NON-INVASIVE OSCILLOMETRIC ASSESSMENT OF THE ARTERIAL PULSE PRESSURE WAVE IN CHILDREN AND ADOLESCENTS

PhD Thesis

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1. INTRODUCTION

The non-invasive assessment of the arterial function is a widely accepted method for stratifying individual cardiovascular risk and for detecting target organ damage in adults. Moreover, we have an increasing volume of evidence concerning impaired vascular function in different diseases in paediatric population. Unfortunately, only few studies with relatively small populations are available which detail the reference values of the arterial function parameters in children and adolescents, because the non-invasive techniques applyied in adults are limited in use in paediatric patients. The aim of our study, therefore, was to determine the reference values of the arterial function parameters in a large healthy population which showed a fair balance in terms of age. We intended to apply a newly developed, invasively validated occlusive-oscillometric device (Arteriograph®, TensioMed Ltd., Budapest, Hungary), which is portable due to its small size, easy-to-use, the measuring procedure is user-independent, fast and painless, which allowed us to expand measurement even into a very young (<6 years) population and within a daily clinical routine.

2. AIMS

a./ To determine the reference values of the aortic pulse wave velocity (PWV_{ao}) in a large healthy population with normal body mass index (BMI) and systolic and diastolic blood pressure aged between 3-18 years, to analyse the physiological background of the observed age-related changes.

b./ To determine the reference values of the aortic augmentation index (Aix_{ao}) and the simultaneously measured return time of the systolic pulse wave (RT) in relation to body height in order to prove the determining role of the body height in characteristics of the Aix_{ao} in childhood.

c./ To determine the reference values of the central (aortic) systolic blood pressure (SBP_{ao}), and to compare them with the reference values of the simultaneously measured peripheral (brachial) systolic blood pressure (SBP_{brach}), to analyze the the background of the age-related changes.

d./ To compare the central (SBP_{ao}) and the peripheral (SBP_{brach}) systolic blood pressure maesured in patients of juvenile essential hypertension (JEH) and in healthy children and adolescents.

3. METHODS, SUBJECTS AND PATIENTS

3,374 apparently healthy Caucasian subjects from Hungary (1,802 boys and 1,572 girls) aged 3-18 years, without any medication, having body mass index and systolic and diastolic blood pressure within the 3^{th} and 97^{th} percentile, as established by the relevant guidelines, were recruited from nursery, elementary and secondary schools.

Data of 217 patients with JEH (173 boys, average age: 15.1±2.2 years, height: 174.4±12.8 cm, weight: 83.1±20.4 kg; 44 girls, average age: 14.3±2.7 years, height: 163.3±13.3 cm, weight: 81.6±20.8 kg) were compared with data of 217 sex- and age matched children and adolescents (173 boys, average age: 15.1±2.2 years, height: 169.4±13.8 cm, weight: 57.9±13.4 cm; 44 girls, average age: 14.3±2.7 years, height: 160.3±12.4 cm, weight: 52.2±13.8 cm).

The arterial function was assessed by Arteriograph. The operating procedure did not, in practice, differ from a standard digital blood pressure measurement. The method is based on the physiological fact that the early (P_1) systolic pulse pressure wave of the aorta generated by the left ventricule ejection, travels along the aorta and is reflected from the area of the aortic bifurcatio, and comes back as a secondary pulse wave (P_2) into the aortic root even in the systole and augments to the primary wave (Figure 1). Occluding the brachial artery by pressurizing the cuff 35-40 mmHg above the actual SBP_{brach} creates easily distinguished, pronounced pressure peaks (P_1, P_2) in the cuff. The time lapses between P_1 and P_2 peaks (Δt) are eaqual to the travel time of the aortic pressure wave from the aortic root to the bifurcation and back. By halving this time and measuring the sternal notch – pubic bone distance (wich is rather close to the true aortic length), the PWV_{ao} can be calculated: PWV_{ao}= Jug-Sy/[Δt/2]. The Aix_{ao} can be calculated as [P2-P1/PP]x100. The pulse pressure in the aortic root (PP) are equal the amplitude of the higher pulse pressure peak (in that case is P_1), the central systolic blood pressure (SBP_{ao}) created as the mean arterial pressure (MAP) and pulse pressure (PP).

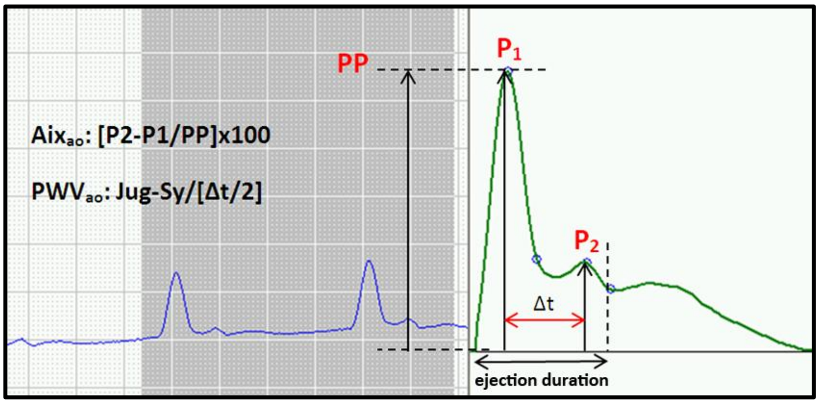

Figure 1

Original pulse pressure curve registered by Arteriograph. P_1; amplitude of the primary pulse pressure wave, P_2; amplitude of the reflected pulse pressure wave, PP; pulse pressure, Aix_{ao}; aortic augmentation index, PWV_{ao}; aortic pulse pressure wave, Jug-Sy; distance between jugulum and symphysis, Δt; return time.

The measurements were taken place with the participant in a calm, supine position after 2-3 minutes of rest. The juvenile essential hypertension was diagnosed lege artis, as the relevant guideline recommended.

Data are reported as mean and SD for continuous data. For data comparison, a Student's *t*-test was used after checking that the assumption of normality was met. A significance level of 0.05 was used for statistical tests. Statistical analysis was performed with the SPSS 15.0 statistical package (SPSS Inc., Chicago, Illinois, USA). Reference percentile curves of PWV_{ao}, Aix_{ao}, RT, SBP_{ao}, SBP_{brach} were obtained with the use of the LMS method, specifically with the LMS Chartmaker software.

To study causal relationships between arterial functional parameters (PWV_{ao}, Aix_{ao}, SBP_{ao}, etc..) and other variables, graphical analyses were used, as multivariate linear regression cannot be applied due to the high multicollinearity among age, anthropetric and hemodynamic parameters.

4. RESULTS

In the examined healthy population both the boys and girls were fairly well balanced in terms of age, whereas 15% of the population was recruited from very young age groups (3-6 years). The patients with JEH were significantly higher and more ponderous, than were the age and sex matched subjects.

a./ Reference values of the PWV_{ao} in a healthy population aged between 3-18 years.

The increase of mean PWV_{ao} turned out to be roughly 1 m/s in both genders from the age of 3 to 18 years, as this parameter increased from 5.5±0.6 to 6.5±0.5 m/s ($p<0.05$) in boys and from 5.6±0.3 to 6.4±0.3 m/s ($p<0.05$) in girls. When comparing the mean PWV_{ao} values in each year between boys and girls, noticible differences were found in the 14-years and 16-year age groups. However, these differences are merely 0.1 and 0.2 m/s, respectively, and so cannot be considered as clinically significant.

Smoothed percentile curves of PWV_{ao} from the 3^{rd} to the 97^{th} for boys and girls are shown in Figure 2.

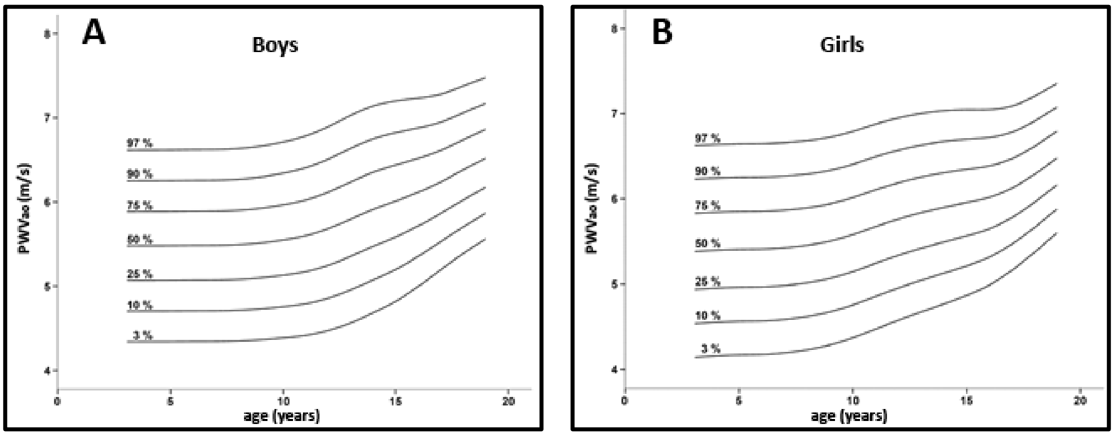

Figure 2

Smoothed percentile curves of PWV_{ao} from 3^{rd} to 97^{th} for boys (A) and girls (B) .

Analysing the curves of the median values of PWV_{ao} in boys and girls, it became clear that the increase was not constant with age, but had more complex dynamics (Figure 2). In both sexes, the PWV_{ao} values exhibit a flat period between 3 and 8 years, with a steeper increase thereafter. The first pronounced increase occured at the age of 12.1 years in boys and 10.4 years in girls.

In Figure 3 we demonstrate the relationship between PWV_{ao}, mean arterial pressure (MAP) and brachial SBP (SBP_{brach}), featuring the median of standardized values of the parameters mentioned in boys and girls. Interestingly, at ages between 3 and 8 years a marked difference was observed in the trend of changes in SBP_{brach}, and MAP versus PWV_{ao}. Although the blood pressure increased continuously, the PWV_{ao} remained practically unchanged in this age range. However, beyond 9 years of age, the blood pressure and aortic stiffness trends basically travelled together.

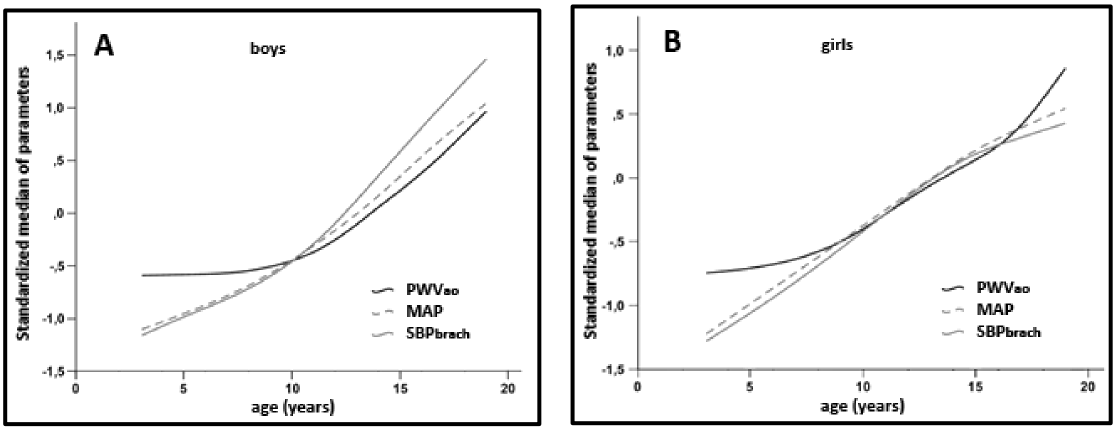

Figure 3

Standardized median curves of aortic pulse wave velocity (PWV_{ao}), mean arterial pressure (MAP) and brachial SBP (SBP_{brach}) related to age for boys (A) and girls (B).

b./ Reference values of the aortic augmentation index (Aix_{ao}) and the simultaneously measured return time of the systolic pulse wave (RT) in relation to body height

The increased aortic augmentation index (Aix_{ao}) observed in infants and small children – which are similar to those measured in adults with different diseases – is a well-known data. This phenomenon is explained by the majority of the authors on the basis of the growing body height. However, this hypothesis still has not been proved directly because in the previous studies the athors measured only the Aix_{ao} and the height of the patients without the return time of the systolic wave reflection (RT) – at least we are not aware of any publication. In the case if the RT is much more shorter in early childhood as at the end of the adolescent age – during this period the body height of the children increases with more than one meter – and also if the RT is increasing proportionally with the body height; we can prove that the growing aortic length plays a decisive role in the age–related physiological decreasing of the Aix_{ao}.

The age-related changes of the Aix_{ao} and RT are shown on Figure 4. There is a remarkably difference regarding Aix_{ao} measured in the early childhood and at the end of puberty. Apparently, the amplitude of the reflected systolic pulse wave (P_2) significantly decreased by the end of the puberty compared to that measured in early childhood; on the other hand, this figure demonstrates that the RT is much more shorter in a small child, than it is in an adolescents.

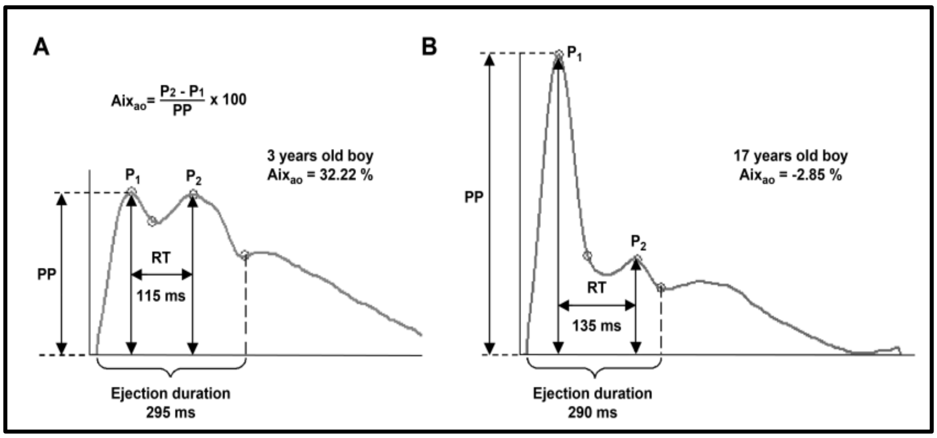

Figure 4.

Original pulse pressure curves registered by Arteriograph in case of 3-years-old (A) and 17-years-old (B) healthy boy.

The above described phenomenon was proved by the measured age-related mean values of Aix_{ao}, as it decreased from 18.6±8.7% to 4.7±4.3% ($p<0.0001$) in boys and from 20.6±11.7% to 8.3±5.0% ($p<0.0001$) in girls, respectively. From the age of 14 the Aix_{ao} were significantly higher in girls ($p<0.02$), and this diffenrence had become even more pronounced from the age of 15 to 18 ($p<0.001$).

Similarly to $Aix_{ao,}$ remarkably changes were observed in RT, which increased from 114.4±17.1 msec to 166.3±20.7 msec ($p<0.0001$) in boys and from 106.2±21.3 msec to 158.2±15.8 msec ($p<0.0001$) in girls between 3 and 18 years of age. Significanct diffenerence between genders was found from the age of 15, RT was higher in boys ($p<0.001$), and this difference had continued to the age of 18 years.

Smoothed reference percentile curves of the Aix_{ao} and the RT from the third to the ninety-seventh are shown on Figure 5. The Aix_{ao} decreased gradually with age in both genders, but this tendency was not constant, it slowed down at the beginning of the puberty significantly. The same phenomenon – with negative prefix – was observed in case of RT, because its increase with age stopped around the puberty. Analyzing the median curves of Aix_{ao} and RT, a difference was found in the timing of these changes between the two genders. The Aix_{ao} tended to decrease with age until around 15 years in boys, and 12 years in girls and then floated thereafter.

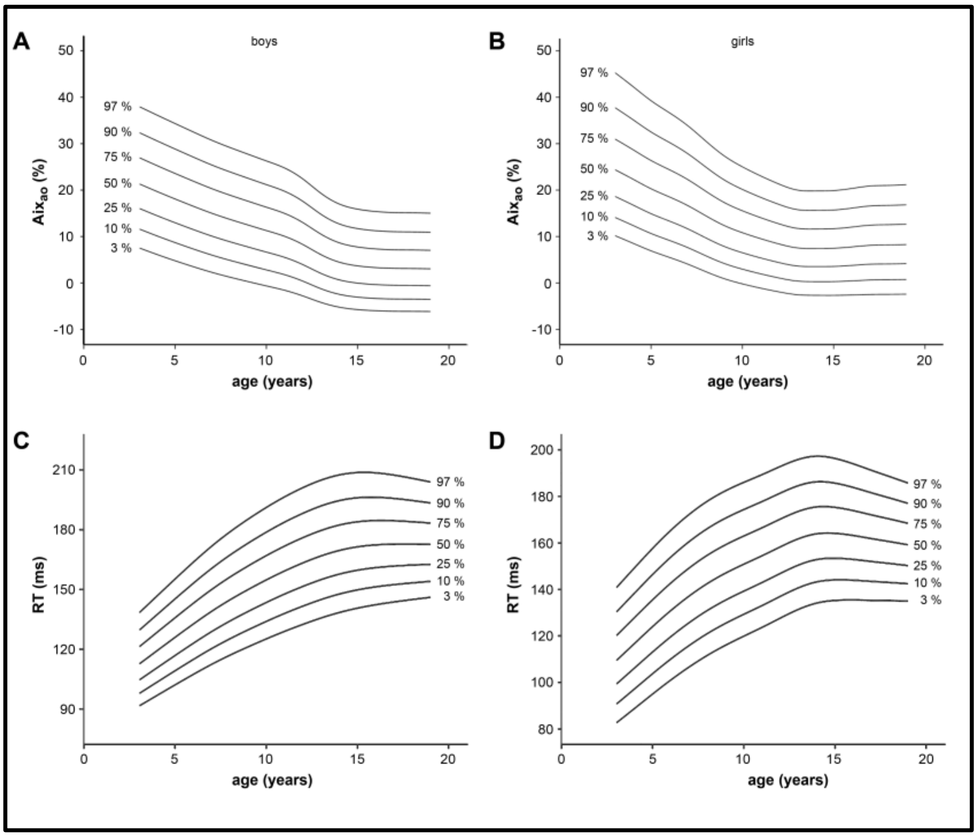

Figure 5

Smoothed percentile curves from 3th to 97th of aortic augmentation index (Aix_{ao}) and return time (RT) related with age for boys (A, C) and girls (B, D).

To study the causal relationships between Aix_{ao} and other variables, graphical analyses were performed. For the graphical analysis we also determined the percentile curves of body height and Jug-Sy distance. Thus, having collected all of the above mentioned parameters, in Figure 6 we were able to demonstrate the relationship between Aix_{ao}, body height, Jug-Sy and RT featuring the changes of the standardized values with age in boys and girls, respectively.

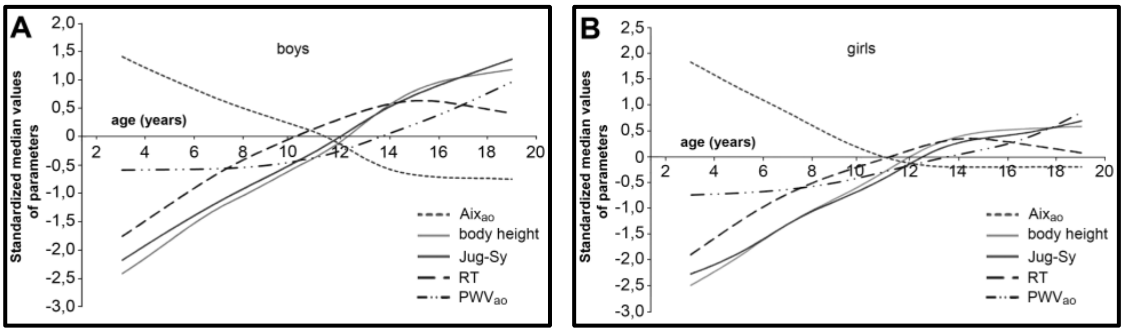

Figure 6

Standardized velocity of median values of aortic augmentation index (Aix_{ao}), body height, distance between jugulum and symphysis (Jug-Sy), return time (RT) and aortic pulse wave velocity (PWV_{ao}) related to age for boys (A) and girls (B).

These complex figures demonstrate that the body height and Jug-Sy were constantly growing until the age of 18 years in both genders. However the decreasing trend of the median Aix_{ao} in boys flattens from the age of 15 years, and the values remain practically unchanged until the age of 18 years while in girls the decrease of the median Aix_{ao} stops earlier (14 years). Similar tendencies were seen with RT, as well. In boys the increase of the median of the RT flattens from the age of 15 years, but in girls this flattening occurs earlier at the 14^{th} year. The mean values of PWV_{ao} were essentially unchanged between age 3 and the start of the puberty, in girls and boys alike. If the travel velocity of the pulse pressure wave (PWV_{ao}) is constant, the increase of time necessary to cover the distance (RT) - and the proportional decrease of Aix_{ao} - can only be caused by the growth of the distance (Jug-Sy, wich is proportional with body height) to be covered. After the start of puberty the PWV_{ao} increases in both genders.

c./ Central (SBP_{ao}) and the peripheral (SBP_{brach}) systolic blood pressure in healthy children and adolescents and in patients with juvenile essential hypertension (JEH)

The SBP_{ao} increased from 96.8±7.1 mmHg to 110.1±7.3 mmHg (p<0.001) in boys and from 97.5±7.8 mmHg to 105.0±7.5 mmHg (p<0.001) in girls between age of 3-18 years, while the SBP_{brach} increased from 103.0±5.5 mmHg to 128.2±8.3 mmHg (p<0.001) in boys and from 102.5±5.1 mmHg to 118.8±8.6 mmHg (p<0.001) in girls, respectively.

The elevation regarding both the SBP_{brach} and SBP_{ao} between the age of 3 and 18 years was higher in boys, than in girls, as the increasing of SBP_{brach} was 25.2 mmHg in boys and 15.3 mmHg in girls (p<0,001), while the increasing of SBP_{ao} was 13,3 mmHg in boys and 8.0 mmHg (p<0,001) in girls, respectively.

From the age of 13 the SBP_{brach} was significantly higher in boys (p<0.01), and this diffenrence had become even more pronounced from the age of 15 to 18 (p<0.001). There is a same situation regrading SBP_{ao}: from the age of 16 the SBP_{ao} was significantly higher in boys (p<0.001), and this diffenrence had continued till the age of 18.

Smoothed percentile curves of the SBP_{ao} and SBP_{brach} measured simoultaneously are shown on Figure 7. Analysing the curves of the median values of SBP_{ao} in boys and girls, it became clear that the increase was not constant with age. In both sexes, the SBP_{ao} and values exhibit a flat period between 3 and 8 years, with a steeper increase thereafter. The first pronounced increase occured at the age of 12.1 years in boys and 10.4 years in girls.

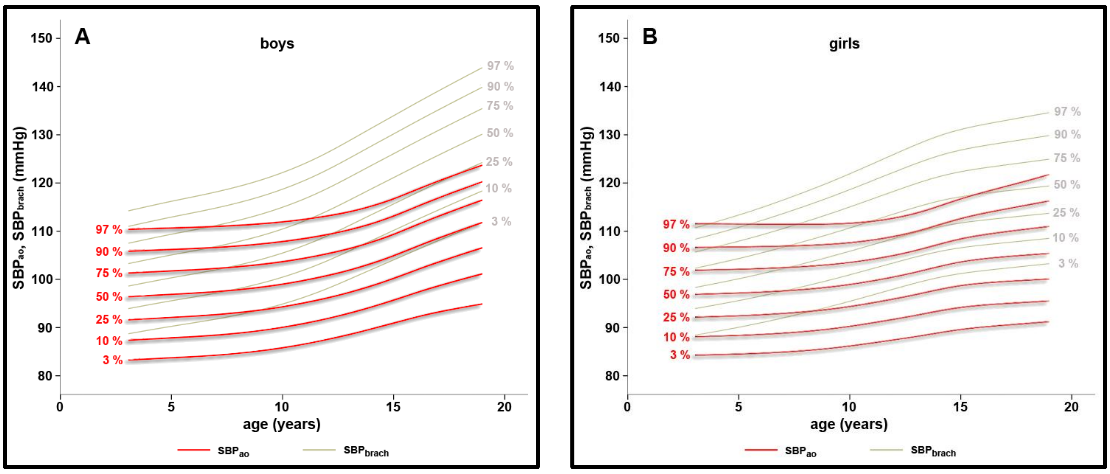

Figure 7

Smoothed percentile curves from the 3rd to 97th of central (SBP_{ao}) (red line) and peripheral (SBP_{brach}) (gray line) blood pressure related with age for boys (A) and for girls (B).

The mean values of the peripheral (SBP_{brach}) and central (SBP_{ao}) systolic blood pressure of the patients with juvenile essential hypertension (JEH) and of the sex- and age matched control groups are shown in Table 1.

Table 1. The mean values of the peripheral and the central systolic blood pressure in patients with juvenile essential hypertension and in sex- and age matched control groups

	BOYS			GIRLS		
	JEH	**control group**	**Student's t-test**	**JEH**	**control group**	**Student's t-test**
n	**173**	**173**	**-**	**44**	**44**	**-**
SBP_{brach} *(mmHg)*	**147.79 ± 12.11**	**121.72 ± 8.84**	**p < 0.001**	**147.32 ± 15.00**	**117.95 ± 6.99**	**p < 0.001**
SBP_{ao} *(mmHg)*	**127.84 ± 10.43**	**106.12 ± 7.27**	**p < 0.001**	**129.38 ± 14.36**	**104.59 ± 6.36**	**p < 0.001**

JEH; juvenile essential hypertension, SBP_{brach}; peripheral (brachial) systolic blood pressure, SBP_{ao}; central (aortic) systolic blood pressure

Obviously, the mean values of the peripheral (SBP_{brach}) and central (SBP_{ao}) systolic blood pressure of the patients with juvenile essential hypertension (JEH) were significantly higher ($p<0.001$) than they were in the sex- and age matched control groups. Interestingly, the SBP_{ao} were significantly lower in both patients' groups (boys and girls) ($p<0.001$) than were the SBP_{brach}, and what is more, the mean SBP_{ao} were in the sex- and age related normal range.

5. DISCUSSION

We applied at first the newly development non-invasive occlusive-oscillometric device (Arteriograph) for measurement of arterial function parameters in children and adolescents.
The most important finding of our study is that we were able to determine the reference values of the arterial function parameters ($PWV_{ao,}$ Aix_{ao}, RT, SBP_{ao}, SBP_{brach}) on the largest database to date of healthy children and adolescents between the ages of 3 and 18 years.
It is a very rapid and painless procedure and is well tolerated even by the youngest participants. The small size of the portable device enabled us to visit kindergartens and schools to collect the database very easily. Newertheless, the operational procedure of the device is fully automatized, and user-independent. On the basis of our experiences the adoption of this technology for routine paediatric practice seems to be realistic.

a./ Reference values of the PWV_{ao} in a healthy population aged between 3-18 years

The overall increase with age of mean PWV_{ao} values was identical in both sexes, only biologically insignificant differences were observed between them. These findings suggest that no significant structural difference exists in the aortic wall between sexes in this age range.
We proved, that the PWV_{ao} does not increase constantly with age. Between 3 and 8 years the median PWV_{ao} values are practically constant for both sexes. A new original finding was, too, that the steepest increas differs in terms of time between boys and girls, that is it occurs at 12.1 years in boys and at 10.4 years in girls. We can hypothesize that this newly observed phenomenon might be explained by the differing onset of adolescence in boys and girls.
When we compared the age-related changes of the median of the standardized values of PWV_{ao}, MAP and SBP_{brach}, a further new and interesting feature appeard. We observed marked differences between the ages of 3 and 8 years in the trends of PWV_{ao}, MAP and SBP_{brach}. Interestingly, the PWV_{ao} remained practically unchanged, whereas the blood pressure trend constantly increased. This rises several physiological questions.
We might suppose that, at a very young age, the aortic wall is so elastic that an increase in blood pressure does not cause any consequential stiffening in the aortic wall. Similarly the practically identical increase of the standardized PWV_{ao} and peripheral blood pressure at the later ages of 10-18 years might be due to a gradual loss of aortic elastic properties. Further, specifically designed studies would be needed to confirm this hypothesis.
Several authors have provided evidence about the changes in the structure and composition of the aortic wallat an early age, specifically that aging causes a loss in elastic properties. It is possible that the continuously increasing blood pressure which occures between the ages of 3 and 18 years may lead to a simultaneous increase in lateral tension in the aortic wall. Than beyond the age of 10-12 years, this load cannot be compensated for as successfully as was the case between 3 and 8 years. Hence, the rise in pressure will inevitably be accompanied by a rise in aortic stiffness and the PWV_{ao} increases.
Whether the abnormally steep increase of PWV_{ao} (e.g. an individual's increase in PWV_{ao} from 25^{th} to 90^{th} percentile whithin a few years) might have pathological value in assessing cardiovascular risk characterized by the accelerated stiffening of the aortic wall is something which remains to be clarified by further, preferably longitudinal examinations.

b./ Reference values of the aortic augmentation index (Aix_{ao}) and the simultaneously measured return time of the systolic pulse wave (RT) in relation to body height

This paper provides the first description of the percentile values from 3rd to 97th of Aix_{ao} and the reference values of the simultaneously measured RT.
Knowing the reference values of the Aix_{ao} and RT related to genders allowed us to discover differences between the genders, namely that the Aix_{ao} was significantly higher in girls than in boys at the age of 14. This difference had become even more pronounced from age of 15 to 18. Difference was also found between the genders regarding RT, which was significantly higher in boys from the age of 15 and thereafter. In addition – although the tendency of the changes was the same for both genders (Aix_{ao} decreased, RT increased linearly in childhood and both processes slowed down at the beginning of the puberty) – the onset of slowing down of this linear changes was different in boys and girls, it happened earlier in girls.
Knowing the RT values we were able to prove our hypothesis presented in the introduction, namely, that simultaneous linear and proportional increase of the body height (Jug-Sy) and RT, and decrease of the Aix_{ao} were found during childhood, until the beginning of the puberty. On the basis of these findings we confirmed that the changes of Aix_{ao} were caused by the increasing RT, namely that the reflected, late systolic pulse pressure wave returns later because of the higher body height (aortic length). Therefore the point of augmentation to the declining slope of the first systolic wave is lower, consequently the Aix_{ao} decreases.

It is also a new finding that the trends of the changes of body height (Jug-Sy), Aix_{ao} and RT were different after the onset of puberty, namely, while the body height (Jug-Sy) increased constantly and linearly after that time, the changes of Aix_{ao} and RT did not follow that trend, on the contrary, the changes of these parameters practically stopped.

Our work is also unique in the aspect that we have percentile values of PWV_{ao} measured simultaneously in the same population, and its trend was unchanged during childhood in both genders. It means that in this interval the spreading velocity of the pulse pressure wave is basically constant independently of age and has no correlation to growth, while after the onset of puberty the PWV_{ao} starts growing in both genders.
On the basis of the above described findings it is proved that the increased Aix_{ao} detected in early childhood can only be caused by the shorter RT due to the shorter aortic length, ie. due to the early return of the reflected systolic pulse wave it augments to a higher point of the declining slope of the first systolic pulse wave, consequently the Aix_{ao} elevates.
We can describe this phenomenon as follows: the mean values of PWV_{ao} were practically unchanged between age 3 and the start of the puberty, in girls and boys alike. If the travel velocity of the pulse pressure wave is constant, the increase of time necessary to cover the distance (RT) - and the proportional decrease of Aix_{ao} - can only be caused by the growth of the length of the distance (Jug-Sy, wich is proportional with body height) to be covered.
The observed changes in the trend of Aix_{ao} after the beginning of puberty – constant increase of body height (Jug-Sy) after the onset of puberty, while both the decrease of Aix_{ao} and the increase of RT slowed down and then stagnated – were caused by the increasing PWV_{ao}. The increasing PWV_{ao} indicates that the characteristics of the aortic wall change, namely the aortic stiffness rises.
The physiological importance of the examined phenomenon (enhanced vawe reflection in infants and small children) may be related to cardiac growth. It is resonable to assume that the enhanced pressure wave reflection is a trigger for the left ventricule performance until the body height reaches its maximum.

c./ Central (SBP_{ao}) and the peripheral (SBP_{brach}) systolic blood pressure in healthy children and adolescents and in patients with juvenile essential hypertension (JEH)

This is the first study which provides detailed description of the percentile values from 3^{rd} to 97^{th} of the central (SBP_{ao}) and the peripheral (SBP_{brach}) systolic blood pressure related to gender measured simultaneously in a healthy population aged 3-18 years.

There was no difference between the genders regarding the mean values of SBP_{ao} in the age period of 3-15 years. Significant difference was observed at first at the age of 16 (SBP_{ao} was lower in girls), which difference had continued therafter. While the mean values of SBP_{ao} were practically unchanged in girls in the age period of 16-18 years, this parameter showed a continuous increasing in boys.

The SBP_{ao} is determined by the aortic wall structure and function – which is characterized by PWV_{ao} – and by the actual cardiac output. No differences were found in SBP_{ao} between genders till the age of 15 years, therefore we may suppose no differences regarding the aortic wall structure and the cardiac output between girls and boys in childhood. During the later age period the boys had became higher and weighter than had done the girls. We speculate, that the higher SBP_{ao} observed in boys is caused by the increased cardiac output, which needs to serve the excessively growing body mass.

Our work is also unique in the aspect that we determined the relationship between the SBP_{ao} and the SBP_{brach} measured simultaneously at first. The mean values of SBP_{brach} were higher during the whole examined age period in both gender, than were the mean values of SPB_{ao}. The increase of the mean values of SBP_{brach} related with age were constant and higher in extent.

The more interest and important finding of our work that we discovered the relationship between the SBP_{ao} and SBP_{brach} in patients with juvenile essential hypertension (JEH). We proved that in group of JEH patients the SBP_{ao} is much more lower, than is the simultaneously measured SBP_{brach}. Hence, it became clear, that while the conventionaly measured SBP_{brach} were very high in the patients group, the SBP_{ao} – which is a determining risk factor for cardiovascular morbidity and mortality – falled into the sex- and age related normal range in all patients.

In summary we presented a detailed description of the age and gender related physiological changes of the arterial function parameteres, such as PWV_{ao}, Aix_{ao}, SBP_{ao} and SBP_{brach} based on a large database measured in a healthy population aged 3-18 years. Analysing our data it became clear that in several cases we coud not find data in the literature to explain the physiological phenomenon observed by us. Hopefully, our work will facilitate further researches in order to answer the opened questions. However, our fidings may contribute to a better understanding of the pathophysiological background of the several diseases with impaired arterial function occur in children and adolescents.

6. NOVEL FIDINGS

1. We applied at first the newly developement, validated, non-invasive, occlusive-oscillometric technique (Arteriograph) for arterial function measurement in children and adolescents.

2. We determined and published the reference values of PWV_{ao} on the largest database to date. We first detailed the specific characteristics of the changes of PWV_{ao} – namely that the PWV_{ao} remains unchanged in the very young despite increasing blood pressure, and we found the gradual increase of PWV_{ao} in adolescence – which is proportionate to the increase in blood pressure.

3. We determined the largest database to date of reference values Aix_{ao} and the simultaneously measured RT. We provided at first evidence about the determining role of the body height (aortic length) in characteristics of the Aix_{ao} in childhood. In children the reflected systolic pulse pressure wave returns earlier because of the shorter body height (aortic length) and not because the stiffer aortic wall.

4. This is the first study which provides detailed description of the percentile values of the central (SBP_{ao}) and the peripheral (SBP_{brach}) systolic blood pressure related to gender measured simultaneously in a healthy population aged 3-18 years. The SBP_{ao} was practically unchanged in the age period of 3-10 years in both gender, after the onset of puberty SBPao showed a continuous increasing in boys and a stagnated in girls.

5. We discovered the relationship between the SBP_{ao} and SBP_{brach} in patients with juvenile essential hypertension (JEH). We proved that in group of patients with JEH the SBP_{ao} is much more lower, than is the simultaneously measured SBP_{brach}.

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8. PUBLICATIONS OF THE AUTHORS

Original papers and letters:

1. **Erzsébet Valéria Hidvégi**, Miklós Illyés, Béla Benczúr, Renáta M. Böcskei, László Rátgéber, Zsófia Lenkey, Ferenc T. Molnár, Attila Cziráki. Reference values of aortic pulse wave velocity in a large healthy population aged between 3 and 18 years. ***J Hypertension***. 2012; 30:2314-21. ***(IF: 3.806)***
2. **Erzsébet Valéria Hidvégi**, Miklós Illyés, Zsófia Lenkey, Ferenc Tamás Molnár, Attila Cziráki. Reference Values of Aortic Pulse Wave Velocity in a Large Healthy Population Aged between 3 and 18 Years – Reply. ***J Hypertension.*** 2013; 31:422-427. ***(Letter; IF: 3.806)***
3. **Erzsébet Valéria Hidvégi**, Miklós Illyés, Ferenc T. Molnár, Attila Cziráki. Evidence about the Determining Role of the Body Height in the Characteristics of the Aortic Augmentation Index in Childhood. ***J Hypertension. (IF: ~3.806,*** *submitted*)
4. László Rátgéber, Zsófia Lenkey, Ádám Németh, **Erzsébet Valéria Hidvégi**, Zsófia Verzár, Miklós Illyés, József Bódis, Attila Cziráki. The effect of physical exercise on arterial stiffness parameters in young sportsmen. ***Acta Cardiologica*. (*IF: 0,604,* *under revision*)**
5. **Hidvégi Erzsébet Valéria**, Illyés Miklós, Molnár T. Ferenc, Böcskei M. Renáta, Benczúr Béla, Lenkey Zsófia, Cziráki Attila. Az aorta pulzushullámterjedési sebesség referencia értékei egészséges gyermekekben és serdülőkben. ***Gyermekgyógyászat.*** 2013; 64:287-291.
6. **Hidvégi Erzsébet Valéria.** Válasz a szerkesztői kommentárra. ***Gyermekgyógyászat.*** 2013; 64:293-294.
7. **Erzsébet Valéria Hidvégi**, Illyés M, Lenkey Zs, Molnár FT, Cziráki A. Reference Values of Aortic Pulse Wave Velocity in a Large Healthy Population Aged between 3 and 18 Years. ***Pediatric Pharmacology.*** 2013; 10:64-71, angol nyelvű, 72-79, orosz nyelvű

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2. **Erzsébet Valéria Hidvégi**, Huberth J, Jákli Gy, Kelemen I, Klemencz H, Illyés M. First database of arterial function (PWV_{ao}, Aix_{brach}, SBP_{ao}) from healthy children and adolescents measured by a new non-invasive oscillometric method (Arteriograph).
5th World Congress of Paediatric Cardiology and Cardiac Surgery, Cairns, Australia 2009; Abstract Book
3. **Erzsébet Valéria Hidvégi**, Huberth J, Jákli Gy, Kelemen I, Klemencz H, Illyés M. The reference values of aortic pulse wave velocity (PWVao) in a healthy population aged 3-18 years and the plausible physiological background of the observed changes. ***Cardiology in the Young.*** 2010; 20(Suppl.2.):S67-68. ***(IF: 0.858)***
4. **Hidvégi Erzsébet Valéria**, Illyés Miklós. Az aorta PWV referencia értékei nagy 3-18 éves korú egészséges populációban. ***Gyermekgyógyászat.*** 2010; 61(5):154.

5. **Hidvégi Erzsébet Valéria**, Illyés Miklós. Centrális és perifériás szisztolés vérnyomás egészséges gyermekekben és serdülőkben valamint juvenilis esszenciális hypertóniás betegekben. ***Gyermekgyógyászat.*** 2011; 62*(*5):197.
6. **Erzsébet Valéria Hidvégi,** Miklós Illyés. Central and Peripherial Systolic Blood Pressure in Healthy Children and Adolescents and in Patients with Juvenile Hypertension. ***Cardiology in the Young.*** 2011; 21(Suppl.1.):S51-52. ***(IF: 0.759)***
7. **Hidvégi Erzsébet Valéria**, Illyés Miklós. Aorta pulzushullámterjedési sebesség referencia értékei 3-18 éves populációban. ***Cardiologia Hungarica.*** 2012; 42(Suppl.A):S44
8. **Erzsébet Valéria Hidvégi,** Miklós Illyés. Reference Values of Aortic Augmentation Index in a Large Healthy Population Aged 3-18 Years. ***Cardiology in the Young.*** 2012; 22(Suppl.1.):S44-45 ***(IF: 0.759)***
9. **Hidvégi Erzsébet Valéria**, Illyés Miklós, Cziráki Attila. Centrális és perifériás szisztolés vérnyomás egészséges gyermekekben és serdülőkben valamint juvenilis esszenciális hypertóniás betegekben. ***Cardiologia Hungarica*.** 2013; 43(Suppl.B):S33.

Reviews:

Doyon A, Kracht D, Bayazit A, Deveci M, Duzova A, Krmar R et al. Carotid Artery Intima-Media Thickness and Distensibility in Children and Adolescents: Reference Values and Role of Body Dimensions. ***(Hypertension, accepted)(IF: 6.207)***

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