Impact of Physical Activity on Glycemic Control and Prevalence of Cardiovascular Risk Factors in Adults With Type 1 Diabetes: A Cross-sectional Multicenter Study of 18,028 Patients

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Diabetes Care 2015;38:1536–1543 | DOI: 10.2337/dc15-0030

OBJECTIVE

Physical activity (PA) can improve cardiovascular risk in the general population and in patients with type 2 diabetes. Studies also indicate an HbA_{1c}-lowering effect in patients with type 2 diabetes. Since reports in patients with type 1 diabetes are scarce, this analysis aimed to investigate whether there is an association between PA and glycemic control or cardiovascular risk in subjects with type 1 diabetes.

RESEARCH DESIGN AND METHODS

A total of 18,028 adults (≥18 to <80 years of age) from Germany and Austria with type 1 diabetes from the Diabetes-Patienten-Verlaufsdokumentation (DPV) database were included. Patients were stratified according to their self-reported frequency of PA (PA0, inactive; PA1, one to two times per week; PA2, more than two times per week). Multivariable regression models were applied for glycemic control, diabetes-related comorbidities, and cardiovascular risk factors. Data were adjusted for sex, age, and diabetes duration. *P* values for trend were given. SAS 9.4 was used for statistical analysis.

RESULTS

An inverse association between PA and HbA_{1c}, diabetic ketoacidosis, BMI, dyslipidemia (all $P < 0.0001$), and hypertension ($P = 0.0150$), as well as between PA and retinopathy or microalbuminuria (both $P < 0.0001$), was present. Severe hypoglycemia (assistance required) did not differ in PA groups ($P = 0.8989$), whereas severe hypoglycemia with coma was inversely associated with PA ($P < 0.0001$).

CONCLUSIONS

PA seemed to be beneficial with respect to glycemic control, diabetes-related comorbidities, and cardiovascular risk factors without an increase of adverse events. Hence, our data underscore the recommendation for subjects with type 1 diabetes to perform regular PA.

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Received 7 January 2015 and accepted 29 April 2015.

This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc15-0030/-/DC1.

A slide set summarizing this article is available online.

There is evidence that regular physical activity (PA) improves well-being and reduces the risk of overweight and noncommunicable diseases as type 2 diabetes, cardiovascular disease (CVD), or some types of cancer (e.g., breast or colon cancers) (1–4). Moreover, PA is associated with a substantial decrease in cardiovascular and all-cause mortality (5).

Compared with the general population, subjects with diabetes are at higher risk to develop CVD and to die of CVD-related complications (6). Studies indicate that in patients with type 2 diabetes the CVD risk profile can be improved through regular PA (7–9). Furthermore, meta-analyses show an HbA_{1c}-lowering effect in patients with type 2 diabetes who engage in regular PA (8,10).

The current literature barely provides evidence on PA-related improvements in glycemic control and CVD risk profile for patients with type 1 diabetes. Previous studies in children with type 1 diabetes suggest an inverse association between PA and HbA_{1c} values (11,12). However, results of meta-analyses are contradictory. Whereas Quirk et al. (13) revealed benefits on glycemic control in children and adolescents with type 1 diabetes, another meta-analysis did not find an association between PA and metabolic control (14). In both meta-analyses, the sample size of studies included was rather low (between 10 and 196 subjects) (13,14). In pediatric patients with type 1 diabetes, regular PA seemed to be linked with a beneficial CVD risk profile (11), a result confirmed by another meta-analysis (15). Concerning microvascular complications (e.g., diabetic nephropathy or diabetic retinopathy), studies are scarce and not consistent. Results of the Pittsburg Insulin-Dependent Diabetes Mellitus (IDDM) Morbidity and Mortality Study suggested an inverse association between the occurrence of microvascular complications and PA (16). In contrast, findings from the Diabetes Control and Complications Trial (DCCT) indicated no beneficial effects (17). Besides potential advantages of PA, adverse effects like the frequency of hypoglycemic events should be considered as well.

The objective of this cross-sectional study was to examine the influence of PA on glycemic control and cardiovascular risk factors in a large cohort of 18,028 adults with type 1 diabetes from Germany and Austria.

RESEARCH DESIGN AND METHODS

Data Source and Subjects

Data were provided by the Diabetes-Patienten-Verlaufsdokumentation (DPV) database, a software for standardized, prospective documentation of diabetes care and outcome. The DPV is currently used by 413 centers from Germany and Austria. Twice a year, anonymized data are transmitted from participating health care facilities to Ulm, Germany, and aggregated into a cumulative database for clinical research and quality assurance. In case of implausibility or inconsistency, data are reported back to the centers for verification or correction. The DPV Initiative is authorized by the Ethics Committee of the University of Ulm, Germany, and data collection by the local review boards.

In March 2014, 338,982 patients from 381 centers were registered in DPV. Patients between 18 and <80 years of age were included. Patients without documentation on PA were excluded, leaving 18,028 subjects (a more detailed flowchart can be found in Supplementary Fig. 1). For each patient, the last year of treatment was analyzed. In case of multiple data sets per patient, data were aggregated. Variables were aggregated as median (e.g., HbA_{1c}), as cumulative sums (e.g., severe hypoglycemia), or as maximum (e.g., antihypertensive drugs). The study population was stratified according to patient self-reported PA as follows: PA0, none (n = 11,357); PA1, one to two times per week (n = 3,459); and PA2, more than two times per week (n = 3,212). At each visit to the physician, the DPV software requires information about patient PA. The protocol includes the frequency of PA (performed for at least 45 min) per week. Patients are asked by the health care team about their PA and its frequency in a standardized question, "How often and how long are you physically active in a typical week?" These data are specific to recreational exercise (including single or group activities as well as self-initiated or organized in sport clubs) and do not include household or transportation activities. Due to the current structure of DPV, information on metabolic equivalents of task (MET) and kind of exercise are not available yet.

Outcome Variables

BMI was calculated as the ratio of the body weight in kilograms and the squared body height in meters (kg/m^2). Overweight was defined as BMI ≥25 to <30 kg/m^2 and obesity as BMI ≥30 kg/m^2. HbA_{1c} was mathematically standardized to the reference range of 20–42 mmol/mol (DCCT, 4.05–6.05%) by applying the multiple-of-the-mean transformation method (18). According to current guidelines, hypertension was defined by increased systolic (≥140 mmHg) or increased diastolic (≥90 mmHg) blood pressure (19) or by the use of antihypertensive drugs. Serum lipids (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) were measured in local laboratories compliant with national guidelines (20). Dyslipidemia was defined by the use of lipid-lowering drugs, decreased values of HDL cholesterol (men, <0.9 mmol/L; women, <1.0 mmol/L), or by at least one increased value of total cholesterol (>5.2 mmol/L), LDL cholesterol (>3.4 mmol/L), or triglycerides (>1.7 mmol/L) (21). Diabetic ketoacidosis (DKA) was diagnosed in patients with a pH value <7.3 or hospital admission due to DKA. Severe hypoglycemia was defined as "an event requiring assistance of another person to actively administer carbohydrates, glucagon, or other resuscitative actions" (22), and hypoglycemia with coma was defined by loss of consciousness or occurrence of seizures. Definitions of diabetic retinopathy and microalbuminuria have previously been described (23).

Statistical Analysis

Descriptive statistics were implemented for the final study population and for patients excluded due to missing information on PA (Table 1). Sociodemographic characteristics and clinical data were presented as median (Q1, Q3), as percentage, or as events/100 patient-years (PY). To compare groups, χ^2 test was used for dichotomous variables, Kruskal-Wallis test for nonparametric continuous variables, and Poisson model for count data. The Holm method (Bonferroni stepdown) was applied to correct P values for multiple comparisons (24).

To account for potential confounding effects (age [in groups 18 to <30, 30 to <45, and 45 to <80 years], sex, and

Table 1—Sociodemographic and clinical data of the final study population and of patients excluded due to missing documentation on PA

	Study population (n = 18,028)	Patients excluded (n = 20,632)	P value*
Age (years)	33.86 (20.18, 52.09)	40.43 (25.13, 54.95)	<0.0001
Male (%)	54.2	52.9	0.0605
Diabetes duration (years)	11.85 (5.90, 21.13)	12.97 (5.41, 24.08)	<0.0001
HbA_{1c} (%)	7.72 (6.80, 8.99)	7.78 (6.84, 9.10)	0.0030
HbA_{1c} (mmol/mol)	60.85 (50.78, 74.74)	61.50 (51.25, 75.96)	0.0030
Insulin dosage (IU/kg/day)	0.74 (0.54, 0.98)	0.69 (0.50, 0.92)	<0.0001
BMI (kg/m^2)	24.56 (22.18, 27.73)	24.67 (22.23, 27.77)	0.8796
Overweight (%)	45.5	46.7	0.2232
Obesity (%)	14.6	14.6	1.0000
Hypertension (%)	39.5	40.2	0.9463
Total cholesterol (mmol/L)	4.88 (4.19, 5.61)	4.91 (4.23, 5.70)	0.0002
LDL cholesterol (mmol/L)	2.70 (2.09, 3.34)	2.69 (2.09, 3.36)	1.0000
HDL cholesterol (mmol/L)	1.47 (1.19, 1.81)	1.50 (1.19, 1.89)	<0.0001
HDL-to-LDL ratio	0.56 (0.40, 0.79)	0.57 (0.41, 0.84)	0.0004
Triglycerides (mmol/L)	1.17 (0.82, 1.77)	1.16 (0.81, 1.75)	1.0000
Dyslipidemia (%)	62.1	63.4	0.2232
Retinopathy (%)	20.3	28.5	<0.0001
Microalbuminuria (%)	20.4	21.3	<0.0001
Hypoglycemia (severe) (events/100 PY)	23.52	23.61	0.6119
Hypoglycemia (coma) (events/100 PY)	6.31	6.42	0.0009
Ketoacidosis (events/100 PY)	5.13	5.07	0.1480
Smoker (%)	26.2	31.1	<0.0001

Data are medians (Q1, Q3) unless otherwise indicated. *P values adjusted for multiple comparisons by Holm method.

diabetes duration [in groups ≤2, >2 to ≤5, >5 to ≤10, and >10 years]), regression models were created to compare outcome variables between PA groups in the study population. Age-specific analysis (age-groups 18 to <30, 30 to <45, and 45 to <80 years) was adjusted for sex and diabetes duration, and sex-specific analysis for age and diabetes duration. Multiple linear regression models were calculated for continuous variables (HbA_{1c}, insulin dosage, BMI, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, HDL-to-LDL ratio, and triglycerides), multiple logistic regression models were used for dichotomous variables (prevalence of overweight, obesity, hypertension, dyslipidemia, retinopathy, and microalbuminuria), and multiple Poisson regression was applied to count data (severe hypoglycemia, severe hypoglycemia with coma, and DKA). Results were given as adjusted means (SE) or as percentage. Due to the multicenter nature of the data, treatment center was entered as a random factor into the model. To optimize iterations, the method of Newton-Raphson was used. Degrees of freedom for confounders in the model were calculated according to Kenward-Roger. Parameters were estimated using restricted maximum likelihood in linear regression and maximum likelihood in logistic and Poisson regression. P value for trend was calculated.

A two-sided P value <0.05 was considered significant. All statistical analyses were implemented with SAS 9.4 (Statistical Analysis Software; SAS Institute, Cary, NC).

RESULTS

Baseline characteristics of the study population and patients excluded due to missing documentation on PA are shown in Table 1.

In the study group, frequency of PA ranged between 0 and 9 times per week. The number of subjects who reported exercising more than two times per week (PA2) was 3,212 (17.8%), 3,459 subjects (19.9%) reported to be physically active one to two times (PA1), and 11,357 (63.0%) were inactive (PA0). Women were more often inactive compared with men (PA0: 66.0 vs. 60.5%, $P < 0.0001$). The percentage of patients in the most active group (PA2) was lower in women compared with men (14.5 vs. 20.6%, $P < 0.0001$). Stratified by age-group (18 to <30, 30 to <45, and 45 to <80 years), the frequency of physical inactivity increased with age (PA0: 48.4 vs. 70.1 vs. 78.0%, $P < 0.0001$). The number of subjects that reported to exercise more than two times per week was highest in the youngest patients, followed by middle-aged and the oldest age-groups (PA2: 25.8 vs. 13.3 vs. 10.0%, $P < 0.0001$).

The median HbA_{1c} of the study population was 7.72% (60.85 mmol/mol), the rate of severe hypoglycemia was 23.52/100 PY, and the rate of hypoglycemia with coma 6.31/100 PY. Forty-five percent of the subjects included were overweight and 14.6% obese. The prevalence of hypertension was 39.5%. Sixty-two percent of the whole study population had any type of dyslipidemia (including patients treated with lipid-lowering drugs).

Glycemic Control and Insulin Dosage

Results of multiple regression models for the whole study population stratified by PA group are given in Table 2.

Table 2—Demographic data and adjusted estimates of glycemic control and cardiovascular risk factors stratified by self-reported frequency of PA

	n	PA0	*n*	PA1	*n*	PA2	*P* value*
Unadjusted demographic data							
Age (years), mean (SD)	11,357	41.84 (18.44)	3,459	31.56 (15.98)	3,212	30.43 (15.80)	<0.0001
Male (%)	11,357	52.1	3,459	53.3	3,212	62.8	<0.0001
Diabetes duration (years), mean (SD)	11,357	16.52 (13.40)	3,459	13.00 (10.79)	3,212	12.43 (10.41)	<0.0001
Adjusted data							
HbA_{1c} (%)	10,978	8.20 (0.05)	3,396	7.92 (0.06)	3,168	7.84 (0.06)	<0.0001
HbA_{1c} (mmol/mol)	10,978	66.13 (0.60)	3,396	63.01 (0.65)	3,168	62.15 (0.66)	<0.0001
Insulin dosage (IU/kg/day)	10,341	0.82 (0.01)	3,172	0.81 (0.01)	2,899	0.79 (0.01)	0.0004
BMI (kg/m^2)	10,948	25.35 (0.07)	3,361	25.12 (0.09)	3,162	24.96 (0.10)	<0.0001
Overweight (%)	10,948	46.5	3,361	44.9	3,162	41.4	<0.0001
Obesity (%)	10,948	15.2	3,361	10.8	3,162	8.4	<0.0001
Systolic blood pressure (mmHg)	11,082	129.42 (0.35)	3,379	129.19 (0.40)	3,153	129.29 (0.41)	0.5932
Diastolic blood pressure (mmHg)	11,076	76.02 (0.23)	3,377	76.27 (0.26)	3,154	75.50 (0.27)	0.0377
Hypertension (%)	11,136	38.2	3,385	37.0	3,157	35.5	0.0150
Total cholesterol (mmol/L)	8,931	5.02 (0.04)	2,764	4.95 (0.04)	2,681	4.91 (0.05)	0.0001
LDL cholesterol (mmol/L)	7,914	2.79 (0.04)	2,403	2.72 (0.04)	2,382	2.75 (0.04)	0.0489
HDL cholesterol (mmol/L)	8,098	1.50 (0.01)	2,468	1.56 (0.01)	2,452	1.60 (0.01)	<0.0001
HDL-to-LDL ratio	7,858	0.63 (0.01)	2,387	0.66 (0.01)	2,375	0.66 (0.01)	<0.0001
Triglycerides (mmol/L)	8,716	1.57 (0.02)	2,675	1.44 (0.03)	2,567	1.39 (0.03)	<0.0001
Dyslipidemia (%)	9,268	66.0	2,832	58.9	2,723	55.9	<0.0001
Retinopathy (%)	6,899	12.2	2,097	8.2	1,975	6.5	<0.0001
Microalbuminuria (%)	9,103	22.0	2,740	15.5	2,609	14.3	<0.0001
Hypoglycemia (severe) (events/100 PY)	11,357	22.18 (0.05)	3,459	20.63 (0.08)	3,209	22.60 (0.09)	0.8989
Hypoglycemia (coma) (events/100 PY)	11,357	5.73 (0.03)	3,459	5.82 (0.04)	3,209	5.05 (0.04)	<0.0001
Ketoacidosis (events/100 PY)	11,357	6.48 (0.03)	3,459	3.99 (0.03)	3,212	2.40 (0.03)	<0.0001

Data are means (SE) unless otherwise indicated. Confounders were age, sex, and diabetes duration. Treatment center was included as a random factor. **P* value for trend.

Estimates were adjusted for sex, age, and diabetes duration.

Patients not physically active had higher HbA_{1c} values compared with their counterparts ($P < 0.0001$). This association was also present in subgroups (all $P < 0.0001$). In the study population and in subgroup analysis, an inverse association between insulin dosage and PA was present. In the entire study population, in all age-groups, and in women, this association reached statistical significance ($P < 0.05$, respectively). Regarding the rate of DKA, an inverse association was found in the whole study population as well as in all subgroups (all $P < 0.0001$). Severe hypoglycemia with coma was lowest in the most active group ($P < 0.0001$). Except for the oldest age-group ($P = 0.1451$), this relationship was present in both sexes and age-groups ($P < 0.0001$, respectively). The rate of severe hypoglycemia (assistance required) did not differ between PA groups ($P = 0.8989$). However, in sex- and age-specific analysis, significant differences were indicated (all $P < 0.0001$). In women and patients aged 45 to <80 years, the most active PA group had higher rates of severe hypoglycemia compared with inactive subjects. In contrast, in men, in 18 to <30 and 30 to <45-year-old subjects, the highest rate was present in the inactive group (Fig. 1*A*).

Diabetes-Related Comorbidities

Results from the logistic regression model revealed that retinopathy and microalbuminuria were more frequent in physically inactive compared with physically active patients (both $P < 0.0001$). This relationship was present in all subgroups (all $P < 0.0001$; except for microalbuminuria in 30–45 years, $P = 0.0004$).

Cardiovascular Risk Factors

In all subjects, an inverse association between PA and BMI as well as between PA and overweight prevalence was found (both $P < 0.0001$). Subgroup analysis revealed this relationship in women, in 30 to <45 and in 45 to <80-year-old patients ($P < 0.01$, respectively). This association was lacking in men and in the youngest age-group (18 to <30 years) (BMI: $P = 0.4281$ and $P = 0.3527$; overweight: $P = 0.9482$ and $P = 0.9218$) (Fig. 2*A*). Obesity prevalence was highest in inactive subjects, irrespective of age or sex (all $P < 0.0001$) (Fig. 2*B*). Whereas systolic blood pressure was not associated with PA ($P = 0.5932$), an inverse association between PA and diastolic blood pressure was found in the whole study population ($P = 0.0377$). Prevalence of hypertension was lowest in the most active patients ($P = 0.0150$). This association was lacking in men ($P = 0.3148$) and in the oldest age-group (45 to <80 years) ($P = 0.5071$) (Fig. 1*B*). Regarding serum lipids, an inverse association with PA was present in the whole study population (Table 2). In men and in the oldest age-group, analysis indicated no association between PA and total cholesterol ($P = 0.1121$ and $P = 0.3525$) and between PA and LDL cholesterol ($P = 0.9937$ and $P = 0.1042$). Overall, dyslipidemia was more common in inactive compared with active subjects, irrespective of age and sex (all $P < 0.0001$).

CONCLUSIONS

In this large cross-sectional multicenter DPV study, we analyzed the association between the frequency of self-reported PA and HbA_{1c}, diabetes-related complications,

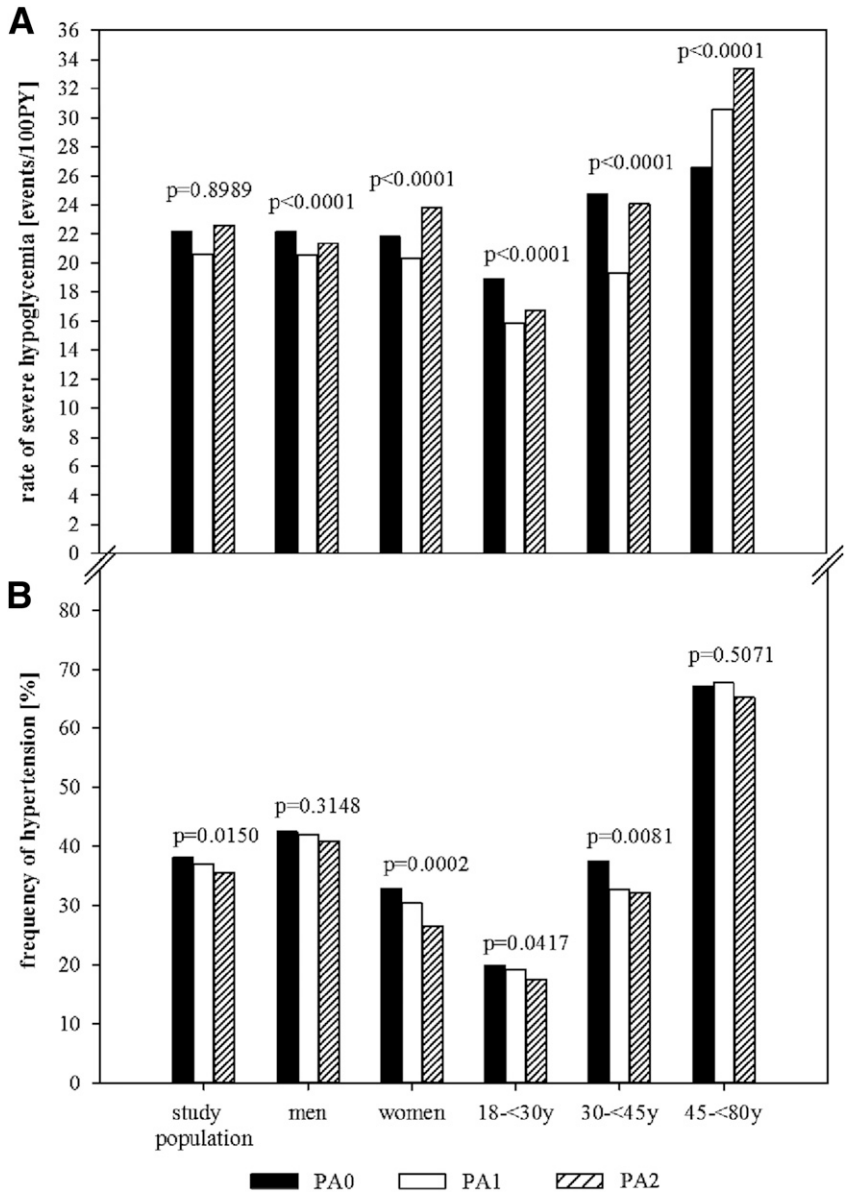

Figure 1—Rate of severe hypoglycemia (*A*) and frequency of hypertension (*B*) of the study population, stratified by sex and age-groups in respect to PA. *P* value for trend.

and cardiovascular risk factors. Overall, outcomes were beneficial in the most active compared with physically inactive subjects.

In the current study, 63.0% of patients included were not physically active. This is higher compared with other studies in the general population. In the German Health Interview and Examination Survey for Adults (DEGS1), interviews with 8,152 German citizens were conducted (25). About one-third reported no PA (men, 33.0%; women, 34.3%) (25). An explanation for the higher percentage of people being physically inactive in our analysis might be the fear or experienced exercise-induced hypoglycemia that is considered as a main barrier in subjects with type 1 diabetes (26).

Multiple regression analysis suggested an inverse association between PA and HbA_{1c}. This is in line with previous DPV studies in pediatric patients (11,12) and with a recently published meta-analysis (13). However, there are also studies that did not find a beneficial effect of PA on HbA_{1c} (14,15,27). Controversial results might be explained by the small sample size of most studies or by different study designs. Due to an aerobic exercise–induced reduction of the blood glucose level and an increase in insulin-stimulated glucose uptake in the muscles, it is discussed whether PA may increase the risk for hypoglycemia in subjects with type 1 diabetes (28). Our data indicate no effect of PA on the rate of severe hypoglycemia in the whole study group. However, we found significant disparities in subgroups. In women and in the oldest age-group (45 to <80 years), the rate of severe hypoglycemia increased with PA, whereas in other subgroups, there was an inverse association. Findings from other studies suggest that counterregulatory responses (neuroendocrine and metabolic homeostatic) during exercise in women may provide greater protection against hypoglycemia compared with men with type 1 diabetes (29). Since we observed a detrimental effect of PA on severe hypoglycemia in females, education in PA might need to be improved in women. Even in the oldest age-group (45 to <80 years), more active subjects had higher rates of hypoglycemia compared with their inactive counterparts. One explanation might be that their last diabetes education dates back several years and that the relevance of PA had not been a major focus. The rate of severe hypoglycemia with coma was lowest in the most active subjects, irrespective of age or sex. Regarding findings from other studies, the effect of PA on the occurrence of hypoglycemia is still controversial, as some studies have shown more hypoglycemic events in physically active subjects with type 1 diabetes (30,31), whereas others have failed to find this relationship (12,32). Moreover, there is a lack of sex- or age-specific analyses. We assume that this is due to the small sample size of most studies (13,14).

To avoid hypoglycemia, patients with type 1 diabetes might reduce their insulin dosage before exercising (14). Hence, due to a lack of insulin, the increasing energy requirement of the muscles during exercise is almost completely covered by free fatty acids, which can lead to DKA (33). In our study population, we found an inverse association between PA and insulin dosage. However, insulin reduction prior to exercise was not documented. Studies also indicate higher levels of counterregulatory hormones (e.g., catecholamines) in physically active compared with inactive

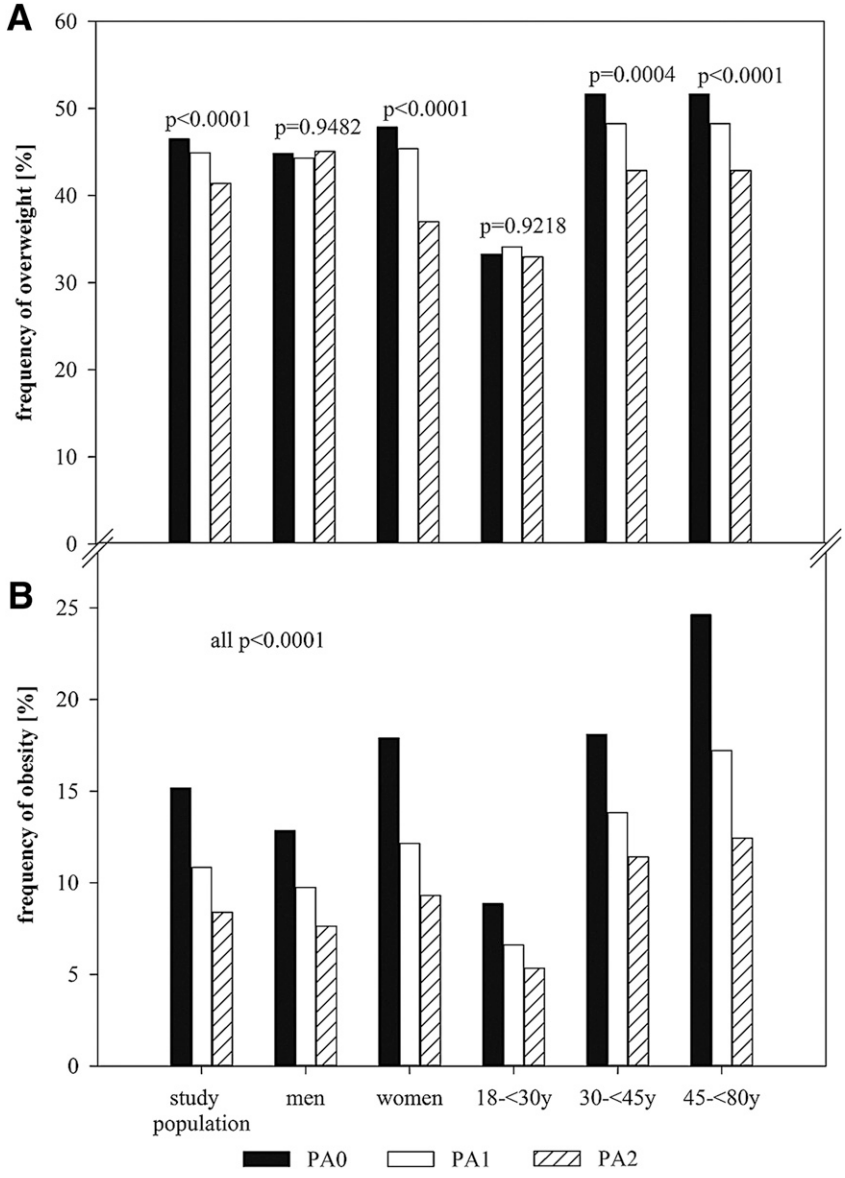

Figure 2—Frequency of overweight (*A*) and obesity (*B*) of the study population, stratified by sex and age-groups in respect to PA. *P* value for trend.

subjects, which may lead to higher rates of DKA (34). However, no adverse effect with respect to a higher rate of DKA was present in our data. On the contrary, PA seemed to decrease the risk of DKA. An explanation might be that physically active subjects are more health conscious compared with inactive subjects and therefore have better diabetes self-management, which may lead to lower rates of DKA. Moreover, blood glucose has to be measured more frequently in physically active subjects, and this in turn may have also contributed to the inverse association between PA and DKA in our study population. Frequencies of retinopathy and microalbuminuria were also lower in active compared with inactive patients. The Pittsburgh IDDM Morbidity and Mortality Study confirmed the inverse association between PA and diabetes complications (16). Six hundred and twenty-eight participants retrospectively estimated their PA during their late childhood. In men, but not in women, the frequency of self-reported PA was inversely related to the risk of nephropathy and neuropathy, whereas retinopathy was not associated with PA (16). Moreover, results of the DCCT study did not indicate beneficial effects of PA on microvascular complications, neither for development nor for progression (17). However, the authors demonstrate that exercising is not harmful in subjects with type 1 diabetes (17). Due to the cross-sectional design of our analysis, no causality can be demonstrated. It therefore remains unclear whether the presence of comorbidities has affected patients' ability to exercise or whether being physically active decreased the risk to develop diabetes-related complications.

Overall, we detected an inverse association between PA and several CVD risk factors in adults with type 1 diabetes. BMI as well as the frequency of overweight and obesity significantly differed between PA groups. The most active subjects had the lowest BMI and were least likely to be overweight or obese. These findings are in line with results of meta-analyses (13,35) and other cross-sectional studies (11,32). Sex- and age-specific analysis of our data revealed in men similar BMI values and overweight prevalences in PA groups. A study in pediatrics with type 1 diabetes also found lower BMI values in female but not in male subjects (11). The authors suspected that this is due to a greater lipolytic response to exercise in women compared with men (36). Regarding blood pressure, we found a beneficial effect of self-reported PA on diastolic blood pressure and hypertension, but not on systolic blood pressure. A previous DPV study in pediatrics with type 1 diabetes (12), a randomized controlled trial in adolescents with type 1 diabetes (37), as well as a recently published meta-analysis in type 2 diabetes confirmed these findings (35). However, there are also studies indicating no improvement (38,39). Our subgroup analysis revealed a marginal, nonsignificant inverse association in men and in patients between 45 and <80 years of age (Fig. 1*B*). According to our definition, patients treated with antihypertensive drugs were considered hypertensive. However, antihypertensives are also described in the treatment of microalbuminuria. Hence, an incorrect assignment might have affected our results. Another explanation could be a higher consumption of sodium chloride in PA1 and PA2 compared with PA0. However, we do not have information on patient diets. In the oldest age-group, duration or intensity of exercise might have been low and therefore the beneficial effect of PA on the prevalence of hypertension was too small. In our

analysis, PA was inversely associated with all serum lipids considered (total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides) and with any type of dyslipidemia. This is in line with a meta-analysis conducted by Chimen et al. (15), which revealed significant decreases in LDL cholesterol and triglycerides as well as an increase in HDL cholesterol in physically active patients with type 1 diabetes. Another meta-analysis also indicated a decrease in triglycerides and additionally in total cholesterol (13), whereas no improvement was present for HDL and LDL cholesterol. However, small sample size, short study duration, as well as lack of adjustments for diet or insulin dosage in studies included were criticized (15).

Strengths and Limitations

The major strength of this study is its large number of subjects included from routine care. Due to the multicenter nature of data collection, variability in the documented data may appear despite standardization of assessments and laboratory procedures by guidelines. A further limitation is the cross-sectional study design. Observed associations cannot prove causal effects. Especially with respect to diabetes-related complications or comorbidities (e.g., CVD or retinopathy), it has to be considered that the ability to exercise might be limited (40). To investigate the role of PA on the occurrence of diabetes-related comorbidities, a longitudinal study design will be needed. Moreover, information on PA was limited, and the quantification of frequency per week was based on subjective estimates by patients. Hence, no detailed information with respect to kind of exercise and METs was available.

Conclusion

Being physically active is associated with reduced cardiovascular risk and better glycemic control without an increase in adverse effects. Therefore, PA should be promoted in patients with type 1 diabetes.

Acknowledgments. The authors thank E. Bollow (Institute of Epidemiology and Medical Biometry, University of Ulm) for statistical analysis and G. Hermann (formerly of the Institute of Epidemiology and Medical Biometry, University of Ulm) for initial discussion. Furthermore, the authors thank all participating centers of the DPV Initiative, especially the collaborating centers in this investigation. A detailed list of the collaborating centers can be found in the Supplementary Data.

Funding. The study was supported by the German Competence Network Diabetes Mellitus (diabetes meta-database) funded by the Federal Ministry of Education and Research (FKZ 01GI1106), now integrated into the German Center for Diabetes Research (DZD). Further financial support was provided by the European Foundation for the Study of Diabetes.

Sponsors were not involved in data acquisition or analysis.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. B.B. created figures and wrote and edited the manuscript. A.H., M.P., D.K., S.Z., F.K., A.M., and J.M.S. contributed to the discussion and reviewed and edited the manuscript. R.W.H. conceptualized the study, contributed to the discussion, and reviewed and edited the manuscript. R.W.H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. An abstract was submitted for consideration in the poster session of the Annual Meeting of the German Nutrition Society (DGE), Halle (Saale), Germany, 11–13 March 2015.

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