Journal of the American College of Cardiology
Vol. 48, No. 9, 2006

ISSN 0735-1097/06/$32.00
Published by Elsevier Inc.
doi:10.1016/j.jacc.2006.07.035

Improvement of Early Vascular Changes and Cardiovascular Risk Factors in Obese Children After a Six-Month Exercise Program

Andreas A. Meyer, MD,* Günther Kundt, PHD,† Ute Lenschow, MD,* Peter Schuff-Werner, PHD,‡ Wolfgang Kienast, PHD*

Rostock, Germany

OBJECTIVES The present study aimed to assess the effect of a 6-month exercise program in obese children on flow-mediated vasodilation (FMD) carotid intima-media thickness (IMT) and cardiovascular risk factors (RF).

BACKGROUND Childhood obesity contributes to adult obesity and subsequent cardiovascular disease. Physical inactivity is a major RF for obesity, endothelial dysfunction, and elevated carotid IMT, culminating in early atherosclerotic disease.

METHODS Sixty-seven obese subjects (age 14.7 $\pm$ 2.2 years) were randomly assigned to 6 months' exercise or non-exercise protocol. We examined the influence of exercises (1 h, 3 times/week) on FMD, IMT, and cardiovascular risk profile.

RESULTS Compared with lean control subjects, obese children demonstrated at baseline significantly impaired FMD (4.09 $\pm$ 1.76% vs. 10.65 $\pm$ 1.95%, $p < 0.001$), increased IMT (0.48 $\pm$ 0.08 mm vs. 0.37 $\pm$ 0.05 mm, $p < 0.001$), and a number of obesity-related cardiovascular RF. Significant improvements were observed in the exercise group for IMT (0.44 $\pm$ 0.08 mm, $p = 0.012$, -6.3%) and FMD (7.71 $\pm$ 2.53%, $p < 0.001$, $+127\%$). This improvement correlated with reduced RF, such as body mass index standard deviation scores, body fat mass, waist/hip ratio, ambulatory systolic blood pressure, fasting insulin, triglycerides, low-density lipoprotein/high-density lipoprotein ratio, and low-degree inflammation (C-reactive protein, fibrinogen).

CONCLUSIONS The present study documented increased IMT, impaired endothelial function, and various elevated cardiovascular RF in young obese subjects. Regular exercise over 6 months restores endothelial function and improves carotid IMT associated with an improved cardiovascular risk profile in obese children. (J Am Coll Cardiol 2006;48:1865–70) © 2006 by the American College of Cardiology Foundation

Child and adolescent obesity strongly relates to early atherosclerosis and obesity-related cardiovascular disease (1). Physical inactivity is instrumental in the development of atherosclerotic cardiovascular disease (2) and might well intermediate between obesity, inflammation, insulin resistance, and early atherosclerosis (3). Greater physical activity reduces cardiovascular risk (4) and is beneficial to weight management, prevention of obesity, and insulin resistance in adults and children (5).

It is universally accepted that disturbed endothelial cell biology, variably including activation, injury, damage, and dysfunction (6), is part of the early pathogenesis of atherosclerosis (7).

Ultrasound evaluation of brachial artery flow-mediated vasodilation (FMD) and carotid artery intima-medial thickening (IMT) is increasingly used for pediatric cardiovascular risk assessment (8) and might present a novel strategy for primary prevention and early therapy. In children, impaired FMD is known to prevail in conditions predisposing atherosclerosis, including familial hypercholesterolemia, type I diabetes, and morbid obesity (9–11). The analysis of short-term exercise studies in a wide population range with endothelial dysfunction showed improvements in vascular function with exercise, with or without concomitant reduced weight and cardiovascular RF (12–14).

Intima-medial thickening in obese children is a focus of ongoing debate. A study of severely obese children produced no evidence of significant differences in carotid IMT, compared with control subjects (11). Results from a larger study, however, demonstrate increased carotid IMT in obese children and potential influence from long-term exercise (15).

In the current study, we sought to determine the effects of 6 months' physical activity in obese children and adolescents on FMD, IMT, and obesity-related cardiovascular disease RF.

METHODS

Study design. Ninety-six obese children (47 boys and 49 girls, age 14.2 $\pm$ 1.9, range 11–16 years) were consecutively recruited when they presented to an established university outpatient department of pediatric endocrinology and cardiology. Obesity was defined as body mass index (BMI) in excess of the 97th percentile for the German pediatric population (16).

The control group consisted of 35 children (17 boys and 18 girls, age 14.7 $\pm$ 2.2, range 12–16 years) without appreciable cardiovascular RF and was selected from children presenting at the same institution for the diagnostic work-up of dizziness

From the *Division of Pediatric Cardiology, Children's Hospital, University of Rostock, Rostock, Germany; and the †Institute of Medical Informatics and Biometry and the ‡Institute of Clinical Chemistry and Laboratory Medicine, University of Rostock, Rostock, Germany. This study was supported by a University of Rostock Medical Faculty research program grant.

Manuscript received April 25, 2006; revised manuscript received June 26, 2006, accepted July 3, 2006.

JACC Vol. 48, No. 9, 2006
November 7, 2006:1865–70

Abbreviations and Acronyms

BMI = body mass index
BP = blood pressure
CRP = C-reactive protein
FMD = flow mediated vasodilation
HDL = high-density lipoprotein
IL = interleukin
IMT = intima-media thickness
LDL = low-density lipoprotein
NO = nitric oxide
RF = risk factor(s)

and minor orthostatic complaints. Children with structural or functional cardiovascular abnormalities were excluded.

At baseline, all patients underwent identical 2-day screening with a multiple RF approach. We ensured group comparability by matching for major baseline characteristics, including family history of atherosclerotic disease, age, gender, and Tanner stages.

The study complied with the Declaration of Helsinki. The study plan was approved by the local ethics committee, and written informed consent was obtained from the parents. Study participation was voluntary; subjects were free to withdraw at any time.

Subjects were randomly assigned to 6 months' exercise or to 6 months' non-exercise. Exclusion criteria were medication of any type; smoking, active participation in any exercise activity ≥30 min more than once/week; participation in organized diet programs; and diabetes, heart, renal, or liver disease.

For all subjects with obesity, the screening protocol was repeated at 6 monthly intervals. The lean control subjects were studied only at baseline.

Of 50 subjects who started the program, only 33 (17 boys and 16 girls, age 13.7 ± 2.1 years), participated sufficiently for inclusion in the second screening protocol. Exclusion criteria were participation in organized exercises less than twice/week, a break in activities for longer than 2 weeks, and total discontinuance of the program. Of 46 subjects of the obese control group, 34 (17 boys and 17 girls, age 14.1 ± 2.4 years) could be recruited for a second risk profile evaluation.

Measurement of risk factors. Anamnestic and anthropometric data were reviewed during 2 days' hospital stay. Body fat mass was assessed by bioelectrical impedance (Data Input Inc., Frankfurt, Germany), expressed as percentage of body weight. A venous blood sample was collected after overnight fasting. Insulin resistance was calculated by homeostasis model assessment (17).

Resting blood pressure (BP) was measured at all extremities by an automatic oscillometric cuff device (Dinamap, Critikon Inc., Tampa, Florida). The 24-h ambulatory BP was measured on the right arm (Space Labs Inc., Issaquah, Washington). The BP data were automatically recorded every 15 min from 8:00 AM to 8:00 PM (daytime BP) and every 30 min from 8:00 PM to 8:00 AM (nighttime BP). The BP studies were excluded from analysis if measurements were invalid or lacking for more than 2 h.

The spiroergometric equipment Oxycon Alpha (Jaeger, Würzburg, Germany) evaluated exercise parameters. All children underwent cycling exercises with a modified Bruce protocol with continuously raised loads; they exercised to exhaustion. Blood pressure was measured during exercise every minute, and the groups were compared at 2 W/kg load. Echocardiography and vascular measurements were taken with a Hewlett-Packard Sonos system (Sonos 5500, Philips Int., Andover, Massachusetts). Left ventricular measurements were derived from 2-dimensional guided M-mode tracings, as recommended by the American Society of Echocardiography (18). Left ventricular mass (LVMMI) was calculated by Devereux-modified American Society of Echocardiography cube equation (19) and indexed to body surface area.

Vascular measurements. Flow-mediated vasodilation and IMT were conducted as previously described (20) at baseline and after 6 months. Endothelium-dependent responses of the right radial artery were measured for each patient subject to International Brachial Artery Reactivity Task Force guidelines (21). A trained, certified pediatrician analyzed FMD and IMT. Intraobserver variability expressed as median absolute difference in the measurements of FMD was 1.03 ± 0.28%. Results of measuring the arterial diameter were highly reproducible with a mean difference of 0.034 ± 0.076. The IMT–intraobserver and IMT–interobserver variability (mean bias) was 0.2% and 1.2%, respectively.

Intervention protocol. Exercises were conducted 3 times/week: on Mondays, swimming and aqua aerobic training (60 min); Wednesdays, sports games (90 min); and Fridays, walking (60 min), supervised by qualified coaches and physiotherapists. Exercises were progressively intensified as individually tolerated. Control subjects did not participate in structured exercises and were instructed to maintain current levels of physical activity. Physical activity was recorded in a 1-week activity protocol, completed by subjects of both groups. There was one consultation with a nutritionist to enhance knowledge about healthy nutrition for children and adolescents for subjects of both groups. Calorie intake was measured at the beginning and after 6 months with a 1-week nutrition protocol and calculated with the Nutriscience Prodi 5.1 expert program (Hausach, Germany). There was no change in calorie intake or diet plan in both groups.

Statistical methods. Data were stored and analyzed with the SPSS statistical package 12.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics were computed for variables of interest and included mean values and SDs of continuous variables and absolute and relative frequencies of categorical factors.

Testing for differences of continuous variables between the study groups was accomplished by the 1-way analysis of variance (ANOVA) or the Kruskal-Wallis 1-way ANOVA, ranked as appropriate. Test selection was based on evaluating the variables for normal distribution, employing the Kolmogorov-Smirnov test. Post hoc comparisons were made after an ANOVA resulted in a significant test. We then