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Arterial compliance measurements in Slovenian children and adolescents

Meritve podajnosti arterij pri slovenskih otrocih in mladostnikih

Katarina Čas,[1] Irena Cossutta,[2] Maruša Esih,[3] Petra Povalej Bržan,[3,4] Nataša Marčun Varda[5]

[1] Slovenj Gradec General Hospital, Slovenj Gradec, Slovenia
[2] University Medical Centre Maribor, Maribor, Slovenia
[3] Faculty of Medicine, Univerity of Maribor, Maribor, Slovenia
[4] Faculty of Electrical Engineering and Computer Science, University of Maribor, Maribor, Slovenia
[5] Department of Paediatrics, University Medical Centre Maribor, Maribor, Slovenia

Correspondence/ Korespondenca:
Maruša Esih, e: esih.marusa@gmail.com

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Abstract

Background: In recent years, the occurrence of cardiovascular risk factors in Slovenian children has been increasing. Pulse wave velocity (PWV) measurement is a non-invasive technique that could contribute to the assessment of cardiovascular disease risk in healthy children for preventive purposes. The aim of this pilot study is to gain reference values for PWV in children, with the purpose of long-term assessment of cardiovascular risk.

Methods: Between April 2018 and June 2019, PWV measurements were performed in 150 children from elementary schools and high-school students in the Maribor area. Every age group consisted of children without associated diseases that could have an impact on PWV. The percentile diagram was outlined with LMS methodology and the curves defined with the function based on "BCCGo" distribution.

Results: We have confirmed that PWV values rise with age (rho = 0.387; $p < 0.001$). Based on the information gathered, we used the LMS method to calculate percentile values of PWV according to age with a graphic presentation. Comparing PWV values, we found that they differ statistically ($H = 23.062$; $p < 0.001$). We also found out that the ratio between systolic and diastolic blood pressure weakly negatively correlates with PWV (rho values = -0.218; $p = 0.043$).

Conclusions: In this pilot study, preliminary age-dependent pediatric reference values of PWV were determined, and the usefulness of the method for preventive purposes due to its non-invasiveness and simplicity was confirmed. Although the results are promising, testing on a larger sample of subjects is necessary with the aim of defining national reference values and using this method in monitoring the cardiovascular health of the Slovenian pediatric population.

Izvleček

Izhodišče: V Sloveniji so pri otrocih dejavniki, ki vplivajo na srčno-žilno ogroženost, v zadnjih letih v porastu. Merjenje hitrosti pulznega vala (PWV) je neinvazivna oblika merjenja srčno-žilne ogroženosti, ki bi se lahko uporabljala za spremljanje ogroženih in navidezno zdravih otrok v preventivne namene. Namen pilotne raziskave je pridobiti referenčne razpone vrednosti PWV pri otrocih, da bi lahko učinkovito dolgoročno spremljali njihovo srčno-žilno ogroženost.

Metode: Med aprilom 2018 in junijem 2019 smo pri 150 otrocih osnovnih ter srednjih šol v Mariboru in okolici izmerili PWV. Za posamezno starostno skupino smo izbrali vzorec otrok in mladostnikov brez pridruženih bolezni, ki bi lahko vplivale na rezultate meritev. Za meritve PWV smo uporabljali metodo aplanacijske tonometrije SphygmoCor. Percentilni grafikon smo izrisali na osnovi metodologije LMS, percentilne krivulje pa s pomočjo funkcije na osnovi distribucije "BCCGo".

Rezultati: Potrdili smo, da vrednosti PWV s starostjo naraščajo (Rho = 0,387; p < 0,001). Z metodo LMS smo izračunali percentilne vrednosti PWV glede na starost in jih predstavili grafično. Ob primerjavi vrednosti PWV smo ugotovili, da se te po starostnih skupinah statistično značilno razlikujejo (H = 23,062; p < 0,001). Ugotovili smo tudi, da razmerje med sistoličnim in diastoličnim krvnim tlakom šibko negativno korelira s PWV (Rho = -0,218; p = 0,043).

Zaključki: V pilotni raziskavi smo pridobili preliminarne pediatrične referenčne razpone vrednosti PWV po starosti in potrdili, da bi se lahko metoda zaradi neinvazivnosti in enostavnosti uporabljala v preventivne namene. Rezultati so obetavni, vendar je potrebno testirati večji vzorec preiskovancev, da bi opredelili nacionalne referenčne vrednosti za uporabo te metode pri spremljanju srčno-žilnega zdravja slovenske pediatrične populacije.

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1 Introduction

Cardiovascular disease has become the leading cause of death in the developed world. Data from the World Health Organization (WHO) shows that they cause 17,9 million deaths each year, 31 % of all deaths in total (1). Several risk factors, modifiable and nonmodifiable, contribute to the development of cardiovascular disease (2-5). Modifiable risk factors can appear in early childhood and increase the risk for cardiovascular disease in later years. Arterial hypertension has a 3-4 % prevalence among children and adolescents; obesity is even more common, being present in 5-7 % of children and adolescents (2,3). The goal of early detection and management of modifiable risk factors is to discover the children with increased risk for cardiovascular events in adulthood among the population of seemingly healthy children. A precise assessment of global pediatric cardiovascular risk is not currently available. According to the algorithms of individual groups of children with probable cardiovascular risk (e.g. children with hypertension), based on the analogy with adults, we can determine the status of all known cardiovascular risk factors. Based on this, we can assess the individual's overall cardiovascular risk. As the number of risk factors increases, their cardiovascular risk escalates exponentially. There are recommendations for at-risk groups of children that can be used in a clinical setting (5,6).

One of the ways to detect cardiovascular risk is to determine the properties of arterial walls, which can be done by measuring arterial stiffness (7). Numerous studies in adults have shown that arterial stiffness, inversely proportional to arterial compliance, is one of the independent risk factors for prediction of cardiovascular events (8-10). Studies on the pediatric population have shown that cardiovascular risk and cardiovascular system complications increase with reduced arterial compliance (11,12). Compliance is a term that describes the absolute change in volume due to a change in pressure (7,13) and decreases as the human body ages. The decline begins in childhood despite the absence of risk factors (14). We have several methods to measure arterial compliance and measuring pulse wave velocity (PWV) is one of them (7).

The pulse wave is defined as the quotient of the distance between the recording sites, measured over the body surface, and the transit time of the arterial pulse along the analyzed arterial segment (7,15). The observed wave, which is described as the result of the pulse wave measurement consists of the incident pulse wave, generated by ventricular ejection, and the reflected wave. The increase in value means a higher afterload and better perfusion of coronary arteries in diastole (7). Studies have shown that PWV is directly dependent on expressed cardiovascular risk factors, similar to the effect obesity has on higher values of PWV (16).

The purpose of our pilot study is to obtain preliminary normal values of arterial vascular compliance parameters for the population of Slovenian children. Based on our own normal values (we would need a bigger sample of children to achieve relevant data) we could find children with higher cardiovascular risk, such as children with obesity or hypertension, in which studies have already shown higher values compared to healthy controls.

2 Materials and methods

2.1 Determining the studied population

150 healthy subjects participated in the study. We sent an invitation to participate in the study to all primary schools and high schools in the Maribor municipality and the wider region. The main inclusion criterion was age between 8 and 18 years. Healthy children without previously known chronic diseases – obesity, hypertension, renal insufficiency and diabetes – were included in the study. Finding these diseases in the individual's medical history was an exclusion criterion. We performed measurements of body height, weight and blood pressure in all enrolled individuals. We obtained consent from the Medical Ethics Committee of the University Medical Centre Maribor on ethical acceptability, application number UKC-MB-KME-10/18.

2.2 Description of methods used

We used the method of applanation tonometry with the SphygmoCor device for conducting PWV measurements. It is a system that assesses arterial stiffness with the SCOR-Vx, SCOR-Px and SCOR-Mx software (At Cor Medical, Australia) (17). In addition to this device we also used computers, printers, semi-automatic and hand-held sphygmomanometers, measuring tape, a weighing scale and electrodes as research equipment. Blood pressure measurement was performed according to measurement recommendations, either semi-automatic or with a hand-held sphygmomanometer (18). The choice of measuring device was dependent on our ability to borrow a semi-automatic blood pressure monitor, which was not available at all times. We included children who had, based on a single measurement, normal blood pressure for their sex and height. Similarly, we also included only children with a normal body mass index (BMI) for their age (19).

The measurements with the SphygmoCor device were performed by only one researcher in primary schools and high schools our enrolled population visited. We performed one measurement per subject, but we repeated it if the program calculated too large an absolute error result.

We gathered the following data for each subject: birth date, sex, systolic and diastolic pressure, body weight, body height, proximal and distal distance, and for each subject we calculated the BMI. The proximal distance was defined as the length between the upper edge of the sternum (suprasternal notch) and the tragus. The distal distance was defined as the length between the suprasternal notch and the wrist. The lengths represented the arterial path distances.

Applanation tonometry is a noninvasive method which enables the measurement of the difference between systolic and diastolic pressure of a surface artery and thus of PWV. A micromanometer is laid onto the skin above the artery and enables measurements of the pulse waveform shape with tonometric sensors. The pulse wave is measured simultaneously with an EKG signal, which enables temporal assesment. We measured the pulse wave of the radial artery on the wrist and the carotid artery on the neck. The SphygmoCor Vx software processes each pulse wave and simultaneously the data from the EKG, so it can calculate the average time difference between the R wave on the EKG and the pressure wave, measured by the tonometer (17).

2.3 Statistical analysis

We analyzed the obtained data with the R programming language. We compared the PWV values between different age groups using the Kruskal-Wallis test and used the Spearman correlation coefficient to check for the relationship between the subject's measured PWV value and their age, blood pressure, the systolic/diastolic blood pressure ratio and absolute measurement error. We assessed the strength of the correlation using Evan's rule (21). Based on the Mann Whitney U test we tested the relationship between sex and PWV. Based on the number and reliability of the measured values we compared blood pressure to PWV values only in older subjects.

Based on the LMS methodology we outlined a percentile growth chart (22), also used by the WHO. We used the »GAMLSS« library in the R programming language (23). The percentile curves were drawn using a function based on »BCCGo« distribution.

3 Results

150 subjects, aged between 8 and 18, participated in the study (Table 1). The median age was 15.4 (interquartile range (IQR) = 6.9 years). Most of the participants (64 %) were female. The median of height and weight was 167 cm (IQR = 11 cm) and 60 kg (IQR = 12 kg).

The average BMI of participants was within normal limits. In the 8-9 age group it was 17.3 kg/m^2 (90th percentile for 8.5-year-old girls 19.65 kg/m^2, and 19.38 kg/m^2 for boys), for the 10-11 age group 17.9 kg/m^2 (90th percentile for 10.5-year-old girls 21.20 kg/m^2, for boys 21.02 kg/m^2), for the 12–13 age group 18.8 kg/m^2 (90th percentile for 12.5-year-old girls 22.91 kg/m^2, for boys 22.64 kg/m^2), for the age group 14–15 years 21.1 kg/m^2 (90th percentile for 14.5-year-old girls 24.35 kg/m^2, for boys 24.05 kg/m^2), for the age group 16–17 years 21.2 kg/m^2 (90th percentile for 16.5-year-old girls 25.02 kg/m^2, for boys 25.18 kg/m^2), for the 18 - year age group 22.1 kg/m^2 (90th percentile for 18-year-old girls 25.28 kg/m^2, for boys 28.78 kg/m^2).

The median of systolic and diastolic pressure was 115 mm Hg (IQR = 16.5 mm

Hg) and 66 mm Hg (IQR = 11.8 mm Hg). The median PWV was 5.65 m/s (IQR = 1.20), and the median of absolute error was 0.50 m/s (IQR = 0.20).

Tables 1 and 2 show the descriptive qualities of the sample and the relationship between observed variables and the measured PWV values.

The results show that age has a statistically significant correlation with the measured values of PWV (Rho = 0.39; p<0,001) (Table 1). When comparing values of PWV in individual age groups (Table 2) we find that PWV values differ statistically significantly (H = 23.062; p<0.001); the lower two age groups have statistically lower values of PWV than the highest two (ages 8–9 vs. 16–17 (p(Dunn) = 0,005); ages 8–9 vs. 18 (p(Dunn) = 0,004); ages 10–11 vs. 16–17 (p(Dunn) = 0,007); 10–11 let vs. 18 (p(Dunn) = 0,004)) (Figure 1).

Based on collected data we calculated the percentile values of PWV depending on age using the LMS method, as shown in Figure 1. A mild rise in PWV values with age can be observed, with the exception of a few deviating values in the youngest group, which are shown in Supplement 1.

The absolute error of performed measurements, which the program itself calculated when it performed each measurement, has a statistically significant correlation with the PWV values (Rho = 0,553; p<0,001). There was no statistically significant correlation between the measured values of PWV and systolic and diastolic blood pressures, but we proved a negative correlation between PWV and the systolic/diastolic blood pressure ratio (Rh0 = -0,218, p = 0.043) (Table 1). The relationship between blood pressure, age

Table 1: Descriptive statistics of investigated parameters and their connection to pulse wave measurements (PWV).

	N	Min	Max	Average value	Median	SD	IQR	Rho	p
Age (years)	150	8.26	18.48	14.39	15.41	3.37	6.94	0.39	**< 0.001**
Weight (kg)	107	27.00	99.00	60.84	60.00	10.97	12.00	0.10	0.288
Height (cm)	107	140.00	193.00	169.33	167.00	9.21	11.00	0.15	0.127
PWV (m/s)	150	4.00	9.30	5.79	5.65	0.95	1.20	/	/
Absolute error (m/S)	146	0.10	1.50	0.49	0.50	0.18	0.20	0.55	**< 0.001**
Systolic blood pressure (mm Hg)	86	93.00	137.00	115.14	115.00	10.43	16.50	0.04	0.704
Diastolic blood pressure (mm Hg)	86	40.00	90.00	66.34	66.00	9.75	11.75	0.15	0.157
Systolic/ diastolic ratio	86	1.32	2.68	1.76	1.74	0.24	0.23	-0.22	**0.044**

N – number of subjects; min – lowest value; max – highest value; SD – standard deviation; IQR – interquartile range; Rho – Spearman correlation coefficient with PWV; p – p value; syst/diast – systolic/diastolic blood pressure

Table 2: Distribution of pulse wave (PWV) measurement in m/s by age group and sex.

	Value	N	Min	Max	Average value	Median	SD	IQR	H	p
Age group	8–9 let	24 (16 %)	4.2	8.1	5.41	5.3	0.94	0.68	23.062 (2)	**< 0.001**
	10–11 let	16 (10.7 %)	4	6.4	5.1	5.15	0.77	1.2		
	12–13 let	20 (13.3 %)	4	7.6	5.72	5.6	1.07	1.53		
	14–15 let	22 (14.7 %)	4.4	7.2	5.82	5.55	0.8	1.18		
	16–17 let	43 (28.7 %)	4.3	8.2	6.03	6.1	0.79	0.85		
	18 let	25 (16.7 %)	4.9	9.3	6.23	6.1	1.03	1.1		
Sex	moški	54 (36 %)	4	8.1	5.73	5.65	0.91	1.18	2720 (1)	0.617
	ženski	96 (64 %)	4	9.3	5.83	5.65	0.97	1.23		

N – number of subjects; min – lowest PWV value; max – highest PWV value; SD – standard deviation; IQR – interquartile range; H – test value (1) Mann Whitney / (2) Kruskal-Wallis; p – p value

and PWV is shown also in Figure 3.

The values of PWV do not have a statistically significant difference based on sex (Table 2). Figure 2 shows the quartile diagrams for PWV values in individual age groups, separated by sex. We can observe slightly higher values of PWV in boys in the 8-9 and 14-15 age groups and a reverse trend in the highest age groups. A statistical comparison isn't of use due to the small sample size.

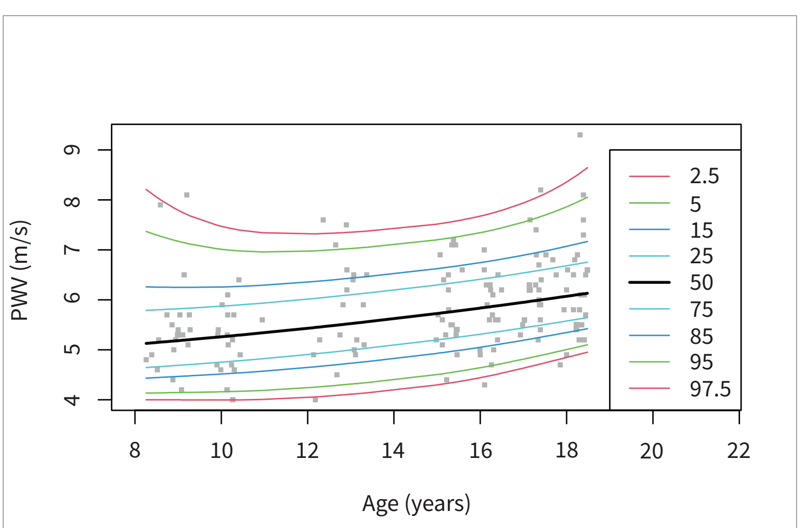

Figure 1: Percentile values of pulse wave velocity (PWV) depending on age, using the LMS method.

4 Discussion

In our study we found that the value of PWV rises with age, similarly to other published research (24). Comparing the values of PWV by age groups, we also found that values of PWV differ statistically significantly by age groups, if we compare the youngest two age groups (8-9 years and 10-11 years) with the oldest (16- 17 years and 18 years).

Arterial hypertension can be present for a long time without symptoms and signs, but it still affects cardiovascular complications and mortality. This is also true for the pediatric population, however, a clinical diagnosis is even harder to make in this age group due to the lack of symptoms. This is why preventive measures for early detection of cardiovascular risk, such as regular measurement of blood pressure and detection of early changes in the cardiovascular system by

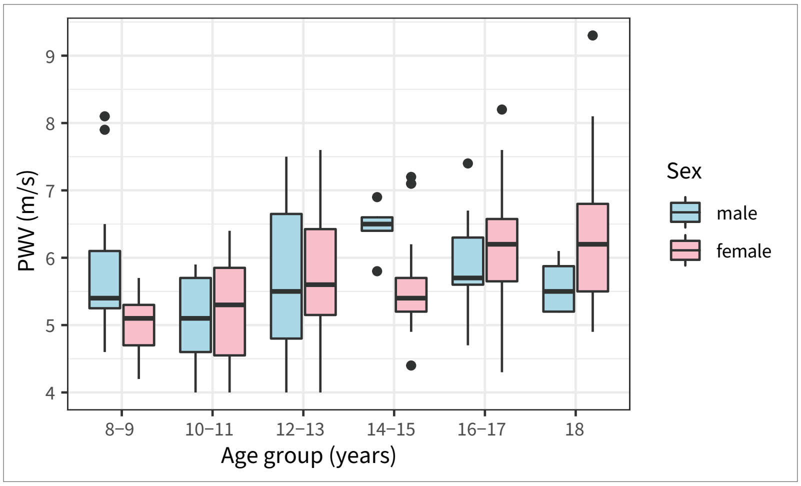

Figure 2: Comparison of the value of pulse wave velocity (PWV) by age group, depending on sex.

methods such as PWV, are so important. The purpose of our pilot study was first to determine the reference range of PWV values of presumably healthy Slovenian children and adolescents to better detect individuals with increased cardiovascular risk.

150 children and adolescents, aged between 8 and 18 years, participated in the study. These are the age groups in which changes, which significantly influence cardiovascular risk, most often appear, especially unhealthy habits, which constitute an important risk factor for future health of the cardiovascular system.

Although our exclusion criteria were obesity and chronic diseases, we cannot exclude the possibility that individual children and adolescents with a subclinical form of one of the chronic diseases, such as hyperlipidemia, were included in the study. We did not measure the laboratory parameters which would confirm this (serum glucose, serum creatinine, lipid fractions) due to the need for venous blood sampling. Included individuals had a normal BMI and blood pressure for their age, sex and height. We have excluded other chronic diseases by talking with the parents of the participating children about possible chronic diseases of their youngster.

Distribution by sex is irregular because of the difficulties of enrolling participants. 64 % of participants were

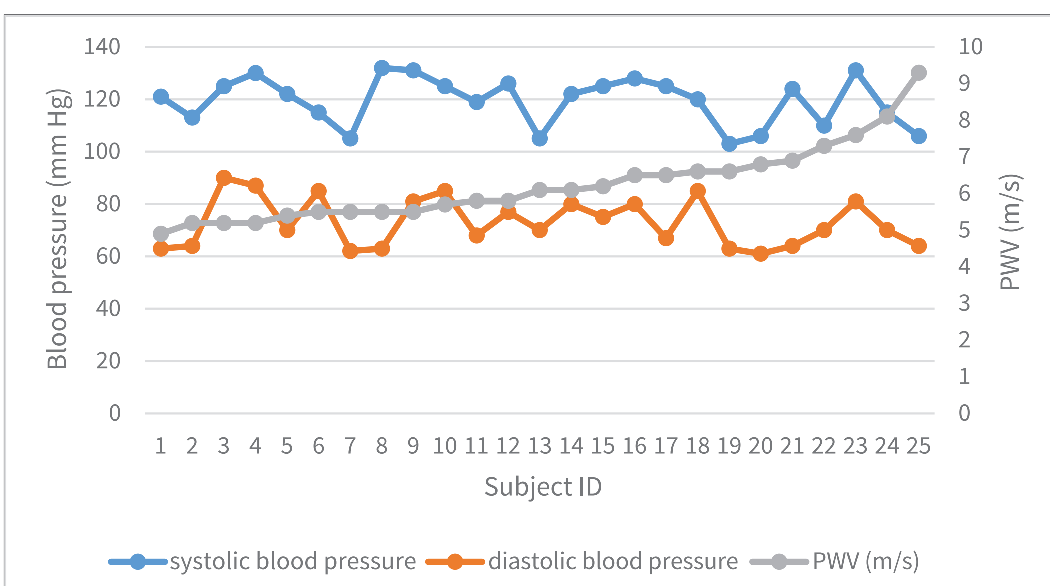

Figure 3: Values of pulse wave velocity (PWV) (m/s) and blood pressure (mm Hg) in 18-year-olds in ascending order based on the measured value of PWV.

female and 36 % were male. We found that PWV values don't differ statistically significantly by sex. Inside individual age groups we found statistically significant differences in PWV between sexes in the youngest age group (8-9 years) and in the 14-15 years age group (Figure 2). We found that boys in these two age groups have statistically significantly higher values of PWV when compared to girls, which was shown for all other age groups in other studies (21). It is interesting that a reverse trend is hinted at in the oldest two age groups, but it is not statistically significant.

Published studies on the effect of blood pressure on PWV have shown that blood pressure and PWV are linked, based on the physiology of the process of the pulse wave transfer (10). For this purpose, we have graphically shown the correlation between PWV and blood pressure for the 18-year-old age group, where no correlation between PWV and systolic and diastolic blood pressure was detected, but there was a correlation between PWV and the systolic/diastolic blood pressure ratio. When measuring blood pressure before the applanation tonometry procedure, we followed the recommendations for correct measurement of blood pressure (18). Because of the different availability of the measuring devices we used both the automatic and hand-held blood pressure monitors, which could have led to differences in measurements.

The obtained measurements were compared with values published by Reusz et al. in June 2010. With the same statistical presentation of results, we compared the 50*th* percentile of each age group and found that the values of PWV are quite different, which speaks in favor of the need to obtain our own normal values of individual populations. The reason for the discrepancy in results is mainly attributed to the many differences in the design of both studies. Reusz et al. used a much larger sample of children and adolescents. They performed measurements with applanation tonometry with the Pulse Pen device, while we used the SphygmoCor applanation tonometer. The location of PWV measurement was above the carotid and femoral arteries in their study, while we measured PWV above the carotid and radial arteries. In the Reusz study they also proved that PWV differs between boys and girls at higher ages, with boys having much higher values of PWV. They also proved that blood pressure values rise linearly with PWV values (25).

Foreign studies (24-26) have demonstrated the usefulness of the PWV measurement method for determining the state of the cardiovascular system in children. Despite its non-invasiveness and relative simplicity, its wide applicability for assessing cardiovascular risk in children and adolescents at the primary level in Slovenia remains questionable. Physicians that perform systematic examinations and are the first to come into contact with the pediatric population do not have the appropriate equipment and knowledge to use applanation tonometry. We see possible problems mainly in financing the purchase of applanation tonometers, the training of providers and standardization of measurements. The disadvantage of this investigation method is also the time required for quality measurement. Perhaps it would make sense to consider introducing one of the commercially available, validated devices that are easier to use in everyday practice, such as Mobil-O-Graph, for preventive purposes, although it also requires standardization and reference values. Last but not least, we also lack a reference method for measuring PWV with which we could confirm the adequacy of measurements and the reliability of the method (7). Some reference values for individual age groups have already been published, but they depend on the specific implementation of the measurement and on the device itself (25,26). In this context, obtaining our own reference values is very important. Our results, as a pilot study, are the basis for achieving this goal.

The weakness of the study is the small sample of individuals on which measurements were performed. In order to be able to present truly representative samples, a larger sample of at least 50 children and adolescents of both sexes for each age group would be needed.

The biggest problem with such research is the unresponsiveness and unwillingness of the respondents and their caregivers to participate. The latter also contributed to the uneven distribution of subjects between the sexes, as more girls than boys responded to the invitation to the study, which is probably the reason why we did not prove the dependence of PWV measurements on sex. We also did not measure the cardiovascular biochemical blood parameters in participants, such as serum glucose and lipid concentrations, as this would unduly burden them.

The goal of the study was to measure the parameters of arterial wall compliance in healthy children to obtain normal values. In its presented form, the study was a pilot study, which needs to be upgraded with a larger sample of children of different ages in order to obtain relevant normal values. We need the latter to diagnose and monitor at-risk children. If we had normal PWV parameters for a healthy population we could use the applanation tonometry as a screening method for cardiovascular risk of the general paediatric population (currently this is not a global practice). With such a screening method we could identify individuals with higher risk among children and adolescents with higher values who are otherwise asymptomatic or unrecognized as endangered (i.e. healthy) and monitor them more intensively during childhood and adolescence and treat them.

In this way, preventive action could be taken at an early stage.

5 Conclusion

Our pilot study determined the preliminary ranges of normal PWV values with respect to age groups and confirmed that PWV values increase with age. The authors hope that this pilot study will be the basis for further research in the direction of defining national PWV reference values and introducing applanation tonometry into clinical practice, which will require an increase in the sample size of participating subjects.

Supplement 1: Percentile values of pulse wave measurement (PWV) according to age, using the LMS method.

	Age (in years)	C2.5	C5	C15	C25	C50	C75	C85	C95	C97.5
1	8	3.998674	4.129372	4.422825	4.630189	5.109561	5.775818	6.26245	7.447932	8.388576
2	9	3.998876	4.145139	4.467315	4.689329	5.183	5.821615	6.250022	7.172877	7.794905
3	10	3.995828	4.160564	4.515303	4.752921	5.260418	5.873389	6.257338	7.013509	7.472231
4	11	4.007248	4.189511	4.573721	4.824641	5.343107	5.938038	6.293762	6.958102	7.338931
5	12	4.046876	4.241771	4.64635	4.905984	5.431089	6.015221	6.355403	6.973304	7.317704
6	13	4.111479	4.314272	4.731159	4.995817	5.524361	6.10207	6.433719	7.027465	7.35373
7	14	4.19238	4.400296	4.824937	5.092616	5.622913	6.19625	6.522543	7.101732	7.417382
8	15	4.298285	4.506068	4.93024	5.197513	5.726818	6.298888	6.624402	7.202154	7.517008
9	16	4.442645	4.641503	5.051408	5.312503	5.836196	6.412368	6.74503	7.344211	7.675497
10	17	4.633127	4.813066	5.192034	5.439476	5.9512	6.540058	6.893423	7.55665	7.939095
11	18	4.847731	5.005575	5.346654	5.576409	6.071938	6.682021	7.072231	7.863001	8.359511

References

1. World Health Organization. Cardiovascular diseases (CVDs). Geneva: WHO; 2019 [cited 2019 Aug 7]. Available from: https://who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
2. Hertiš T, Petek T, Marčun Varda N. The prevalence of elevated blood pressure in a sample of Slovene children and adolescents: a pilot study. Zdrav Varst. 2018;57(2):72-80. DOI: 10.2478/sjph-2018-0010 PMID: 29651318
3. Gabrijelčič Blenkuš M. Prekomerna prehranjenost in debelost pri otrocih in mladostnikih v Sloveniji. Gradivo za Odbor DZ RS za zdravstvo. Ljubljana: Inštitut za varovanje zdravja Republike Slovenije; 2013 [cited 2018 May 8]. Available from: https://www.nijz.si/sites/www.nijz.si/files/uploaded/prekomerna_prehranjenost_in_debelost_pri_otrocih_in_mladostnikih_v_slo.pdf.
4. Gorjup V, Kamenik B, Kanič V, Lainščak M, Letonja M, Lobnik A, et al., eds. Izbrana poglavja o srčno-žilnih boleznih. Maribor: Medicinska fakulteta; 2015.
5. Falkner B. Hypertension in children and adolescents: epidemiology and natural history. Pediatr Nephrol. 2010;25(7):1219-24. DOI: 10.1007/s00467-009-1200-3 PMID: 19421783
6. de Ferranti SD, Steinberger J, Ameduri R, Baker A, Gooding H, Kelly AS, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association. Circulation. 2019;139(13):e603-34. DOI: 10.1161/CIR.0000000000000618 PMID: 30798614
7. London GM, Pannier B. Arterial functions: how to interpret the complex physiology. Nephrol Dial Transplant. 2010;25(12):3815-23. DOI: 10.1093/ndt/gfq614 PMID: 20947536
8. Vlachopoulos C, Terentes-Printzios D, Laurent S, Nilsson PM, Protogerou AD, Aznaouridis K, et al. Association of estimated pulse wave velocity with survival: a secondary analysis of SPRINT. JAMA Netw Open. 2019;2(10):e1912831. DOI: 10.1001/jamanetworkopen.2019.12831 PMID: 31596491
9. Dasgupta K, Rosenberg E, Joseph L, Trudeau L, Garfield N, Chan D, et al. Carotid femoral pulse wave velocity in type 2 diabetes and hypertension: capturing arterial health effects of step counts. J Hypertens. 2017;35(5):1061-9. DOI: 10.1097/HJH.0000000000001277 PMID: 28129250
10. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, et al. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. J Am Coll Cardiol. 2014;63(7):636-46. DOI: 10.1016/j.jacc.2013.09.063 PMID: 24239664
11. Urbina EM. Abnormalities of vascular structure and function in pediatric hypertension. Pediatr Nephrol. 2016;31(7):1061-70. DOI: 10.1007/s00467-015-3188-1 PMID: 26275663

12. Močnik M, Nikolič S, Varda NM. Arterial compliance measurement in overweight and hypertensive children. Indian J Pediatr. 2016;83(6):510-6. DOI: 10.1007/s12098-015-1965-2 PMID: 26666902
13. London GM, Marchais SJ, Guerin AP, Pannier B. Arterial stiffness: pathophysiology and clinical impact. Clin Exp Hypertens. 2004;26(7-8):689-99. DOI: 10.1081/CEH-200031982 PMID: 15702623
14. Lunder M, Janić M, Skarlovnik A, Turk M, Habjan S, Šabovič M. Staranje arterijskega sistema. Zdrav Vestn. 2012;81:653-63.
15. Guyton AC, Hall JE. Textbook of medical physiology. 11th ed. Edinburg: Churchill Livingstone; 2006.
16. Hudson LD, Rapala A, Khan T, Williams B, Viner RM. Evidence for contemporary arterial stiffening in obese children and adolescents using pulse wave velocity: A systematic review and meta-analysis. Atherosclerosis. 2015;241(2):376-86. DOI: 10.1016/j.atherosclerosis.2015.05.014 PMID: 26071661
17. AtCor MedicalSphygmoCor XCEL. Naperville: AtCor Medical Pty Ltd; 2018 [cited 2017 Dec 16]. Available from: http://atcormedical.com/healthcare-professionals/products.
18. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens. 2016;34(10):1887-920. DOI: 10.1097/HJH.0000000000001039 PMID: 27467768
19. Kromeyer-Hauschild K, Wabitsch M, Kunze D, Geller F, Geiß HC, Hesse V, et al. Perzentile für den Body-mass-Index für das Kindes- und Jugendalter unter Heranziehung verschiedener deutscher Stichproben. Monatsschr Kinderheilkd. 2001;149(8):807-18. DOI: 10.1007/s001120170107
20. Papaioannou TG, Stamatelopoulos KS, Gialafos E, Vlachopoulos C, Karatzis E, Nanas J, et al. Monitoring of arterial stiffness indices by applanation tonometry and pulse wave analysis: reproducibility at low blood pressures. J Clin Monit Comput. 2004;18(2):137-44. DOI: 10.1023/B:JOCM.0000032809.71793.b8 PMID: 15362275
21. Wuensch K, Evans J. Straightforward statistics for the behavioral sciences. J Am Stat Assoc. 1996;91(436):1750. DOI: 10.2307/2291607
22. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. Stat Med. 1992;11(10):1305-19. DOI: 10.1002/sim.4780111005 PMID: 1518992
23. Rigby RA, Stasinopoulos DM. Generalized additive models for location, scale and shape. Appl Stat. 2005;54(3):507-54. DOI: 10.1111/j.1467-9876.2005.00510.x
24. Kis E, Cseprekál O, Kerti A, Salvi P, Benetos A, Tisler A, et al. Measurement of pulse wave velocity in children and young adults: a comparative study using three different devices. Hypertens Res. 2011;34(11):1197-202. DOI: 10.1038/hr.2011.103 PMID: 21796122
25. Reusz GS, Cseprekal O, Temmar M, Kis E, Cherif AB, Thaleb A, et al. Reference values of pulse wave velocity in healthy children and teenagers. Hypertension. 2010;56(2):217-24. DOI: 10.1161/HYPERTENSIONAHA.110.152686 PMID: 20566959
26. Hidvégi EV, Illyés M, Benczúr B, Böcskei RM, Rátgéber L, Lenkey Z, et al. Reference values of aortic pulse wave velocity in a large healthy population aged between 3 and 18 years. J Hypertens. 2012;30(12):2314-21. DOI: 10.1097/HJH.0b013e328359562c PMID: 22990356