

**Impact of physical activity on cardiovascular risk factors in children with type 1 diabetes:
a multicenter study of 23,251 patients**

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Short title: Impact of physical activity in diabetic children

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Introduction

Type 1 diabetes is associated with a high risk for early atherosclerotic complications. Patients with type 1 diabetes have a four- (in men) to eightfold (in women) excess risk of coronary heart disease compared to the general population (1). It has been shown that type 1 diabetic patients aged 20-39 years had a fivefold higher risk of dying from cardio- and cerebrovascular events compared to healthy individuals (2). Development of atherosclerotic lesions in healthy subjects begins upon childhood. In children with type 1 diabetes, who had died an unnatural death, an asymptomatic increase of the intima-media thickness of the common carotid artery was found (3). Known risk factors for vascular complications are long standing diabetes, age, poor glycemic control, smoking, hypertension, obesity and dyslipidemia (4,5,6). In a recent study, 69% of the pediatric patients with type 1 diabetes were found to have one or more cardiovascular risk factors (7). Thus, there is an urgent need of prevention strategies to reduce these risk factors in childhood and adolescence.

We recently showed that frequency of regular physical activity (RPA) represents an important factor influencing glycohemoglobin and, in girls, BMI (8). The present study focuses on the impact of RPA on further cardiovascular risk factors in children with type 1 diabetes such as plasma lipids and blood pressure.

Research design and methods

Data were provided by the Pediatric Quality Initiative (9) including anonymized longitudinal data of 23,251 patients (3-18 years) with type 1 diabetes from 209 centers in Germany and Austria. The data are continuously generated by the participating centers using the DPV software (Diabetes Software for Prospective Documentation) and after anonymization transmitted to the Pediatric Quality Initiative for central

analysis. Plausibility of the data is reviewed twice a year and inconsistent data are reconfirmed with the centers.

In this cross-sectional study (DPV-Science database, October 2006), the following cardiovascular risk factors were evaluated: plasma lipids (Chol, HDL-C, LDL-C and TG), blood pressure, HbA1c, and Body Mass-Index (BMI). Laboratory methods are standardized nationwide and follow criteria for quality management defined by the German Medical Association (10). Dyslipidemia was defined as Chol >200 mg/dl (5.2 mmol/l), HDL-C <35 mg/dl (0.91 mmol/l), LDL-C >160 mg/dl (4.1 mmol/l) or TG >150 mg/dl (1.7 mmol/l) (11). Normative blood pressure data developed by the Task Force on Blood Pressure Control in children served as reference values (12). For comparison, the HbA1c values were standardized and transformed to the DCCT normal range (13).

Patients were grouped by the frequency of their self-reported RPA as follows: RPA0=none (n=10,392), RPA1 = 1-2x/week (n=8,607), RPA2 = \geq 3x/week (n=4,252). At every visit at the diabetologist, the DPV software requires information about the frequency of the patient's RPA. This is exercise performed at least once a week for at least 30 minutes. Intensity of the sportive activity is not protocolled. School sports are not included. The study protocol was approved by the human subjects committee of the University of Ulm, Germany.

The data were evaluated statistically using the Kruskal-Wallis test for comparison among groups followed by the Holm adjustment (Bonferroni stepdown) in case of multiple comparisons (SAS for Windows, Version 9.1). Multiple linear regression analysis was performed to extract possible explanatory variables affecting the levels of Chol, HDL-C, LDL-C and TG, HbA1c and blood pressure. P

values $<.05$ were considered statistically significant.

Results

Mean HbA1c was 7.9%. Frequency of RPA ranged between 0-9x per week (average 1.29x). 44.7% of the patients were not physically active, 37.0% of them performed RPA once or twice per week and 18.3% performed more than twice per week. Age of the patients was higher with increasing frequency of RPA ($p<.00001$). Frequency of RPA was higher in boys than in girls ($p<.01$).

37.9% of the patients showed dyslipidemia. Elevation of Chol or of TG were the most frequent types of dyslipidemia (24.3% and 25.8% respectively) followed by elevated LDL-C (14.2%) and decreased HDL-C (3.1%). With increasing frequency of RPA, the percentage of patients with dyslipidemia decreased from 41.2% in RPA0 to 36.0% in RPA1 and 34.4% in RPA2 ($p<.00001$). Girls had higher values of Chol, LDL-C, HDL-C, and TG than boys ($p<.001$). In girls, with increasing frequency of RPA, we found lower levels for Chol ($p<.015$), LDL-C ($p<.005$), and TG ($p<.00001$) and higher levels for HDL-C ($p<.00001$) whereas in boys, there were differences only for HDL-C ($p<.00001$) and TG ($p<.0005$). Increasing frequency of RPA was associated with lower Chol, LDL-C and TG in age group 15-18 years, whereas in age group 9-14 years, it was associated with lower LDL-C and higher HDL-C. In age group 3-8 years only the effect on HDL-C reached significance. Multiple analysis revealed that HDL-C and TG were influenced by the frequency of RPA whereas Chol and LDL-C were not.

8.1% of the patients had elevated systolic and 3.1% showed elevated diastolic blood pressure. Concerning systolic or diastolic blood pressure, there was no difference between the RPA groups. However, multiple analysis revealed that the percentage of patients having elevated diastolic blood

pressure was lower in group RPA1 and RPA2 than in group RPA0 ($p<.005$).

Multivariate analysis with HbA1c as the dependent variable revealed that frequency of RPA was one of the most important influencing factors for HbA1c. HbA1c was lower in patients with higher frequency of RPA ($p<.00001$), this effect was found in both sexes and in every age group. Other influencing factors lowering HbA1c were young age ($p<.0001$), male sex ($p<.0001$), and diabetes duration ($p<.0001$). Higher levels of HbA1c were associated with higher levels of Chol, LDL-C and TG ($p<.0001$ each) and lower HDL-C ($p<.01$).

Conclusion

Increasing physical activity is associated with a beneficial cardiovascular risk profile in children with type 1 diabetes such as lower lipoproteins and diastolic blood pressure and with better glycemic control. There are positive interactions between these parameters. Therefore, physical activity should represent an important issue in education of children and adolescents with type 1 diabetes and be performed regularly by these patients. The percentage of children with type 1 diabetes not performing any regular physical activity should be reduced.

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References:

1. Swerdlow AJ, Jones ME: Mortality during 25 years of follow-up of a cohort with diabetes. *Int J Epidemiol* 25:1250–1261, 1996
2. Laing SP, Swerdlow AJ, Slater SD, Botha JL, Burden AC, Waugh NR, Smith AWM, Hill RD, Bingley PJ, Patterson CC, Qiao Z, Keen H: The British Diabetic Association Cohort Study, II: cause-specific mortality in patients with insulin-treated diabetes mellitus. *Diabet Med* 16:466-471, 1999
3. Järvisalo MJ, Putto-Laurila A, Jarri L, Lehtimäki T, Solakivi T, Rönnemaa T, Raitakari OT: Carotid artery intima-media thickness in children with type 1 diabetes. *Diabetes* 51:493-498, 2002
4. Zieske AW, Malcolm GT, Strong JP: Natural history and risk factors of atherosclerosis in children and youth: the PDAY study. *Pediatr Pathol Mol Med* 21:213-237, 2002
5. The Diabetes Control and Complications Trial Research Group: The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus. *N Engl J Med* 329: 977-986, 1993
6. Soedamah-Muthu SS, Chaturvedi N, Toeller M, Ferriss B, Reboldi P, Michel G, Manes C, Fuller JH, The EURODIAB Prospective Complications Study Group: Risk factors for coronary heart disease in type 1 diabetic patients in Europe. *Diabetes Care* 27:530-537, 2004
7. Schwab KO, Doerfer J, Hecker W, Grulich-Henn J, Wiemann D, Kordonouri O, Beyer P, Holl RW: Spectrum and prevalence of atherogenic risk factors in 27.358 children, adolescents and young adults with type 1 diabetes – Cross sectional data from the German diabetes documentation and quality management system DPV. *Diabetes Care* 29:218-225, 2006
8. Herbst A, Bachran R, Kapellen T, Holl RW: Effects of physical activity on glycaemic control in children with diabetes mellitus type 1 (T1DM). *Arch Pediatr Adolesc Med* 160:573-577, 2006
9. Hecker W, Grabert M, Holl RW, for the German Paediatric Diabetology Group: Quality of paediatric IDDM care in Germany: a multicenter analysis. *J Pediatr Endocrinol Metab* 12:31-38, 1999
10. Richtlinie der Bundesärztekammer zur Qualitätssicherung quantitativer laboratoriumsmedizinischer Untersuchungen. *Deutsches Ärzteblatt* 100:A 3335-3338, 2003
11. American Academy of Pediatrics: National Cholesterol Education Program: report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. *Pediatrics* 89:522-584, 1992
12. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. *Pediatrics* 98:649-658, 1996
13. The DCCT Research Group: Feasibility of centralized measurements of glycated hemoglobin in the Diabetes Control and Complications Trial: a multicenter study. *Clin Chem* 33:2267-2271, 1987

Tables:**Table 1:** Baseline characteristics of the investigated 18,392 patientsData are presented in means \pm SD

RPA = regular physical activity per week:

RPA 0 = none, RPA 1 = 1-2x/week, RPA 2 = \geq 3x/week

*Kruskal-Wallis-Test with Holm-Correction for multiple testing

n.s. = not significant

	RPA 0	RPA 1	RPA2	P value*
N	10,392	8,607	4,252	
Age (years)	12.7 \pm 4.3	12.6 \pm 3.7	13.9 \pm 3.1	< .00001
BMI-SDS	0.52 \pm 0.9	0.48 \pm 0.9	0.47 \pm 0.8	<.002
Diabetes duration (years)	4.7 \pm 3.8	4.7 \pm 3.7	5.1 \pm 3.8	< .00001
HbA1c (%)	8.1 \pm 1.9	7.8 \pm 1.6	7.8 \pm 1.6	< .00001
Any dyslipidemia (% of patients)	41.2 \pm 49	36.0 \pm 48	34.4 \pm 47	< .00001
TG (mg/dl)	126 \pm 102	114 \pm 85	114 \pm 92	< .00001
Chol (mg/dl)	181 \pm 48	178 \pm 45	176 \pm 38	< .00001
LDL-C (mg/dl)	99 \pm 35	96 \pm 35	95 \pm 32	< .0001
HDL-C (mg/dl)	61 \pm 19	63 \pm 19	63 \pm 17	< .00001
Elevated systolic blood pressure (% of patients)	8.4 \pm 28	7.5 \pm 26	8.6 \pm 28	n.s.
Elevated diastolic blood pressure (% of patients)	3.5 \pm 18	3.2 \pm 17	1.9 \pm 14	< .0001