conclusions: The higher values of arterial stiffness found in overweight/obese adolescents, by both methods used, reinforce the contribution of excess weight to vascular injury in early life. The comparison of these two methods, seldomly reported in the literature so far, contributes with much needed data to help the establishment of easy-to-use methods for arterial stiffness assessment and identification of higher risk individuals.

Key words: Pulse wave velocity; Arterial stiffness; Pulse wave analysis by ambulatory brachial cuff-based oscillometry; Childhood obesity; Cardiovascular Risk

ABBREVIATIONS

ABPM, ambulatory blood pressure monitoring

ASI, arterial stiffness index

BMI, body mass index

BP, blood pressure

cf-PWV, carotid-femoral pulse wave velocity

cIMT, carotid intima-media thickness

CV, cardiovascular

DBP, diastolic blood pressure

HDL, high density lipoprotein

hs-CRP, high sensitivity C-reactive protein

LDL, Low density lipoprotein

PWA, pulse wave analysis (by ambulatory brachial cuff-based oscillometry)

PWV, pulse wave velocity

SBP, systolic blood pressure

SD, standard deviation

WHO, World Health Organization

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

In developed countries, the prevalence of obesity among children and adolescents has been increasing, in association with the tendency for the adoption of sedentary lifestyles and habits of consumption of energy-dense foods[1]. Fat accumulation is known to lead to the development of several cardiovascular (CV) risk factors and metabolic derangements, such as hypertension, dyslipidemia, and insulin resistance. It has also been acknowledged that obesity constitutes an important risk factor for the development of preclinical vascular wall abnormalities and atherosclerosis progression[2,3,4]. In fact, the acceleration of the process of atherosclerosis, a common denominator in CV diseases, was demonstrated to begin early in life in obese children, tracking into adulthood and contributing to a higher risk of cardiovascular morbidity and premature mortality[5].

Several methods have been used to evaluate vascular health, including arterial structure, endothelial function, and arterial function[1,6]. Firstly, the measurement of carotid intima-media thickness (cIMT), as well as the assessment of the coronary arteries calcification, are forms of arterial structure evaluation, based on ultrasound probe and computed tomography images, respectively. However, cIMT is technically difficult to measure in children, due to its anatomical conditions and compliance and requires expensive equipment and a high level of technical knowledge[7]. The need for thoracic irradiation is a significant limitation in the evaluation of coronary arteries calcification in children[1]. Secondly, the flow-mediated vasodilation or peripheral arterial tonometry can also be used for the assessment of the endothelial function, but its use is somehow limited by the expensive equipment required for the evaluation[7]. Finally, several previous studies have demonstrated that arterial stiffness is a non-invasive and dynamic measure of arterial function that can be used for prognostic assessment of cardiovascular risk[1,8,9] and as a predictive value for the occurrence of cardiovascular events and all-cause mortality[7,10,11].

Arterial stiffness can be measured using pulse wave velocity (PWV)[6]. Currently, PWV between the carotid and femoral arteries (central arterial stiffness) is an increasingly used method due to its ease of determination and reliability[7,10,11]. Although easily measured using a pressure sensor (tonometry applanation), PWV is dependent on several variables, such as age, height, sex, race, and blood pressure (BP)[12,13]. Furthermore, there are no well-established reference values nor standardized method for its assessment, especially in children[10,14,15]. More recently, pulse wave analysis by ambulatory brachial cuff-based oscillometry (PWA) was developed as another noninvasive method to evaluate arterial stiffness[16,17]. This method has also been studied as an independent predictor of CV morbidity and mortality, closely correlated to PWV[16,18]. This method

of arterial stiffness assessment stands out by the possibility of being obtained through repeated measurements, in different day-to-day situations, during daytime activities and during sleep, for example[19]. The use of the 24-hour ambulatory blood pressure monitoring (ABPM) devices to additionally measuring PWA is expected to represent a great advantage, especially in children and adolescents, mainly by representing an easily accessible method, independent of the observer and less influenced by motion and other possible disturbances[1,18].

Arterial stiffness is known to be directly associated with aging, increasing with age, and to be influenced by several CV risk factors[20], such as obesity. Several studies have shown that PWV is higher among obese children, possibly representing another marker of increased of CV risk during lifetime[7,12,13,21,22,23]. Several studies have shown that arterial stiffness increases in obese individuals, especially in the transition between childhood and adulthood, a period of constant change and adaptation, namely at vascular level, suggesting that the degree and duration of obesity might influence the CV phenotype[24]. Few studies have studied the association between arterial stiffness estimated by PWV and by PWA. Studies in diabetic children showed a significant correlation of PWA and PWV values, suggesting that the PWA method might be more reliable than others previously used[25]. In hypertensive adolescents, some studies reported higher PWA values, suggesting that this marker might represent a good complement to conventional BP monitoring, as a proxy of risk of target-organ damage[26]. Despite the promising results of the previous studies of PWA, estimated by ambulatory brachial cuff-based oscillometry, its usefulness in children and adolescents and its applicability in the clinical practice still needs to be confirmed in future studies, ideally with a longitudinal follow-up during lifetime[1,19].

In the present study, we aimed to characterize the arterial stiffness of nonoverweight and overweight/obese adolescents, followed in the Generation XXI birth-cohort, evaluated by carotid-femoral pulse wave velocity (cf-PWV) and by PWA, and to compare the estimation of this parameter obtained by these two methods.

METHODS

Study design and sample

We studied adolescents aged 12-14 years that have been followed since birth in a previously established cohort study (Generation XXI, Porto-Portugal)[27]. Of the original cohort (n=8647), 4590 children attended a face-to-face follow-up visit at 7 years of age, thus being eligible for the ObiKid project - a specific project aiming to clarify the impact of childhood obesity and associated co-morbidities on the kidney. The ObiKid project evaluated a subsample of 313 participants at 8-9 years of age[28]. The detailed specifics of screening and enrollment of participants to the original ObiKid project can be found in previous publications[28]. In the present project, we aimed to reevaluate all the ObiKid participants, previously included in the 8-9 years of age evaluation. The participants were contacted to be enrolled in the ObiKid 2.0 reevaluation, 18 refused to participate due to personal constraints, 41 could not be contacted, 77 were unable to schedule visits during the recruitment period (mostly due to COVID19 constraints). None of the ObiKid participants was excluded from the present reevaluation due to exclusion criteria [chronic diseases (genetic, renal, or metabolic) and 4 were excluded for chronic usage of medication (affecting BP or glucose or lipid metabolism)]. A total of 55 participants were excluded for not having completed the evaluation, with either ABPM or cf-PWV measurements. A total of 118 were finally included in the present study.

Data collection and variable definition

The study visits took place at the Public Health and Forensic Sciences and Medical Education Department, Faculty of Medicine - University of Porto. Anthropometric measurements and general physical examinations were performed, according to standard procedures and as previously reported[29]. Body mass index (BMI) was calculated (Kg/m^2), and BMI-for-age values were classified into 2 categories: (1) nonoverweight [≤+1 standard deviation (SD)], (2) overweight (>1SD and ≤+2SD)/obesity (>2SD), according to the World Health Organization (WHO) reference data for BMI z-score[30].

Carotid-femoral PWV analysis was performed by a single trained cardiopneumology technician with a portable device (Micro Medical, model PulseTrace PWV PT4000, Kent, UK). After a 5 min rest, in a supine position, the distance between carotid and femoral arteries was assessed as the distance of suprasternal notch to the umbilicus and from there to the measuring point at the femoral arterial minus the suprasternal notch to the measuring point at the carotid artery. Electrocardiogram registry was performed simultaneously, allowing the software to calculate the time from the peak

of the R-wave to the foot of the pulse wave at the carotid and femoral arteries, respectively. Digital volume pulse waveform had to fill 2/3 of the display with little or no noise and artefact to be considered and 3 measurements of PWV were performed and averaged for analysis.

ABPM was performed during 24 hours with a portable non-invasive oscillometric BP recorder, with PWA (Mobil-O-Graph ®, I.E.M. GmbH, Germany), in the non-dominant arm and with a cuff size appropriate chosen according to the circumference of the adolescent´s arm. BP measurements were automatically evaluated at 20-minute intervals during the daytime (08.00 AM until 08:00 PM) and at 30-minute intervals during the night-time (00:00 PM until 06:00). For acceptance, a minimum monitoring duration of 24 hours with gaps of less than 2 hours was required. The readings were used to calculate mean 24 hours, day and night mean arterial pressure, systolic blood pressure (SBP) and diastolic blood pressure (DBP). For PWA, from 8:00 AM until 11:59 PM 4 recordings were obtained and from 00:00 AM until 7:59 AM 2 recordings were obtained. Firstly, the oscillometric BP was measured and then there was a re-inflation to the diastolic BP level, recording, for 10 seconds, a pulse waveform that was calibrated considering the systolic and diastolic brachial BP. Then, using a generalized transfer function, ARCSolver algorithm, the PWA was generated.

A venous blood sample was collected from all participants, after an overnight fast of at least 8 hours. All standard blood analyses, which included lipid profile (total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides), glucose, insulin, and high sensitivity C-reactive protein (hs-CRP), were performed at the Clinical Pathology Department of Centro Hospitalar Universitário São João, Porto. Insulin resistance was determined using the homoeostasis model assessment index (HOMA-IR).

Ethics

The ObiKid study was approved by the Ethics Committee of Centro Hospitalar Universitário de São João, E.P.E., and Faculty of Medicine of the University of Porto. It complies with the Helsinki Declaration, the guidelines for the ethical conduct of medical research involving children[31] and the current national legislation. Written informed consent from parents (or their legal substitute) and verbal assent from adolescents were obtained, concerning information and biological samples gathering.

Statistical analysis

Statistical analysis was performed using IBM® SPSS® Statistics 26.0. The variables are presented as mean and SD or n (%), as appropriate. Differences between groups in continuous variables were evaluated with Student's T-tests. Bivariate associations were assessed by Pearson correlation tests. Two-sided $p < 0.05$ was considered significant. To evaluate the agreement between methods of

arterial stiffness determination (PWV and PWA), calculation of differences (means ± SD), accuracies (within 10, 30, and 50%), and absolute bias (i.e., average difference between cf-PWV and total PWA) were performed and Bland Altman charts were plotted.

RESULTS

A total of 118 children (54.2% male) aged 14 years old were included in the present study. Demographic, anthropometric, and cardiovascular variables are shown in **Table I**, by classes of BMI (nonoverweight, n=77; overweight/obesity, n=41). Overweight/obese individuals presented higher 24-h SBP and daytime DBP, when compared to their nonoverweight counterparts. No significant differences were found in the prevalence of hypertension or absence of dipping between the groups. Overweight/obese adolescents presented significantly lower levels of HDL cholesterol and higher levels of fasting insulin, HOMA-IR, and hs-CRP (**Table I**)**.**

Compared to nonoverweight, the overweight/obese adolescents presented significantly higher levels of cf-PWV (6.71 ± 1.22 vs. 6.07 ± 0.89, p=0.005), total PWA (4.61 ± 0.199 vs. 4.53 ± 0.22, p=0.038) and daytime PWA (4.67 ± 0.196 vs. 4.57 ± 0.21, p=0.008) (**Figure 1**).

When comparing the two techniques, significant positive correlations between cf-PWV and PWA were only found in the overweight/obese group, during the nighttime period ($r=0.336$; $p<0.05$) (**Table II**).

In **Table II**, we summarize the agreement between cf-PWV and PWA. The PWA value that seemed to have the closest performance to cf-PWV (both higher correlation coefficients and higher accuracy values) and to present the most similar results in the nonoverweight and overweight/obesity groups was the nighttime PWA. The Bland-Altman plots for each PWA value (total, daytime, and nighttime) using cf-PWV as the reference, for nonoverweight and overweight/obesity groups, are presented in **Figure 2**.

DISCUSSION

In the present study, which involved a large sample of nonoverweight and overweight/obese adolescents, we showed that the overweight/obese group presented significantly higher values of arterial stiffness, as measured by cf-PWV and by total and daytime PWA. Interestingly, when analyzing the correlation between the two methods of arterial stiffness estimation, only nighttime PWA showed to be significantly correlated to cf-PWV values, and exclusively among the group of overweight/obese adolescents. The overweight/obese group also presented higher values of cardiovascular risk markers such as ambulatory BP, insulin resistance as estimated by HOMA-IR, blood lipids and hs-CRP. These findings are in line with several previous studies on the CV risk associated with overweight and obesity[23,32].

The finding of higher values of cf-PWV and consequently greater arterial stiffness in overweight/obese adolescents, when compared to their nonoverweight counterparts, is also in accordance with several previous studies in children and adolescents[13,22,24,33,34]. Nonetheless, regarding cf-PWV some other studies have demonstrated the opposite, with findings of lower PWV values among overweight/obese, or even no relationships being found between PWV and obesity[35,36,37]. A study with 501 children and adolescents showed a positive association between PWV and BP, but an inverse association between PWV and BMI, with the authors reporting that obesity blunted the expected increment in PWV of hypertensive and high-normal BP subjects[36]. Another study with 6816 children and adolescents, aged 3 and 18 years old, could not find differences in PWV levels between normal and overweight individuals[37]. Some of these contradictory findings have been interpreted as possibly related to a compensatory vasodilation secondary to the metabolic changes of obesity, thus justifying lower PWV values in obese individuals[35]. Nonetheless, our results of higher PWV values in the overweight/obese adolescents are in line with 2 recently published meta-analysis on the impact of obesity on arterial stiffness which found that BMI is positively associated with central PWV[22,33].

Regarding PWA, we also found higher values in overweight/obese adolescents. A previous study in hypertensive children and adolescents reported higher PWA and higher BP values in hypertensive patients when compared to non-hypertensive controls[38]. There are few studies using PWA especially in pediatric age, but in a study involving adults with end-stage kidney disease, with PWA estimated using the same device used in our study, the authors also reported a positive association with BMI[17]. To our knowledge, to date, no studies exist comparing PWA levels in nonoverweight and overweight/obese children or adolescents.

In fact, one of our main aims was to evaluate the agreement between PWV and PWA in the estimation of arterial stiffness in adolescents. We were able to find a moderate correlation between cf-PWV and PWA but only in the overweight/obese adolescents' group and when considering the nighttime PWA values. We expected a stronger positive correlation between the different PWA (total, daytime, nighttime) and cf-PWV, both methods of arterial stiffness evaluation, especially in overweight/obese adolescents. Despite the moderate correlation found in our study, previous studies in adults have shown that PWA by ambulatory brachial cuff-based oscillometry seems to be reliable and highly reproducible, thus probably representing a promising tool for CV risk prediction[16]. A recent paper on the current evidence and perspectives about 24-hour ambulatory PWA states that PWA provide extra information to cf-PWV regarding arterial stiffness[19]. In fact, since PWA corresponds to the average of several readings and since its measurements are taken outside the office environment, some authors even hypothesize that this method might have a better predictive value than cf-PWV[39].

The closest association between nighttime PWA and cf-PWV might be related to the fewer possible external interferences occurring during nighttime measurements. A previous study analyzing PWA acquired by the same device reported that the values obtained were influenced by physical activity and emotional stress[40]. Furthermore, another study in obese children and adolescents found a positive relationship between cf-PWV and nighttime SBP in the obese group[41]. The authors justified this finding by the high distension pressure in the systole, where tension on the arterial wall is transferred and supported by fibers of less extensible collagen, making the arterial wall more stiffed[41]. In fact, the PWA, as mentioned above, is estimated taking into consideration the both SBP and DBP, but the fact that PWA seems to be more related to nighttime BP values needs to be clarified and further investigated.

Our study addresses an expanding area of investigation and reinforces the association between obesity and arterial stiffness, already present in adolescents. We were able to include a large sample of adolescents, homogeneous in terms of age, for which extensive evaluation of CV markers was available, including cf-PWV, PWA, ABPM, total cholesterol, LDL and HDL cholesterol, triglycerides among others. The assessment of PWV, especially in obese individuals, may be difficult and subject of some variability, with some determinations possibly overestimating the real value of this parameter, but the fact that all measurements were performed by a single trained cardiopulmonary technician, probably helped to minimize this possible bias and limitation. PWV has been accepted as a validated standard method for arterial stiffness measurement, mainly due to its low cost, feasibility, and reproducibility. In addition, PWA by ambulatory brachial cuff-based

oscillometry is an innovative method for estimating CV risk, since it depends on the same device used to measure ABPM, with no need for other invasive methods.

In the present study, considering our main aim, we analyzed data of a specific evaluation, during adolescence, but in the future, it will be interesting to explore the long-term evaluation of this group of individuals, whose CV data, including PWV is available also from the prepubertal period.

Conclusions

The early determination of CV risk is extremely important especially during the pediatric age, in particular, in individuals with overweight and obesity. The study of methods to improve our ability to identify individuals at higher risk of future adverse CV events will contribute to put in motion early actions of prevention. We believe to have contributed with additional data on the correlation between cf-PWV and PWA, which increases the interest of this innovative method of arterial stiffness estimation. Since PWA is a non-invasive, convenient, and easy-to-use method, an especially important aspect in the age group studied, our results reinforce that further studies are needed to better clarify this association, in the pediatric setting. Another important point to consider in the future would be the identification of adequate reference values, established in a large and representative sample of individuals in different pediatric age groups, allowing for a better use and applicability of PWA in the clinical practice.

REFERENCES

1. P S, M PT. Methods to evaluate arterial structure and function in children - State-of-the art knowledge. *Adv Med Sci*. 2017;62(2):280-294. doi:10.1016/J.ADVMS.2017.03.001

2. DS F, DA P, SR S, et al. The contribution of childhood obesity to adult carotid intima-media thickness: the Bogalusa Heart Study. *Int J Obes (Lond)*. 2008;32(5):749-756. doi:10.1038/SJ.IJO.0803798

3. McMahan CA, Gidding SS, Malcom GT, Tracy RE, Strong JP, McGill HC. Pathobiological determinants of atherosclerosis in youth risk scores are associated with early and advanced atherosclerosis. *Pediatrics*. 2006;118(4):1447-1455. doi:10.1542/PEDS.2006-0970

4. GS B, SR S, W B, WP N, RE T, WA W. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med*. 1998;338(23):1650-1656. doi:10.1056/NEJM199806043382302

5. SR S, W B, WA W, GS B. Adolescent overweight is associated with adult overweight and related multiple cardiovascular risk factors: the Bogalusa Heart Study. *Metabolism*. 1996;45(2):235-240. doi:10.1016/S0026-0495(96)90060-8

6. Aggoun Y, Szezepanski I, Bonnet D. Noninvasive assessment of arterial stiffness and risk of atherosclerotic events in children. *Pediatr Res*. 2005;58(2):173-178. doi:10.1203/01.PDR.0000170900.35571.CB

7. C P, ED M, G R. Utility of arterial stiffness assessment in children. *Cardiol Young*. 2018;28(3):362-376. doi:10.1017/S1047951117002402

8. Vogel RA, Benitez RM. Noninvasive assessment of cardiovascular risk: from Framingham to the future. *Rev Cardiovasc Med*. 2000;1(1):34-42.

9. GF M, SJ H, RS V, et al. Arterial stiffness and cardiovascular events: the Framingham Heart Study. *Circulation*. 2010;121(4):505-511. doi:10.1161/CIRCULATIONAHA.109.886655

10. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: "establishing normal and reference values." *Eur Heart J*. 2010;31(19):2338-2350. doi:10.1093/EURHEARTJ/EHQ165

11. H S, J H, K H, H S, K K. A population-based study of arterial stiffness index in relation to cardiovascular risk factors. *J Atheroscler Thromb*. 2005;12(3):175-180. doi:10.5551/JAT.12.175

12. JD S, SL F, KE M. Arterial Stiffness in Children: Pediatric Measurement and Considerations. *Pulse (Basel)*. 2014;2(1-4):69-80. doi:10.1159/000374095

13. Correia-Costa A, Correia-Costa L, Caldas Afonso A, et al. Determinants of carotid-femoral pulse wave velocity in prepubertal children. *International Journal of Cardiology*. 2016;218:37-42. doi:10.1016/J.IJCARD.2016.05.060

14. C Y, W H, D X. Noninvasive measurement and evaluation of arterial stiffness. *Conf Proc IEEE Eng Med Biol Soc*. 2005;2005:5483-5485. doi:10.1109/IEMBS.2005.1615724

15. D T, A D, B S, et al. Aortic Pulse Wave Velocity in Healthy Children and Adolescents: Reference Values for the Vicorder Device and Modifying Factors. *Am J Hypertens*. 2015;28(12):1480-1488. doi:10.1093/AJH/HPV048

16. Papaioannou TG, Argyris A, Protogerou AD, et al. Non-invasive 24 hour ambulatory monitoring of aortic wave reflection and arterial stiffness by a novel oscillometric device: the first feasibility and reproducibility study. *Int J Cardiol*. 2013;169(1):57-61. doi:10.1016/J.IJCARD.2013.08.079

17. Vaios V, Georgianos PI, Vareta G, et al. Age dependence of brachial cuff-based ambulatory PWV in end-stage kidney disease patients undergoing long-term peritoneal dialysis. *Perit Dial Int*. 2022;42(1):65-74. doi:10.1177/0896860821996927

18. EV H, AE J, Z L, C B, A C, M I. Updated and revised normal values of aortic pulse wave velocity in children and adolescents aged 3-18 years. *J Hum Hypertens*. 2021;35(7):604-612. doi:10.1038/S41371-020-0374-9

19. Omboni S, Posokhov IN, Kotovskaya Y v., Protogerou AD, Blacher J. Twenty-Four-Hour Ambulatory Pulse Wave Analysis in Hypertension Management: Current Evidence and Perspectives. *Current Hypertension Reports*. 2016;18(10). doi:10.1007/s11906-016-0681-2

20. NB K, MU G, SG G, SS D. Effect of age and Blood Pressure on Surrogate Markers of Atherosclerosis in Patients with Type 2 Diabetes Mellitus. *J Clin Diagn Res*. 2014;8(6). doi:10.7860/JCDR/2014/7859.4438

21. S S, K K, T N, K C, D T, V K. Ambulatory hemodynamic patterns, obesity, and pulse wave velocity in children and adolescents. *Pediatr Nephrol*. 2020;35(12):2335-2344. doi:10.1007/S00467-020-04694-1

22. AT C, AA P, KC H, GG S, C P, AM D. Obesity and arterial stiffness in children: systematic review and meta-analysis. *Arterioscler Thromb Vasc Biol*. 2015;35(4):1038-1044. doi:10.1161/ATVBAHA.114.305062

23. AT C, KC H, C P, GG S, AM D. Childhood obesity and cardiovascular dysfunction. *J Am Coll Cardiol*. 2013;62(15):1309-1319. doi:10.1016/J.JACC.2013.07.042

24. F D, Y C, K B, W O, P F. Increased rate of arterial stiffening with obesity in adolescents: a five-year follow-up study. *PLoS One*. 2013;8(2). doi:10.1371/JOURNAL.PONE.0057454

25. S T, Y B, T Ü, Y T, U E, B Ç. Evaluation of arterial stiffness in children with type 1 diabetes using the oscillometric method. *J Diabetes Complications*. 2016;30(5):864-867. doi:10.1016/J.JDIACOMP.2016.03.012

26. Ntineri A, Kollias A, Bountzona I, et al. Twenty-four-hour ambulatory central blood pressure in adolescents and young adults: association with peripheral blood pressure and preclinical organ damage. *J Hypertens*. 2020;38(10):1980-1988. doi:10.1097/HJH.0000000000002518

27. PS L, M KJ, A A, et al. Pregnancy and birth cohort resources in europe: a large opportunity for aetiological child health research. *Paediatr Perinat Epidemiol*. 2013;27(4):393-414. doi:10.1111/PPE.12060

28. L CC, AC A, F S, et al. Decreased renal function in overweight and obese prepubertal children. *Pediatr Res*. 2015;78(4):436-444. doi:10.1038/PR.2015.130

29. Durão C, Severo M, Oliveira A, et al. Evaluating the effect of energy-dense foods consumption on preschool children's body mass index: a prospective analysis from 2 to 4 years of age. *Eur J Nutr*. 2015;54(5):835-843. doi:10.1007/S00394-014-0762-4

30. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ*. 2007;85(9):660-667. doi:10.2471/BLT.07.043497

31. N M, P B, G B, et al. Guidelines for the ethical conduct of medical research involving children. Royal College of Paediatrics, Child Health: Ethics Advisory Committee. *Arch Dis Child*. 2000;82(2):177-182. doi:10.1136/ADC.82.2.177

32. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. *BMJ*. 2012;345(7876). doi:10.1136/BMJ.E4759

33. Lona G, Hauser C, Köchli S, et al. Association of blood pressure, obesity and physical activity with arterial stiffness in children: a systematic review and meta-analysis. *Pediatr Res*. 2022;91(3):502-512. doi:10.1038/S41390-020-01278-5

34. Çelik A, Özçetin M, Yerli Y, et al. Increased aortic pulse wave velocity in obese children. *Turk Kardiyoloji Dernegi arsivi : Turk Kardiyoloji Derneginin yayin organidir*. 2011;39(7):557-562. doi:10.5543/TKDA.2011.01694

35. Dangardt F, Osika W, Volkmann R, Gan LM, Friberg P. Obese children show increased intimal wall thickness and decreased pulse wave velocity. *Clin Physiol Funct Imaging*. 2008;28(5):287-293. doi:10.1111/J.1475-097X.2008.00806.X

36. Lurbe E, Torro I, Garcia-Vicent C, Alvarez J, Fernández-Fornoso JA, Redon J. Blood pressure and obesity exert independent influences on pulse wave velocity in youth. *Hypertension*. 2012;60(2):550-555. doi:10.1161/HYPERTENSIONAHA.112.194746

37. AE J, EV H, M I, et al. Childhood Obesity: Does it Have Any Effect on Young Arteries? *Front Pediatr*. 2020;8. doi:10.3389/FPED.2020.00389

38. GS S, A K, PP G, J P, LG R. Ambulatory arterial stiffness index, pulse pressure and pulse wave velocity in children and adolescents. *Hypertens Res*. 2010;33(12):1272-1277. doi:10.1038/HR.2010.178

39. Stabouli S, Kollios K, Nika T, Chrysaidou K, Tramma D, Kotsis V. Ambulatory hemodynamic patterns, obesity, and pulse wave velocity in children and adolescents. *Pediatr Nephrol*. 2020;35(12):2335-2344. doi:10.1007/S00467-020-04694-1

40. Luzardo L, Lujambio I, Sottolano M, et al. 24-h ambulatory recording of aortic pulse wave velocity and central systolic augmentation: a feasibility study. *Hypertens Res*. 2012;35(10):980-987. doi:10.1038/HR.2012.78

41. Hvidt KN, Olsen MH, Holm JC, Ibsen H. Obese children and adolescents have elevated nighttime blood pressure independent of insulin resistance and arterial stiffness. *Am J Hypertens*. 2014;27(11):1408-1415. doi:10.1093/AJH/HPU055

Table I. Demographic, anthropometric, and cardiovascular variables, in nonoverweight and overweight/obesity groups, separately.

	WHO BMI z-score classification		
	Nonoverweight	Overweight/obesity	
	n=77	n= 41	*p*
Demography and anthropometry			
Age (months)	170.8 ± 2.28	170.90 ± 2.13	0.746
Male sex	44 (57.1%)	20 (48.8%)	0.385
Weight (Kg)	53.8 ± 6.7	72.25 ± 11.65	< 0.001
Height (cm)	165.1 ± 7.8	165.30 ± 7.82	0.907
BMI	19.7 ± 1.9	26.35± 3.12	< 0.001
24-h ambulatory blood pressure			
24-hour systolic BP (mmHg)	111 ± 7	114 ± 6	0.079
z-score	-0.59 ± 0.91	-0.23 ± 0.70	0.028
24-hour diastolic BP (mmHg)	65 ± 5	66 ± 5	0.173
z-score	-0.52 ± 1.00	-0.25 ± 0.83	0.138
Daytime systolic BP (mmHg)	113 ± 8	116 ± 6	0.023
z-score	-0.91 ± 0.90	-0.47 ± 0.72	0.008
Daytime diastolic BP (mmHg)	67 ± 6	68 ± 5	0.132
z-score	-0.93 ± 0.93	-0.69 ± 0.76	0.149
Nighttime systolic BP (mmHg)	108 ± 7	108 ± 7	0.803
z-score	0.39 ± 0.94	0.52 ± 0.77	0.461
Nighttime diastolic BP (mmHg)	60 ± 5	61 ± 6	0.344
z-score	0.64 ± 0.87	0.84 ± 0.96	0.243
Hypertension	25 (32.5%)	19 (46.3%)	0.138
Absence of dipping pattern (mmHg)	54 (70.1%)	24 (30.8%)	0.205
Laboratorial parameters			
Total cholesterol (mg/dL)	148.3 ± 33.1	146.6 ± 25.6	0.774
LDL cholesterol (mg/dL)	85.1 ± 25.3	87.1 ± 21.8	0.676
HDL cholesterol (mg/dL)	51.8 ± 9.0	46.5 ± 6.5	0.002
Triglycerides (mg/dL)	66.6 ± 27.9	64.9 ± 22.2	0.731
Fasting glucose (mg/dL)	86.6 ± 5.9	86.3 ± 6.9	0.846
Fasting insulin (μIU/mL)	11.2 ± 4.4	13.7 ± 5.1	0.011
HOMA-IR	2.41 ± 1.0	2.93 ± 1.2	0.016
hs-CRP (mg/L)	0.2 (0.1-0.5)	0.5 (0.2-0.9)	0.003

The values presented are mean ± standard deviation, median (25^{th}-75^{th} percentiles), or n (%). The BMI classes are according to the WHO classification for BMI z-score values[30].

BMI, body mass index; BP, blood pressure; LDL, low density lipoprotein; HDL, high density lipoprotein; HOMA-IR – homeostasis model assessment of insulin resistance; hs-CRP, high sensitivity C-reactive protein.

Table II. Accuracy and bias of carotid-femoral pulse wave velocity compared to pulse wave analysis by ambulatory brachial cuff-based oscillometry, in nonoverweight and overweight/obesity adolescents.

	Total		Daytime		Nighttime	
	Nonoverweight	Overweight/ obesity	Nonoverweight	Overweight/ obesity	Nonoverweight	Overweight/ obesity
cf-PWV, mean ± SD	4.53 ± 0.23*	4.61 ± 0.20*	4.57 ± 0.21*	4.67 ± 0.20*	4.44. ± 0.26*	4.47 ± 0.25*
PWA – cf-PWV, mean ± SD	1.55 ± 0.93	2.10 ± 1.18	1.51 ± 0.93	2.03 ± 1.21	1.64 ± 0.93	2.24 ± 1.15
Accuracy 10%, %	13.0	2.4	14.3	2.4	11.7	4.9
Accuracy 30%, %	67.5	53.7	68.8	58.5	59.7	39.0
Accuracy 50%, %	98.7	97.6	98.7	97.6	98.7	97.6
Correlation coefficient between cf-PWV and PWA	-0.066	0.252	-0.074	0.130	0.001	0.366**

The nonoverweight group includes children with thinness and normal weight and the overweight/obesity group includes children with overweight or obesity, according to the WHO classification for BMI z-score[30].

* p<0.001, Paired t-test in comparison with cf-PWV.

** p<0.05, Pearson correlation.

cf-PWV, carotid-femoral pulse wave velocity; PWA, pulse wave analysis by ambulatory brachial cuff-based oscillometry.

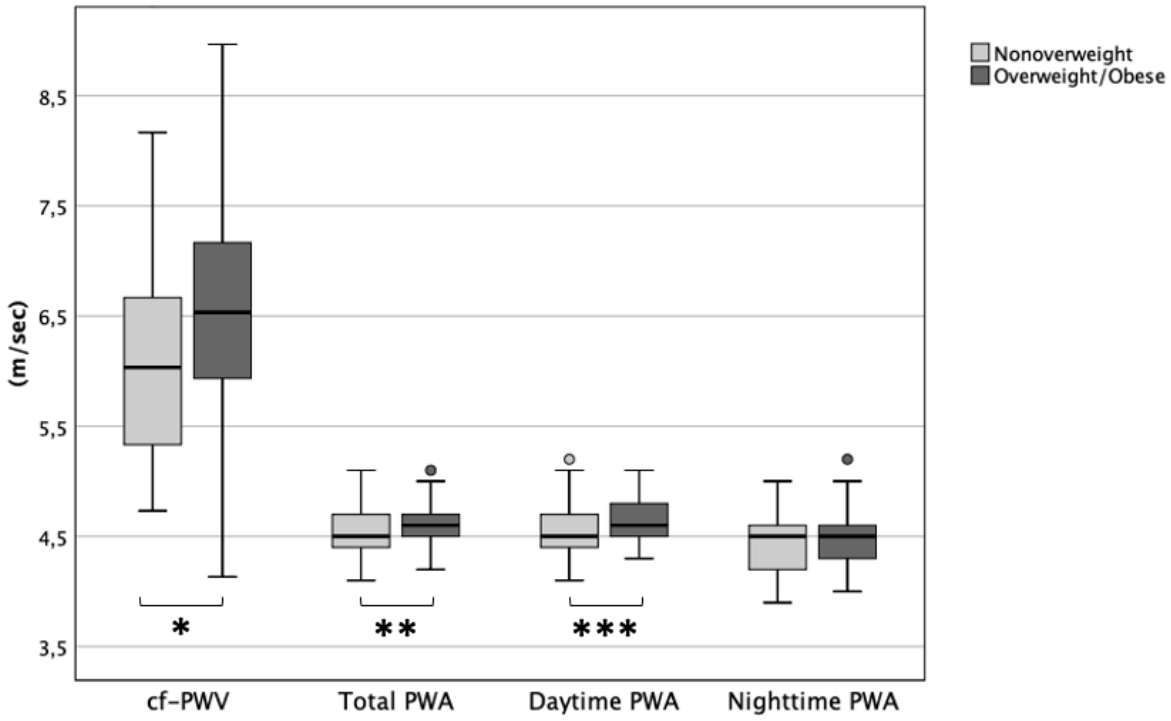


Figure 1. Comparison of carotid-femoral pulse wave velocity and pulse wave analysis by ambulatory brachial cuff-based oscillometry, in nonoverweight and in overweight/obese adolescents.

The BMI classes are according to the WHO classification for BMI z-score values[30].

* p=0.005.

** p=0.038.

*** p=0.008.

cf-PWV, carotid-femoral pulse wave velocity; PWA, pulse wave analysis by ambulatory brachial cuff-based oscillometry.

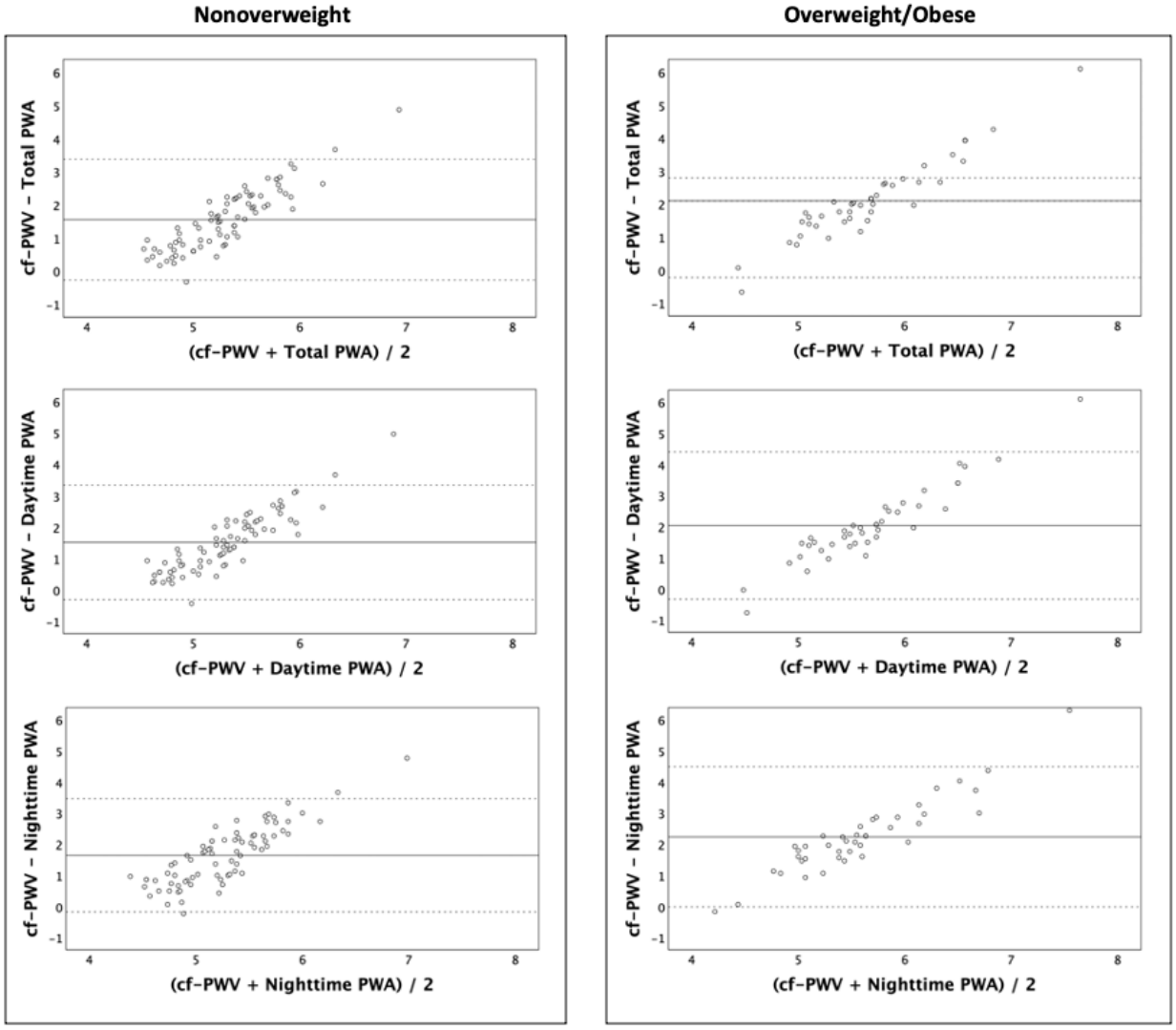


Figure 2. Bland-Altman plots of the carotid-femoral pulse wave velocity in comparison of pulse wave analysis by ambulatory brachial cuff-based oscillometry (total, daytime, and nighttime), for nonoverweight and overweight/obese subjects.

The horizontal full line represents the mean difference between cf-PWV and PWA, and the horizontal dashed lines the limits of agreement.

The BMI classes are according to the WHO classification for BMI z-score values[30].

cf-PWV, carotid-femoral pulse wave velocity; PWA, pulse wave analysis by ambulatory brachial cuff-based oscillometry.

INSTITUTO DE **CIÊNCIAS BIOMÉDICAS ABEL SALAZAR**