

Application of the Measurement of Carotid Intima-Media Thickness for Prediction of the Essential Hypertension in Children

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Hypertension is a major risk factor for progression of the atherosclerotic process and for developing of degenerative cardiovascular diseases in adulthood. The aim of this study is to evaluate how the measurement of carotid intima - media thickness for prediction of essential hypertension in children can be used. The study group included 81 children and the control group 61 children, all aged between 5 - 17 years and 11 months old, and admitted in Children Hospital Brasov in the period of 2009 - 2014. The study protocol included: BMI, blood pressure and Doppler echography of the common carotid artery for each group. Mean age of the patients from the study group was 13.67 years, 43.20 % girls and 56.80 % boys, while in the control group, the mean age was 14.07 years, 54.10% girls and 45.90 % boys. 70.37% of the children from the study group presented obesity, while in the control group 40.98% were obese. The IMTC study group ranged from 0.52 - 0.69 mm and the limits of the normotensive subjects were 0.32 - 0.54 mm. In both groups the obese patients were found to have increased carotid artery intima-media, which means that IMTC was positively correlated with BMI ($p=0.000001$). It is necessary to identify diagnostic methods easily applicable for children, allowing involvement of the characteristics of the arterial wall in the degenerative pathological processes. Increased intima-media ratio is positively correlated with high values of blood pressure.

Keywords: carotid intima - media thickness, hypertension, children

The incidence of essential hypertension in children is in continuous progress despite efforts of the medical staff to prevent the disease and to educate people regarding long term effects. Hypertension is a major risk factor for progression of the atherosclerotic process, and also for degenerative cardiovascular diseases developing in adulthood [1]. Today is obvious that this unfavorable outcome is common at blood pressure values of 115/75 mmHg in children and the risk doubles with each rise of the blood pressure (with 20/10 mmHg) [2].

There is a strong interaction between high blood pressure values, dysfunction of the vascular endothelium and atherosclerosis. This determines transformation of the vessels in a rigid system impairing the blood flow and maintaining hypertension. Constant high blood pressure values lead firstly to endothelial dysfunction and then to structural alterations of the arterial vessels [3]. The presence of the endothelial dysfunction maintains the hypertension progression [4]. One of the earliest change is the apparition of the atherosclerotic plaque and this was observed in young subjects as early as aged two [5]. These structural changes of the arterial vessels can be proved using Doppler echography of the common carotid artery, respectively measurement of the intima-media thickness (IMTc). Our study aims to investigate the existence of a correlation between hypertension and IMTc.

Experimental part

Methods

The study group included 81 children, boys and girls, aged between 5 and 17 years and 11 months, admitted in Children Hospital Brasov between 2009-2014. In these batches, repeated measurements of blood pressure show

high levels for age, gender and height. The patients with secondary hypertension were excluded (1 case). (Secondary hypertension). The control group included 61 children, boys and girls, also with age between 5 and 17 years and 11 months, with normal values of blood pressure.

The study protocol included:

Measurement of weight and height; the body mass index (BMI) was calculated according to the formula: $BMI = W/H^2$, where W = weight (kilos), H = height (meters).

Blood pressure was determined according to *The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents* [6].

Doppler echography of the common carotid artery for each group. We used ultrasound machine Fukuda. The examinations were performed with linear transducer with 12.5-13 MHz. The principle of the examination was to expose the common carotid artery (which can be assimilated with a pipe) and to evaluate the anterior and posterior walls and the blood flow. In a normal system the flow should be laminar without turbulence because the walls are smooth without asperities like atherosclerotic plaque. The dimensions of the walls should be less than 0.40 mm.

Subjects were examined in a quiet ambient, thermal comfort, noise free, after 15 min break from physical effort. Examination position was supine, face up and head turned to the opposite side of the examined artery (45°). We performed manually 5 measurements for each wall (anterior and posterior); a distance of 1 cm for the left and the right carotid artery was used to study the arithmetic

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average of the values obtained. The data were compared with the values considered normal for the age group[8].

Statistical analysis: We used ANOVA statistical calculation method applied for continuous variables and chi-square test to compare groups. We considered statistically significant a p value < 0.05.

Methodology of measurement of IMTc

We had measured the carotid intima-media thickness (IMTc) by analyzing B-mode ultrasound imaging which was obtained manually in real time. Ultrasound examination was performed by a single person with a linear transducer with 12.5-13 MHz frequency, with an ultrasound imaging system Fukuda. The examinations were performed in a quiet room, after 15 minutes of resting, with patient lied on bed in dorsal decubitus position with head rotated at 45° on the opposite side of the carotid artery which was examined. With this technique it can be visualized 2 parallel echogenic lines separated by an anechoic space, at the common carotid artery. The 2 lines means the blood-intima and media-adventitia interfaces. The distance between the 2 lines has the significance of the thickness of the intima-media complex. The measurements were made at 1 cm from carotid bulbous, for the both anterior and posterior wall. We made 5 determinations for each wall, for right and left common carotid artery and we used the mean value in our study. We compared the values obtained with the normative values.

Results and discussions

The study group involved 81 patients who, at admission were detected with blood pressure values (fig. 1) greater

than the 95th percentile for age, sex and class. 46 were boys (56.79%) and 35 girls (43.20%). The ages of the subjects ranged from 5.9 years to 17.11 years (mean age 13.67 years). The control group included 61 subjects, 28 boys (45.90%) and 33 girls (54.09%), aged 5.7 to 17.10 years (mean age 14.07 years). In the study group, 57 children (70.37%) presented obesity (BMI > 95th percentile), 10 children (12.34%) were overweight (BMI between 85 and 95 percentile) and 14 (17.28%) were normal weight (BMI < 85). In the control group 29 (47.54%) children had normal weight (BMI < 85), 7 subjects (11.47%) were overweight (BMI between 85 and 95 percentiles) and 25 subjects (40.98%) were obese (BMI > 95th percentile). Demographic and clinical data are presented in table 1.

In the study group in which most children were obese or overweight systolic blood pressure was higher as expected for the age and gender. In the control group the systolic blood pressure was normal for age and gender. There is a significant difference between the two groups; 44 subjects (56.41 %) of the study group registered BP values > 99th percentile for age, gender and class, which shows occurrence of severe HTAE early.

Following IMTC, we noticed a positive correlation to hypertension (fig. 2), this correlation was significantly higher in hypertensive subjects compared to normotensive. All subjects who were later confirmed as having elevated blood pressure had increased IMTC and even registered as having characteristic complications such as hypertension and left ventricular hypertrophy modification of retinal vessels in eye fundus examination. In addition, the subjects

	CONTROL GROUP			STUDY GROUP			P
	cases	media	std.dev	cases	media	std.dev	
Age	53	14.06	2.79	78	13.83	3.16	0.673102
WB	32	3139.34	562.60	49	3301.02	632.74	0.244134
W	53	54.31	17.56	78	64.64	20.14	0.478138
H	53	1.528	0.1386	78	1.547	0.1684	0.002925
BMI	53	23.01	6.65	78	26.37	4.79	0.001016
SBP	53	107.04	6.14	78	133.47	15.41	0.000000
DBP	53	63.75	7.33	78	77.86	11.60	0.000000
IMTc	50	0.37	0.06	75	0.43	0.06	0.000000

Table 1
DEMOGRAPHIC
CHARACTERISTICS, CLINICAL
FEATURES OF THE STUDY
GROUP AND CONTROL
GROUP

WB = weight of birth; W = weight; H = height; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; IMTc = intima-media thickness at carotid artery.

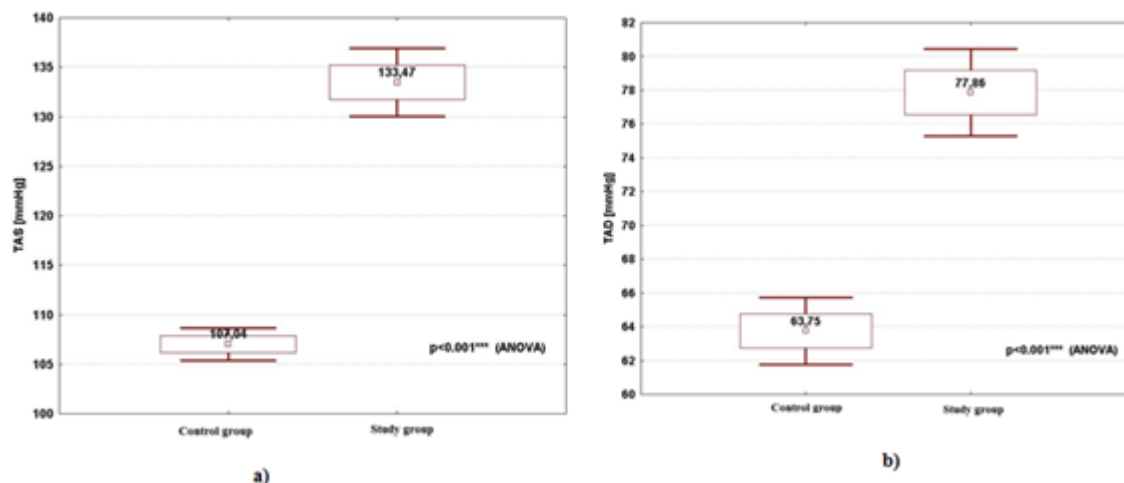


Fig. 1. The variations of blood pressure in both groups;
A) SBP. B) DBP

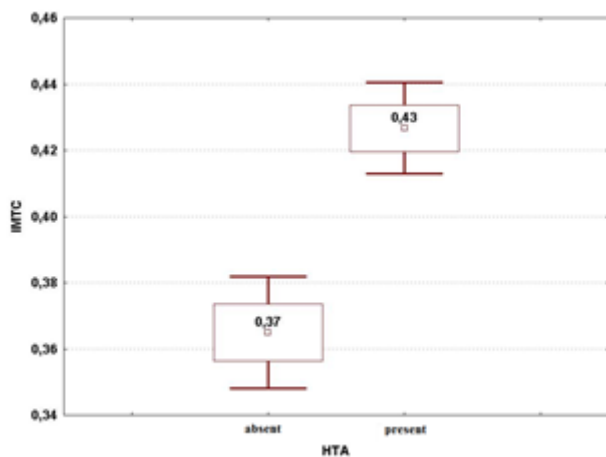


Fig. 2. Correlation between high values of BP and IMTC

associated high blood pressure values and obesity (BMI > 95th). The IMTC in the study group ranged from 0.52 to 0.69 mm and for normotensive subject's limits were 0.32 to 0.54 mm.

For all patients from the study, obesity was found increased when compared to carotid artery intima-media policy.

In the study group we noticed a positive correlation between IMTC, TAS values ($p = 0.0001$) (fig. 3) and DBP ($p = 0.0001$) (fig. 3). Patients with SBP and DBP values greater than the 99th percentile were those who experienced the most severe changes in intima-media ratio (values greater than 0.5 mm). One possible explanation could be that the condition of increased pressure exerted on artery walls correlated with the time factor (how long these mechanical forces act on the arterial wall), causes changes in the tissue structure (live, with intense metabolism), making it a rigid structure like a tube. Clearly, the time factor plays an important role in modifying IMTC because in these subjects there is evidence that hypertension was installed for at least 6 months before the examination.

In the control group, 17 subjects (27.86%) had increased IMTC but they were normotensive obese (BMI > 95th) suggesting that this could be also the consequence of atherosclerotic changes.

In our study, age of onset of HTAE was between 10 to 17 years in 72 subjects (88.88%) and 6 to 10 years old in 9 subjects (11.12%). Although the percentage is small and statistically insignificant, we must highlight the young age of onset. Scientific literature offers references for lowering the age of onset at 10-12 years. A significant number of subjects had elevated BP and arterial vascular damage

revealed by increased IMTC. This may be an argument to support apparition of the condition for at least 6 months prior. Pathological processes occurring in the arterial wall, consequences of the high pressure can be emphasized using Doppler ultrasound by measuring intima-media thickness pressure. Increased intima-media ratio is an evidence for structural changes in the arterial wall.

We applied this method in the present study outlining bilateral common carotid artery measurements as being the hallmark of a well-defined tube wall thickness that can be monitored using the Doppler technique and so we managed to emphasize the presence of structural changes in case of high pressure. This thickness variations are complex pathophysiological process arguments for atherosclerosis and plaque formation, which both deform the interface with the bloodstream and determine turbulent blood flow in the arteries. The study found that the value of IMTC is higher in children with high blood pressure compared to children who had normal blood pressure (positive correlated to systolic blood pressure and diastolic blood pressure).

In the study group IMTC values were increased for both obese and normal weight patients, thus showing that high blood pressure regime itself may determine, over time, not only endothelial dysfunction but permanent structural changes in the arterial wall. On the other hand, we cannot ignore the fact that in our study, the proportion of obese subjects was significant for both groups of children (high blood pressure and normal blood pressure).

Moreover, we noticed that increased IMTC positively correlated with BMI. Thus, we observed a slight association between obesity and increased IMTC [9, 10] and therefore it is difficult to specify the exact contribution of each of the two variables (blood pressure and obesity) in the process of reconfiguration of the arterial wall and blood flow alteration. It is certain that endothelial dysfunction and vascular endothelial structural changes are common in both obesity and hypertension and that between the two disorders a close interdependence occurs. It would be interesting to study the functional parameters such as vascular distensibility, vascular arterial geometry and flow-mediated vasodilation.

Carotid intima media thickness is one of the most studied parameters regarding evaluation of the atherosclerosis and hypertension not only in adults but also in children and adolescents [11]. In the present study we had demonstrate that IMTC has a strong correlation with high levels of blood pressure (BP) in childhood. In these subjects we found structural modifications of the common carotid artery characterized by augmented wall thickness as a prove of

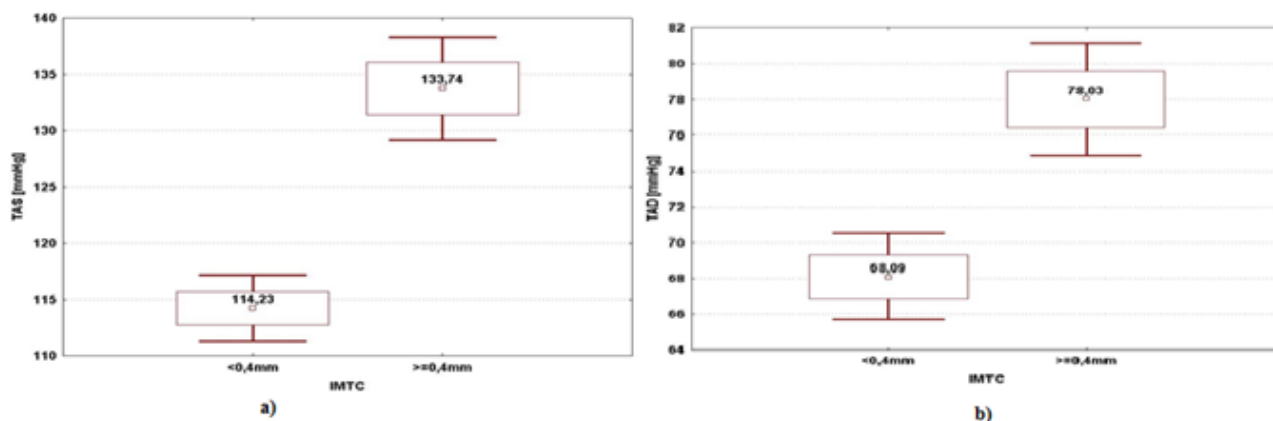


Fig. 3. The variation of IMTC with blood pressure
A) SBP B) DBP

the early atherosclerotic modification that had already taken place despite of early age. Glagov et al.[12] had described for the first time arterial remodeling and the correlation of this with atherosclerosis process.

It is very difficult to evaluate cardiovascular risk in children and to find proper and valuable methods to define this [13] although it is widely accepted that degenerative cardiovascular diseases begins in childhood [14]. In our study group the youngest was five years old and it was a surprise to find that even so young structural impairment in carotid artery was already present confirming the hypothesis of early onset of the atherosclerosis [15]. The study had revealed that one of the most important factor that is affecting carotid IMT is blood pressure, both systolic and diastolic values. Many trials had been studied the impact of blood pressure (systolic, diastolic, mean value, 24-hours continuous monitoring) on the carotid IMT and had demonstrated that high levels of these factors determine the increasing of the intima-media thickness and the antihypertensive treatment determine the regression of IMT [16]. Date of the present study showed that carotid IMT is correlated not only with high levels of systolic blood pressure and diastolic blood pressure but with the body mass index (BMI); children with normal values of blood pressure but with BMI above 95 percentiles had demonstrated enlargement of the carotid IMT. Now we know that metabolic syndrome is including features as hypertension and obesity and our study showed the primary importance of BP and BMI in determining early abnormalities of the arterial wall.

Our findings are similar with other studies that had demonstrated this correlation [13, 17,18]. Carotid intima-media thickening is reflecting the presence of subclinical atherosclerotic changes even in childhood and predict the future cardiovascular events in adulthood.

Conclusions

Elevated blood pressure values in pediatric patients is a fact and moreover, essential hypertension is a disease common in children aged 10. It is necessary to identify the diagnostic methods easily applicable to children: noninvasive, reproducible, allowing involvement of the characteristics of the arterial wall in understanding and handling of the degenerative pathological processes.

Measures of the intima-media vessel wall ratio of the common carotid artery using Doppler echocardiography appears to meet these requirements. Increased intima-media ratio is positively correlated with high blood pressure values, both systolic and diastolic hypertension and represents an indicator for structural changes occurring after high pressure works on the endothelium.

Because there is a positive correlation between BMI values and IMTC we can conclude that the determination of this ratio provides useful information regarding the onset and progression of atherogenesis long before clinical signs of organ involvement appear.

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