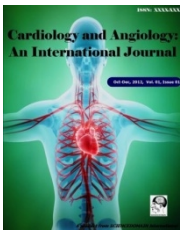

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Early Detection of Atherosclerosis in Primary School Children

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Authors' contributions

This work was carried out in collaboration between all authors. Author VN designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors EL and AL managed the literature searches, did all measurements under cardiologist's supervision and the questionnaires in the primary school children, put all data in Excel. Author SB performed statistical analysis and made corrections of the manuscript according to the reviewers opinion. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Purpose: The aim of this study was to determine the correlations of age, sex, anthropometric measurements, pulse rate, blood pressure, and family history of cardiovascular disease with early atherosclerosis in children.
Methods: Between December 2011 and January 2012 we included 112 children of primary school »Osnovna šola Bojana Ilicha Maribor«, whose parents consented and signed the inform consensus. We made a questionnaire about cardiovascular diseases in child's family. We measured blood pressure, pulse rate, body height, weight, waist circumference. We performed ultrasound measurement of carotid artery intima-media thickness (IMT). The data were processed using the SPSS statistical program.
Results: Body mass index (BMI) ($r=0.246$; $p<0.009$), waist circumference ($r=0.198$; $p<0.036$) systolic ($r=0.282$; $p<0.003$) and diastolic blood pressure ($r=0.282$; $p<0.003$) were positively correlated with carotid artery IMT. In addition, those with family history of cardiovascular diseases had higher carotid artery IMT ($p<0.0001$) at baseline. A multivariable logistic regression analysis revealed that family history of cardiovascular disease was associated with carotid artery IMT ($p<0.0001$).

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Conclusion: Higher levels of BMI, waist circumference, and arterial blood pressure were correlated with higher carotid artery IMT in children. In addition, the presence of family history of cardiovascular disease was independently associated with carotid artery IMT in children.

Keywords: Atherosclerosis; cardiovascular risk factors; carotid artery intima-media thickness; body mass index; abdominal obesity.

1. INTRODUCTION

Cardiovascular diseases (CVD) (myocardial infarction, ischemic stroke and peripheral artery disease) are leading cause of death in most developed countries [1]. Many risk factors for CVD are modifiable by specific preventive measures. In the worldwide Interheart study of patients from 52 countries, nine potentially modifiable factors accounted for over 90 percent of the population-attributable risk of a first myocardial infarction: smoking, dyslipidemia, arterial hypertension, diabetes, obesity, psychosocial factors, daily consumption of fruits and vegetables, regular alcohol consumption, and regular physical activity [2].

Autopsy studies in children and young adults, who have died from non-cardiovascular causes, demonstrated an early development of atherosclerosis. They detected vascular changes, which are associated with CVD in adults: changes in vessel anatomy (increased intima-media thickness (IMT)), mechanical changes (decreased arterial distensibility or increased stiffness), and physiologic changes (decreased flow mediated vasodilatation) measured before the death of the children. Clinically, cardiovascular risk factors such as obesity, dyslipidemia, arterial hypertension are predictive of increased carotid IMT in young adults and adolescents [3-9]. Individuals with early and more severe atherosclerotic changes were more likely to have one or more cardiovascular risk factors [10,11]. This has been illustrated in two reports that used the surrogate end point of carotid artery IMT. In a cohort of 486 adults ages 25 to 37 from the Bogalusa Heart Study, higher values of low-density lipoprotein (LDL) cholesterol and increased body mass index (BMI) in childhood were independent predictors to greater carotid IMT of young adults [5]. Moreover, in a larger cohort study from Finland of 2229 adults ages 24 to 39 years, carotid artery IMT was significantly associated with LDL cholesterol, systolic blood pressure, BMI, and smoking in childhood [6]. Another studies show that young adults with increased carotid IMT detected by ultrasound have an increased likelihood of a cardiovascular event (myocardial infarction and stroke) [7]. In addition, increased IMT is found in adolescents with familial hyperlipidemia, in children with a parent who has a history of premature myocardial infarction and in children with diseases associated with a high-risk for CVD, such as Kawasaki disease with coronary aneurysms [8].

Notably, the process of atherosclerosis begins early in childhood. Most children have slight atherosclerotic vascular changes, but some have progressive atherosclerosis because of additional risk factors (obesity, diabetes, arterial hypertension) [12]. The aim of our study was to evaluate the relationship between carotid artery IMT values in a population of children with family history of CVD, blood pressure, BMI or abdominal obesity.

2. MATERIALS AND METHODS

We included 112 children of the last three years of the primary school »Osnovna šola Bojana Ilicha Maribor«, whose parents consented and signed the inform consensus, from December

2011 to January 2012. The study was designed as a research project for competition »Mladi za napredek Maribora« (»Young for Maribor progress«).

A questionnaire report was filled by parents about family history of CVD in first and second-line relatives (myocardial infarction, ischemic stroke and peripheral artery disease). We helped them, if they needed any explanation. Each child brought us his parents' questionnaire, when he came on measurements in a peaceful and warm school room. We measured blood pressure and pulse rate at rest, two times sequential, in two minutes intervals. We took the mean value of the two consecutive measurements, at the accuracy of 1 decimal site. An electronic Omron's device with a cuff, which covered at least two thirds of the left upper arm, was used. During the measurement the child seat on a chair with his left forearm resting on a table. We measured body weight in kilograms, at the accuracy of 1 decimal site, body height and waist circumference at the level of upper anterior iliac spines and the umbilicus, in the centimetres, at the accuracy of 1 decimal site. We performed the ultrasound measurement of left carotid artery IMT. For measurements portable ultrasound Philips T-Max, two-dimensional ultrasound technique, colour-doppler ultrasound technique, and linear probe L 9-3 was used. The IMT measurements were performed by single researcher. We took the mean value of both measurements-one and two centimetres below the bifurcation of the common carotid artery to the internal and external carotid artery, in millimetres, at the accuracy of 1 decimal site. During the measurements, a child was lying supine on a massage table, with a neck turned right.

All data are presented as mean±SD. Pearson's correlation coefficient was used to find out the correlation between different variables (height, weight, BMI, waist circumference, systolic and diastolic blood pressure, pulse rate, IMT and age of the children). 95% confidence interval (CI) of Pearson's correlation coefficient was calculated. The Mann-Whitney test was used to compare the children with and without family history of CVD and with different variables. The multiple logistic regression analysis was used to evaluate the relationship between children with a family history of CVD and atherosclerosis risk factors (BMI, waist circumference, systolic and diastolic blood pressure, age of the children).

Relationship was considered statistically significant at p less than 0.05. Statistical analysis was performed by using SPSS for Windows, version 19.0.1 (SPSS Inc, Chicago, IL).

3. RESULTS

Baseline characteristics of study population are presented in (Table 1). There were 53 boys (47.3%) and 59 girls (52.7%) aged from 11 to 15 years old. The mean age was 13±0.9 years.

There were positive correlations of carotid artery IMT with age ($r=0.282$; $p<0.003$; CI 0.1-0.463), body height ($r=0.247$; $p<0.009$, CI 0.064-0.430), and body weight ($r=0.298$; $p<0.001$; CI 0.117-0.478). Additionally, there was positive correlation of carotid artery IMT with waist circumference ($r=0.198$; $p<0.036$; CI 0.13-0.383), BMI ($r=0.246$; $p<0.009$; CI 0.063-0.429) (Figs. 1 and 2), systolic ($r=0.282$; $p<0.003$; CI 0.1-0.463) and diastolic blood pressure ($r=0.282$; $p<0.003$; CI 0.1-0.463) (Fig. 3).

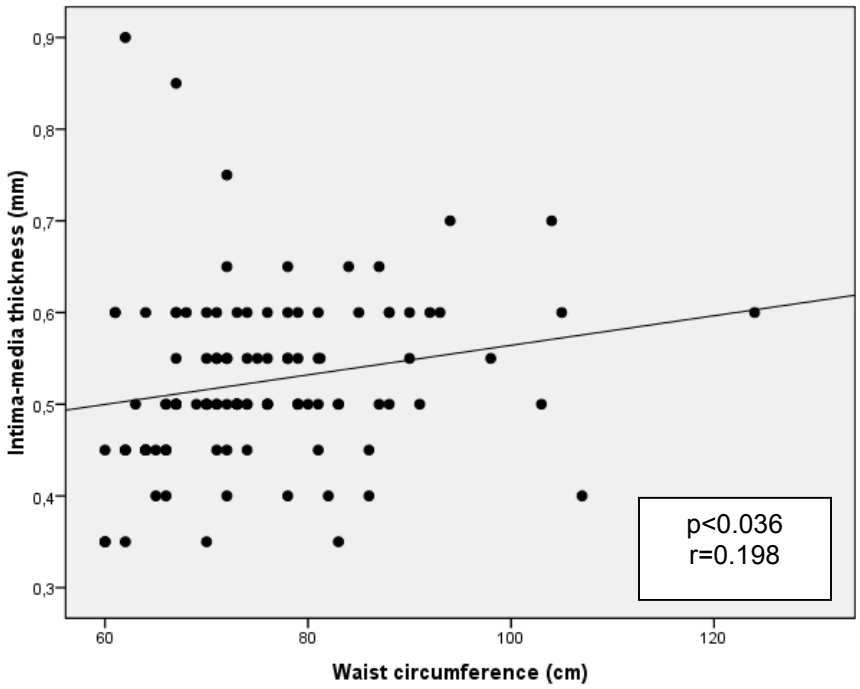

Fig. 1. The correlation between carotid artery IMT and waist circumference

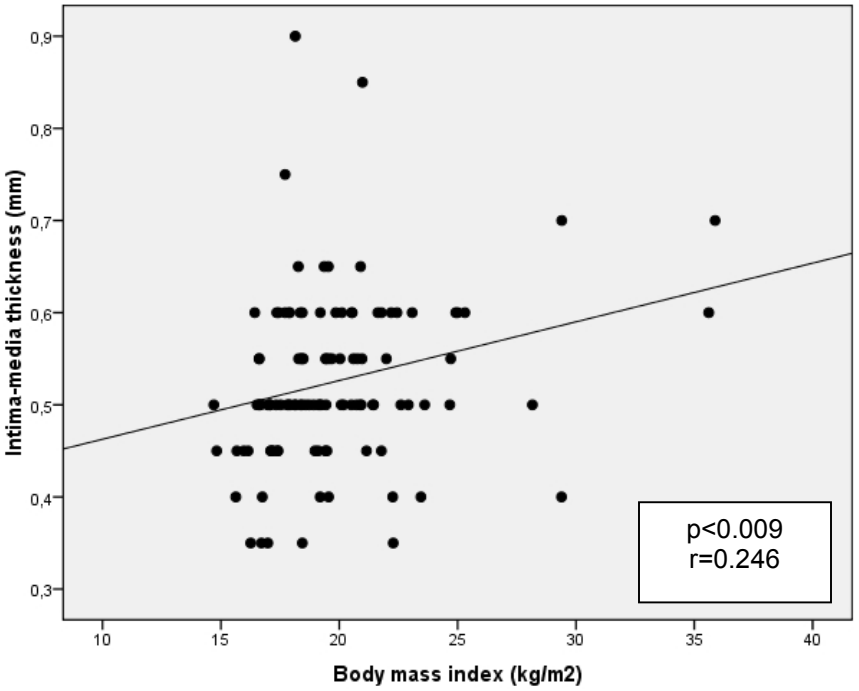

Fig. 2. The correlation between carotid artery IMT and BMI

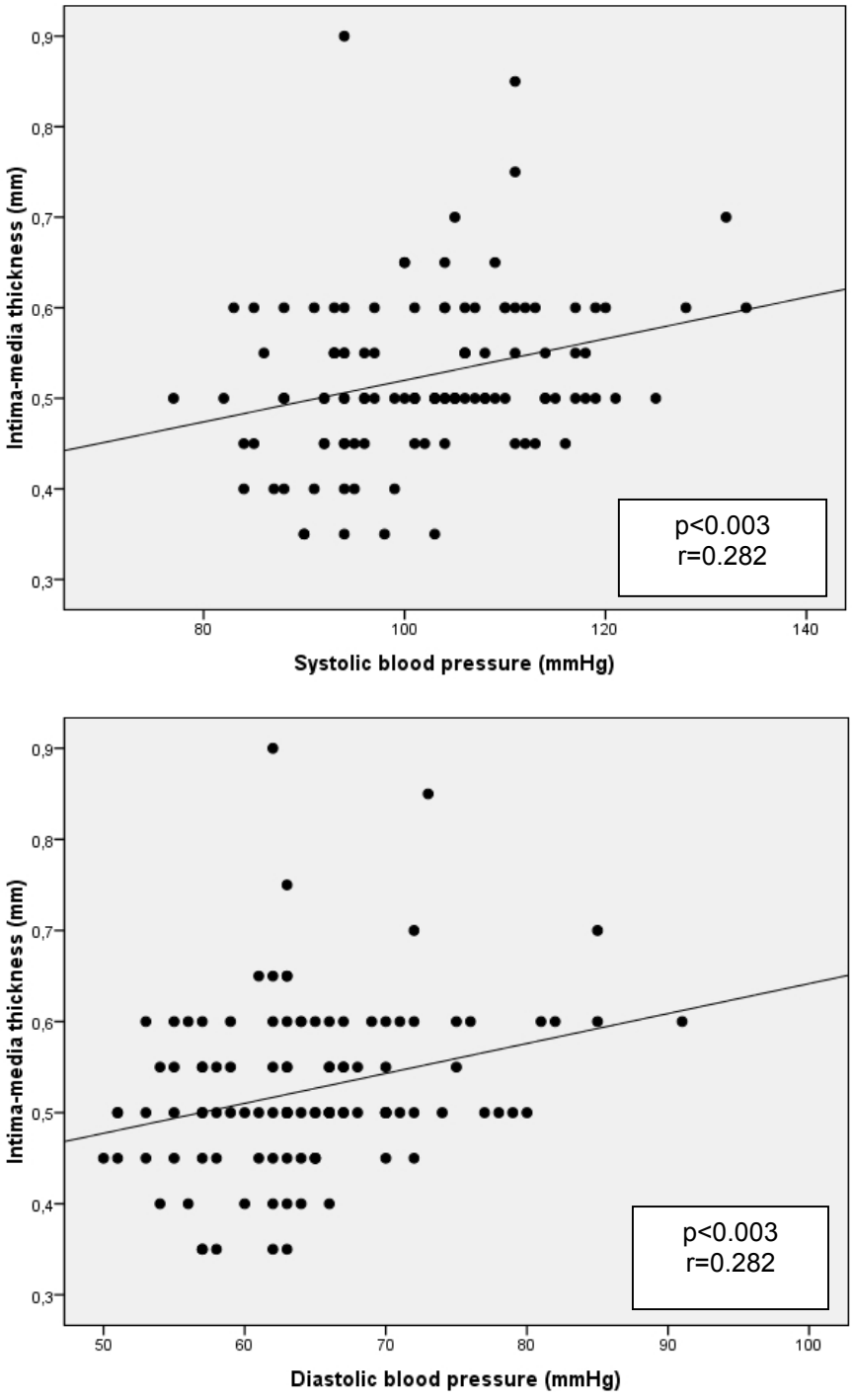

Fig. 3. The correlation between carotid artery IMT and systolic and diastolic blood pressure

Table 1. Basic caracteristics of study population

Variable	Unit	All N=112	Boys N=53	Girls N=59	p-value*
Age (mean±SD)	years	13±0.9	13±0.7	13 ±1.0	1.0
Height (mean±SD; (range))	cm	163.9±9.4; (139-193)	166.5±9.6; (145-193)	161.6±8.6; (139-185)	**0.0052**
Weight (mean±SD; (range))	kg	53.5±12.3; (36.4-114.1)	56.4±12.8; (36.2-114.1)	50.8±11.3; (36.2-89.5)	**0.0015**
Waist circumference (mean±SD; (range))	cm	75.6±11.2; (60-124)	79.2±10.8; (60-124)	72.4±10.7; (60-107)	**0.0011**
Body mass index (mean±SD; (range))	kg/m^2	19.8±3.5; (14.7-35.88)	20.2±3.4; (15.96-35.61)	19.4±3.7; (14.7-35.88)	0.2378
Systolic pressure (mean±SD; (range))	mmHg	102.2±11.2; (77-134)	105.6±9.4; (87-128)	99.2±11.9; (77-134)	**0.0022**
Diastolic pressure (mean±SD; (range))	mmHg	64.5±7.8; (50-91)	64.5±7.1; (51-91)	64.5±8.5; (50-85)	1.0
Heart rate (mean±SD; (range))	beats/min	84.9±13.0; (52-121)	85.2±13.1; (52-121)	84.6±13.0; (58-113)	0.8085
Intima-media thickness (mean±SD)	mm	0.5±0.09	0.52 ± 0.07	0.5±0.10	0.2277
Family history- cardiovascular diseases (%)	presence	45 (40.2)	19 (35.8)	26 (44.1)	0.8007

**difference of variables between sexes bold=statistically significant difference*

Table 2. The comparison of children with and without family history of CVD with different variables

Variable	Unit	Group 1 (N=45; Male/ female 19/26) children with positive family history of CVD	Group 2 (N=67; Male/ female 34/33) children with negative family history of CVD	p-value*
Age (mean ± SD)	years	13.2 ±0.82	12.9±0.83	0.071
Waist circumference (mean±SD)	cm	76.6±11.97	74.9±10.73	0.448
Body mass index (mean±SD)	kg/m^2	19.84±3.3	19.74±3.69	0.88
Systolic pressure (mean±SD)	mmHg	101.96±12.55	102.04±11.25	0.969
Diastolic pressure (mean±SD)	mmHg	65.6±8.78	64.12±7.68	0.347
Intima-media thickness (mean±SD)	mm	0.59±0.09	0.48±0.07	**0.0001**

**difference of variables between groups bold=statistically significant difference*

The sub-analysis for sex showed that there was a positive correlation between IMT and systolic blood pressure (r=0.305; p<0.026; CI 0.037-0.565), but not diastolic blood pressure (p=0.308) in boys. However, a positive correlation of IMT with systolic (r=0.314; p<0.015; CI 0.059-0.535) and diastolic blood pressure (r=0.362; p<0.005; CI 0.11-0.587) in girls was found.

When we omitted the outlier(s) with high waist circumference and BMI>35kg/m^2, the correlation remained significant for systolic and diastolic pressure but not for waist circumference and BMI.

There were 45 children with family history of CVD (40%); three of them had a parental history of CVD (2.7%), other 42 had a CVD history for second-line relatives (37.3%). We found that the children with family history of CVD had significantly higher IMT than children without family history of CVD (p<0.0001). Those with family history of CVD were relatively older and had greater waist circumference, BMI, diastolic blood pressure but lower systolic blood pressure (Table 2 above). Furthermore, the logistic regression analysis showed the presence of family history of CVD was associated with carotid artery IMT (p<0.0001).

4. DISCUSSION

Our study showed that age, higher blood pressure and BMI were positively correlated with carotid artery IMT in children. The findings were consistent with previous studies that the process of atherosclerosis begins since childhood and mainly for those children with metabolic abnormalities and hypertension. In addition, the presence of family history of CVD was associated with higher carotid artery IMT. As compared to previous studies, the correlation was only described in children's first-line relatives who had history of premature myocardial infarction. However, we described the association of children's family members including both first- and second-line relatives with prior CVD history (myocardial infarction, ischemic stroke and peripheral artery disease) with carotid IMT.

Our study had some limitations. First, the sample size was relatively small. Second, our questionnaire might be difficult to understand, if somebody didn't know, what is myocardial infarction or ischemic stroke, for example. However, we try to give all parents some oral explanation, so they could understand all questions. Third, we didn't try to establish diagnosis of hypertension or obesity in children with higher IMT values, because of the fact that the blood pressure and BMI percentiles are based upon gender, age, and height [13,14]. Therefore, we only tried to prove the correlation between higher values of blood pressure, BMI and carotid artery IMT. We are aware of low but still statistically significant correlation coefficients. Finally, we didn't ask, how many cardiovascular events were in each family history, but only, if they were present or not, if the family history was positive or negative for cardiovascular events.

5. CONCLUSION

In conclusion, higher levels of BMI, waist circumference, arterial blood pressure levels were correlated with higher carotid artery IMT in children. In addition, the presence of family history of CVD was independently associated with carotid artery IMT in children.

CONSENT

All authors declare that written informed consent was obtained from the parents of all included children.

ETHICAL APPROVAL

All authors hereby declare that the study has been approved by National Ethics Committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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