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Original article

PREDICTORS OF CAROTID INTIMA MEDIA THICKNESS IN OBESE ADOLESCENTS

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Abstract: Our aim was to assess cardiovascular risk factors that may predict increased carotid intima media thickness (cIMT) in obese children and adolescents. Children and adolescents were included in the cross-sectional study if they were aged 9-19 years and had primary obesity. Besides anthropometric and biochemical measurements, ambulatory blood pressure monitoring, measurement of carotid intima media thickness and exercise stress test were performed. We included 103 obese patients and divided them according to the ambulatory blood pressure findings in two groups: obese patients with and without ambulatory hypertension. There were 49 obese patients with and 54 without ambulatory hypertension Univariate analysis showed that there was a significant positive correlation of cIMT with age (r = 0.334, p= 0.001), body mass index (r = 0.288, p = 0.004), waist circumference (r = 0.352, p = 0.000), hip circumference (r = 0.288, p = 0.004), night-time systolic blood pressure (r = 0.226, p = 0.027), and peak diastolic blood pressure on exercise test (r = 0.241, p = 0.018). In a stepwise model, age, waist circumference and peak diastolic blood pressure on exercise test were independent predictors of cIMT.

Key words: Ambulatory blood pressure monitoring, Hypertension, Obesity, Intima media thickness, Exercise stress test.

INTRODUCTION

Epidemy of obesity lead to rise in prevalence of arterial hypertension (1). Rise in the number of children with hypertension will lead to increased number of complications. Clinical significance of hypertension is in effect of blood pressure on cardiovascular systemleading to left ventricular hypertrophy and increased carotid intima media thickness (cIMT). Long term effect of elevated blood pressure results in pathologic remodeling of arterial blood vessels with increased cIMT (2). Increased cIMT can predict increased risk of stroke and myocardial infarction in adults (3).

Our aim was to ascertain cardiovascular risk factors that may predict increased cIMT in obese children and adolescents.

PATIENTS AND METHODS

Cross-sectional study was performed at University Children's Hospital between October 2008. and June 2014. Children and adolescents were included in the study if they were aged 9-19 years and had primary obesity. Exclusion criteria was secondary hypertension, which was diagnosed according to recomended investigations of hypertension in children (4).

The study was approved by the hospital Ethics committee. Written informed consent from parents and written assent from subjects were obtained.

Office blood pressure (BP)

The average of three office BP measurements using a mercury sphygmomanometer was used for analysis. Measurements were taken after at least 5 minutes of rest with an appropriate cuff size. To control for the differences in age and body size, BP index was calculated for each patient as mean office BP divided with 95th percentile for age, gender and height (4). Office hypertension was determined when indexed office systolic and/or diastolic BP was ≥ 1.

Ambulatory blood pressure monitoring (ABPM)

All ABPM measurements were obtained on an outpatient basis using an oscillometric device (Space-

Lab 90217, Seattle, WA, USA). BP index was calculated (mean BP > 95th percentile for gender and height) for 24-hour, daytime and night-time BP according to the data from the European multicenter study (5). Ambulatory hypertension was defined as mean day-time systolic or diastolic BP index ≥ 1 or BP load above 25%.

Measurement of carotid intima media thickness

Measurement of carotid intima media thickness was performed according to standardiyed protocol on ultrasound device Simens Acuson x300 Ultrasound System (Siemens Medical Solutions, Mountain View, CA, USA). Radiologist was not aware of the blood pressure status of the patient. Patients were seating 10 minutes prior to measurement. Longitudinal view in B mode of distal carotid artery was scanned with linear probe. cIMT was measured at 1 cm proximal to bifurcation. Mean value of six measurements was used for further analysis. We used reference values of cIMT acquired in a study of 247 healthy children (6).

Exercise stress test

Exercise stress test was performed on a Schiller Cardiovit Ergo-Spiro CS-200 treadmill (Schiller AG, Baar, Switzerland) according to the modified Bruce protocol (7). Blood pressure and heart rate were measured before test, during maximal exercise, and after the test. The test was stopped when the subjects refused to continue despite encouragement.

Data analysis

Descriptive statistics are expressed as percentages or means ± SD. Continuous variables were tested for normal distribution by the Shapiro-Wilk test. Chi-square test was used to compare dichotomous variables between groups. Univariate regression analysis was used to investigate the relationships between cIMT and anthropometric, biochemical, and BP-related parameters among obese subjects. All parameters that had significant correlation with cIMT were included in stepwise multiple linear regression model. Stepwise multiple linear regression analysis was used to determine independent predictors of cIMT. Statistical significance was assumed at $p < 0.05$. Data were analyzed using SPSS version 13 (SPSS, Chicago, IL).

RESULTS

We included 103 obese patients referred for ambulatory blood pressure monitoring (ABPM) in the study. Patients were divided according to the ABPM findings in two groups: obese patients with and without ambulatory hypertension. The anthropometric and blood pressure characteristics of 103 obese patients classified according to ambulatory BP levels are described in Table 1. Age and gender were not significantly different between the two groups. There were no significant differences in anthropometric characteristics, exercise stress test, cIMT or biochemical results between the groups (Table 1 and 2).

Stepwise multiple regression analysis was performed to investigate the independent predictors of cIMT

Table 1. *Anthropometric characteristics, exercise stress test and intima media thickness*

	Obese with hypertension (n = 49)	Obese without hypertension (n = 54)
Gender (male %)	67.3	72.2
Age (years)	14.1 ± 2.0	14.1 ± 2.3
BMI (kg/m^2)	29.4 ± 3.2	30.0 ± 3.8
Waist circumference (cm)	95.5 ± 8.8	98.1 ± 10.3
Hip circumference (cm)	99.4 ± 9.5	102.6 ± 10.6
Resting heart rate (bpm)	86 ± 10	89 ± 14
Systolic BP at maximum exercise (mmHg)	187 ± 19	183 ± 16
Diastolic BP at maximum exercise (mmHg)	57 ± 10	56 ± 8
Heart rate at maximum exercise (bpm)	187 ± 7	187 ± 7
Intima media thickness	0.43 ± 0.05	0.44 ± 0.05

[a] $p < 0.05$ between obese with hypertension (OHT) and obese without hypertension (ONT)
BMI, body mass index; BP, blood pressure

Table 2. *Biochemical results of the study groups*

	Obese with hypertension	Obese without hypertension
Urea (mmol/L)	4.1 ± 0.9	4.2 ± 1.0
Creatinine (ìmol/L)	75.7 ± 14.7	77.8 ± 16.4
Ac. uricum (mmol/L)	328.8 ± 61.6	360.6 ± 89.6
Sodium (mmol/L)	140.0 ± 1.8	140.3 ± 1.6
Potassium (mmol/L)	4.4 ± 0.3	4.3 ± 0.3
CRP (mg/L)	2.9 ± 2.2	4.8 ± 9.2
HOMA-IR	3.6 ± 2.0	3.9 ± 1.8
Triglyceride (mmol/L)	1.2 ± 0.6	1.1 ± 0.6
Total cholesterol (mmol/L)	4.3 ± 1.1	4.3 ± 0.9
HDL cholesterol (mmol/L)	1.1 ± 0.2	1.1 ± 0.3
LDL cholesterol (mmol/L)	2.6 ± 1.1	2.7 ± 0.8

[a] $p < 0.05$ between obese with hypertension (OHT) and obese without hypertension (ONT)
CRP, C reactive protein
HOMA-IR, homeostasis model assessment of insulin resistance

Table 3. *Best model for determining independent predictors of cIMT in obese children and adolescents (adjusted $R^2 = 0.192$, $p < 0.001$)*

Independent variable	ß	95% CI	p
Waist circumference (cm)	0.223	0.007-0.237	0.038
Peak diastolic blood pressure on exercise test (mmHg)	0.241	0.033-0.241	0.011
Age (years)	0.243	0.079-1.142	0.025

in obese subjects. Univariate analysis showed that there was a significant positive correlation of cIMT with age (r = 0.334, p= 0.001), body mass index (r = 0.288, p = 0.004), waist circumference (r = 0.352, p = 0.000), hip circumference (r = 0.288, p = 0.004), night-time systolic blood pressure (r = 0.226, p = 0.027), and peak diastolic blood pressure on exercise test (r = 0.241, p = 0.018). Hence, these variables were included as potential predictors of cIMT in a stepwise multiple regression analysis. In a stepwise model, age, waist circumference and peak diastolic blood pressure on exercise test were independent predictors of cIMT (Table 3). Carotid IMT was not correlated with casual BP or with any of the ABPM parameters.

DISCUSSION

Arterial hypertension is one of the most important cardiovascular risk factors. It is observed that even slight changes in blood pressure levels might cause significant change in hypertension-induced morbidity (8). Consequently, additional survey of blood pressure status in childhood could improve future cardiovascular health of adults. Hence, blood pressure measurement is recommended as essential part of pediatric exam (4). ABPM is considered as superior method in comparison to casual blood pressure measurement as it can better predict hypertension induced target organ damage (9).

Primary hypertension has become the dominant form of hypertension in adolescents due to escalation of obesity. Hypertension is also the most important modifiable risk factor for atherosclerosis. Therefore, a notion that pediatric hypertension often remains undiagnosed deserves closer attention (10).

Our study did not find significant differences in exercise stress test results between obese subjects with and without hypertension. This could be explained with early stopping of exercise stress test in obese subjects.

Obesity is well established independent predictor of cardiovascular diseases in adults (11). In addition to effect via metabolic, endocrine and inflammatory parameters known to increase risk of cardiovascular diseases, obesity also has a direct influence on alterations in structure and function of blood vessels (12).

Previously it was considered that obese children and adolescents are population less prone to cardiovascular diseases. However, a recent report declared that cardiovascular damage associated with obesity occurs even in childhood (13). In comparison with children who lived between 1986. and 1989, modern youth has increased cardiovascular risk (14). Given the increased prevalence of obesity in XXI century this seems to be common issue of health care systems around the world.

Carotid IMT measurement allows noninvasive detection of early arteriosclerotic changes (15). Preclinic form of cardiovascular diseases may last for decades, hence detection of disease in presymptomatic phase during childhood allows timely management (16). The most important predictive risk factors of cIMT in children with primary hypertension were systolic and pulse pressure (17, 18).

Previous investigations performed in children with primary hypertension did not find correlation of office blood pressure measurement and cIMT, but there was a significant correlation between cIMT and several parameters of ABPM (19), such as day-time systolic blood pressure load and day-time systolic blood pressure index, which are parameters of hypertension severity. Our results revealed correlation of cIMT and night-time systolic blood pressure.

Sorof showed that cIMT was directly correlated with BMI and left ventricular mass index in children with primary hypertension (2). Since obesity may occur prior to overt hypertension (20), obese children have increased risk for future cardiovascular complications. In obese children cIMT was associated with BMI, systolic blood pressure, fasting glucose level, HOMA resistance index, basal insulin, resistin and decrease of adiponectin level. When adjusted for gender and BMI, only adiponectin level remained as independent predictor of cIMT (21).

In contrast to previous studies in children and adults (22, 23), our findings revealed correlation of cIMT in obese children with with age, body mass index, waist circumference, hip circumference, night-time systolic blood pressure, and peak diastolic blood pressure on exercise test.

According to literature review, association of cIMT with blood pressure parameters during exercise test was not investigated. Our findings indicate that peak diastolic blood pressure on exercise test, in addition to age and waist circumference, is predictor of cIMT.

Previous research established association of obesity and cIMT (24,25,26). Obese children have increased cIMT compared with normal weight children independent of blood pressure influence (27). Correlation between cIMT and waist circumference is in concert with previous results, which noted the importance of

central obesity in children as an independent cardiovascular risk factor.

It is still not clear how structural changes of blood vessel evolve with aging of obese adolescents. Future longitudinal investigations should analyze progression of cardiovascular disorders, their influence on health and future structure and function of blood vessels.

CONCLUSION

In conclusion, age, waist circumference, and peak diastolic blood pressure on exercise test may predict cIMT in obese children and adolescents.

Abbrevations

cIMT — carotid intima media thickness
BP — blood pressure
ABPM — Ambulatory blood pressure monitoring
BMI — body mass index

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Conflict of interest

The authors declare that there are no conflicts of interest.

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Sažetak

PREDIKTORI DEBLJINE INTIME I MEDIJE KAROTIDNIH ARTERIJA KOD GOJAZNIH ADOLESCENATA

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Cilj rada je ispitati faktore rizika kardiovaskularnih oboljenja (biohemijski parametri, vrednost krvnog pritiska) koji utiču na povećanje debljine intime i medije karotidnih arterija (cIMT) kod gojazne dece i adolescenata. U studiju preseka su uključeni deca i adolescenti koji su ispunjavali kriterijume za ulazak ispitanika u studiju: uzrast od 9 do 19 godina i primarna gojaznost. Pored antropometrijskih i biohemijskih merenja učinjena su sledeća ispitivanja: merenje krvnog pritiska 24-časovnim ambulatornim merenjem, ultrasonografsko određivanje debljine intime i medije karotidnih arterija, i test opterećenja fizičkim naporom. U ispitivanje je uključeno 103 gojazna pacijenta koji su prema vrednostima krvnog pritiska pri ambulatornom monitoringu podeljeni u 2 grupe – gojazni pacijenti sa hipertenzijom i gojazni pacijenti bez hipertenzije. Grupu gojaznih pacijenta sa hipertenzijom činilo je 49 ispitanika, dok je u grupi gojaznih pacijenata bez hipertenzije bilo 54 ispitanika. Pronađena je statistički značajna korelacija cIMT sa uzrastom (r = 0,334, p= 0,001), indeksom telesne mase (r = 0,283, p = 0,005), obimom struka (r = 0,352, p = 0,000), obimom kukova (r = 0,288, p = 0,004), noćnim sistolnim krvnim pritiskom (r = 0,226, p = 0,027), i dijastolnim krvnim pritiskom pri maksimalnom opterećenju pri testu opterećenja fizičkim naporom (r = 0,241, p = 0,018). Multipla linearna regresija je pokazala da su uzrast, obim struka, i dijastolni krvni pritisak pri maksimalnom opterećenju nezavisni prediktori cIMT.

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