Clinical Characteristics and Outcome of 467 Patients With a Clinically Recognized Eating Disorder Identified Among 52,215 Patients With Type 1 Diabetes: A Multicenter German/Austrian Study

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OBJECTIVE

To compare clinical characteristics and outcome of type 1 diabetes mellitus (T1DM) between patients with and without a clinically recognized eating disorder (ED).

RESEARCH DESIGN AND METHODS

A total of 52,215 T1DM patients aged 8 to <30 years from the prospective diabetes data acquisition system DPV were analyzed. A total of 467 patients had an additional diagnosis of ED according to DSM-IV criteria (anorexia nervosa [AN], *n* = 141 [female: 94.3%]; bulimia nervosa [BN], *n* = 62 [90.3%]; and EDs not otherwise specified, including binge-eating disorder [EDNOS], *n* = 264 [74.2%]). Groups were compared using multivariable regression. Cox proportional hazard ratios were calculated for the association between ED and retinopathy.

RESULTS

After adjustment for age, sex, and duration of diabetes, patients with ED revealed higher HbA_{1c} (no ED vs. AN, BN, or EDNOS, respectively: 8.29 ± 0.01% [67.1 ± 0.1 mmol/mol] vs. 8.61 ± 0.15% [70.6 ± 1.6 mmol/mol], 9.11 ± 0.23% [76.1 ± 2.5 mmol/mol], or 9.00 ± 0.11% [74.9 ± 1.2 mmol/mol]) and a higher rate of pathological insulin injection sites (48.4 vs. 64.3, 64.1, or 62.1%). Furthermore, ketoacidosis (5.7 ± 0.1 vs. 12.1 ± 2.1, 18.0 ± 4.1, or 12.9 ± 1.6 events per 100 person-years) and hospitalization (54.9 ± 0.3 vs. 89.3 ± 6.0, 132.0 ± 12.7, or 91.0 ± 4.4 per 100 person-years) were more common, and duration of hospital stay was longer (4.81 ± 0.01 vs. 11.31 ± 0.21, 18.05 ± 0.48, or 8.44 ± 0.13 days per year). All *P* values were <0.05. Patients with BN and EDNOS had a 2.5-fold (95% CI 1.3–4.8) and a 1.4-fold (0.8–2.3) higher risk for retinopathy, whereas AN patients had no increased risk (0.9 [95% CI 0.4–2.3]).

CONCLUSIONS

Diabetes health care professionals should be aware of comorbid EDs in pediatric/young-adult T1DM patients. An ED diagnosis is associated with worse metabolic control and higher rates of diabetes complications.

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The standard treatment regimen for type 1 diabetes mellitus (T1DM) requires a major focus on food and eating pattern, multiple daily insulin injections, weight control, and exercise. Intensive insulin therapy is associated with increasing body weight (1). Combined with the typical body changes during puberty, the perfect body image, and the social pressure for slimness, especially in females, the diabetes diagnosis as well as the burden of treatment may contribute to psychological disorders such as depression, fear of gaining weight, dysfunctional cognitive control of eating, or diagnosed eating disorders (EDs).

Previous studies indicated a relationship between T1DM and EDs or subthreshold variants (2–6). One study revealed an almost twofold higher prevalence in females with T1DM compared with nondiabetic subjects (2). However, there are studies in the literature revealing no association between the two conditions (7,8). Different assessment methods and definitions of eating problems used among previous studies might be possible explanations. EDs are more common in females than in males. This might be one reason why most previous studies investigated females only. The DSM-IV distinguishes three types of ED (9): anorexia nervosa (AN), bulimia nervosa (BN), and EDs not otherwise specified (EDNOS). The latter includes binge-eating disorder (BED). Underweight is the clinically most obvious sign in patients with AN. BN and EDNOS are clinically less obvious, and identification is most complete by targeted screening. In clinical settings, BN or EDNOS are therefore often underdiagnosed.

Knowledge on characteristics and outcome of T1DM with clinically recognized comorbid ED is still limited and often based on small sample sizes. To our best knowledge, this study is the first extensive report to compare demographics and diabetes-related outcome parameters between T1DM with and without comorbid ED. Contrary to most previous studies, different types of ED were distinguished, and males were not excluded. We hypothesized that T1DM patients with comorbid ED have worse metabolic control, different insulin therapy, and increased rates of complications compared with patients without ED.

RESEARCH DESIGN AND METHODS

Data Source and Subjects

The basis for the present research was the German/Austrian standardized, multicenter, prospective, computer-based diabetes data acquisition system DPV (www.d-p-v.eu). Within the DPV Initiative, 392 specialized diabetes care centers currently use DPV for standardized documentation of diabetes diagnosis and patient care. (See Supplementary Data for a detailed list.) Patient demographics, type and onset of diabetes, metabolic control, treatment regimen, and comorbidities are entered into the electronic health record. Twice a year, participating centers transmit their locally documented data anonymously to Ulm, Germany, for central analyses (10,11) and quality assurance. In case of inconsistent data, participating centers are requested to correct data entries. All plausible data are aggregated into a cumulative database. The ethics committee of the University of Ulm has approved the DPV Initiative.

Until March 2013, demographic and clinical data of 303,986 patients with any type of diabetes were available in the database (Fig. 1). For the present analysis, T1DM patients aged 8 to <30 years, with age at diabetes onset >6 months, no biopsy-proven celiac disease, and documented insulin dosage, body weight, and height were considered. The final study population comprised 52,215 pediatric and young-adult T1DM patients from 354 German and 26 Austrian centers (Fig. 1).

For distinction between patients with and without ED, the database was searched for the additional lifetime diagnosis of ED. According to DSM-IV classification (9), 467 subjects identified with comorbid ED were subdivided into three groups: *1*) AN, *2*) BN, and *3*) EDNOS, including BED. Identification and classification of EDs was made using ICD-10/DSM-IV codes and the respective German terms entered by diabetologists at each site. Patients had either already received an ED diagnosis based on ICD-10/DSM-IV criteria by trained psychologists or diabetologists made the diagnosis jointly with psychologists or child psychiatrists.

For each patient included, the last 2 years of treatment were analyzed. In case of multiple data sets per patient, data were aggregated.

Demographics and ED Characteristics

Migratory background was defined if either the patient or at least one parent was born outside Germany/Austria.

The formula from Du Bois and Du Bois (12) was used to estimate patient's body surface (BS). BMI SD score (BMI-SDS) was calculated using national reference data from the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) study for patients <18 years old and from the second German National Nutrition Survey for patients ≥18 years old as described elsewhere (13,14). Beside current BMI-SDS, lowest BMI-SDS ($BMI\text{-}SDS_{min}$) documented in DPV was analyzed.

Typical ED characteristics like lanugo and amenorrhea were ascertained by searching the database for the respective search terms.

Diabetes-Related Outcome Variables

For adjustment for differences among laboratory methods, the multiple of the mean method was applied to mathematically standardize HbA_{1c} measurements to the Diabetes Control and Complications Trial (DCCT) reference range (4.05–6.05%; 20.7–42.6 mmol/mol) (15). Current HbA_{1c} and maximum HbA_{1c} during the course of diabetes ($HbA_{1c\,max}$) were evaluated, excluding HbA_{1c} values at onset or during the first 3 months of diabetes.

Hypertension was defined as an elevated median blood pressure or the use of antihypertensive medication at least once during the last two treatment years. In patients aged <18 years, an average systolic and/or diastolic blood pressure ≥95th percentile for age, sex, and height was classified as elevated (16). Normative blood pressure values were obtained from the 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents (16). In patients ≥18 years old, elevated blood pressure was defined as systolic and/or diastolic blood pressure >140/90 mmHg (17). The use of lipid-lowering agents at least once during the last two treatment years and/or a blood lipid value on average above (below) the following thresholds was defined as dyslipidemia: total cholesterol >5.2 mmol/L, LDL >3.4 mmol/L, HDL <0.9 mmol/L, and triglycerides >1.7 mmol/L (18).

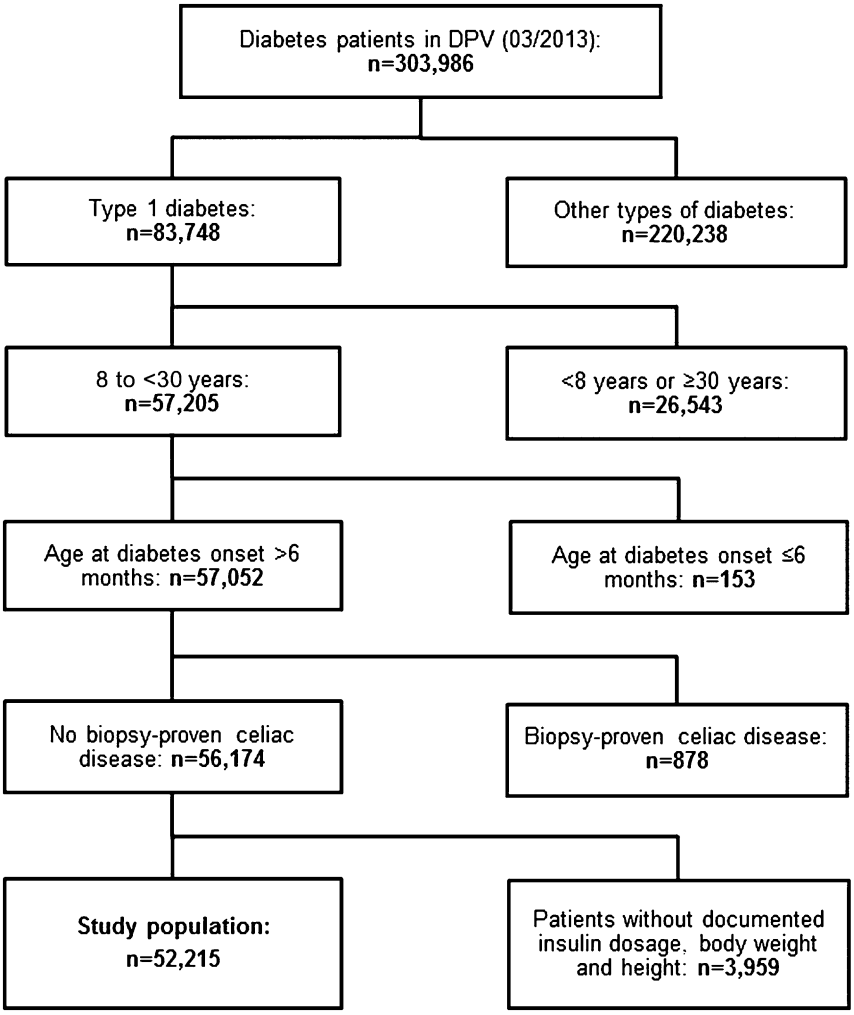

Figure 1—Flowchart for the selection of study population. Only T1DM patients aged 8 to <30 years, with age at diabetes onset >6 months, with no biopsy-proven celiac disease, and with documented insulin dosage, body weight, and height were included in the analysis.

Diabetic ketoacidosis was diagnosed in patients with a blood pH value <7.3 or a clinical diagnosis of diabetic ketoacidosis associated with inpatient care. Definitions of severe hypoglycemia, hypoglycemia with coma, diabetic retinopathy, and microalbuminuria have previously been described (19).

Statistical Analysis

Data analysis was implemented using SAS 9.3 (SAS Institute, Cary, NC). Median and quartiles were used as descriptive statistics for continuous variables and proportions for categorical variables. To account for potential confounding effects (e.g., age, sex, duration of diabetes), hierarchical, multivariable regression models were created to compare diabetes-related outcome variables between groups. Linear regression was used for continuous variables, logistic regression for binary data, and Poisson regression for count data with time under risk as offset. Age was categorized as 8 to <15 years, 15 to < 20 years, and 20 to <30 years and duration of diabetes as <2 years and ≥2 years. Based on observed marginal frequencies of demographical variables (age, sex, duration of diabetes), adjusted estimates (means ± SEM) were calculated for all outcomes. For the model with HbA_{1c} as target variable, additional adjustments for frequency of self-monitoring of blood glucose (SMBG) and interaction between SMBG and ED were made. The between-within method was applied to compute denominator degrees of freedom. Parameters were estimated using restricted maximum likelihood in linear regression and maximum likelihood in logistic or Poisson regression.

For evaluation of risk for the occurrence of retinopathy or microalbuminuria and for accounting for covariates, Cox proportional hazard models with duration of diabetes as the underlying time metric were created. Presence and type of ED and age at diabetes onset were included as categorical variables. Age at diabetes onset was divided in 5-year categories, beginning with 6 months to <5 years and ending with 25 to <30 years. The Breslow method was applied to adjust for ties. Results are presented as hazard ratios (HRs) with 95% CIs. Two-sided *P* values <0.05 were considered statistically significant.

RESULTS

Baseline Characteristics

A clinically recognized comorbid ED was present in 0.9% of T1DM patients (1.6% of T1DM females). AN was reported in 0.27% of patients (94.3% female), BN in 0.12% of patients (90.3%), and EDNOS in 0.51% of patients (74.2%). Patients with ED were significantly older

(median no ED vs. ED 15.8 years [quartile 1; quartile 3 12.7; 17.5] vs. 16.8 years [15.0; 18.1]; $P < 0.001$) and had longer duration of diabetes (5.2 years [2.2; 8.8] vs. 6.5 years [3.4; 10.6]; $P < 0.001$), and significantly fewer subjects had a migratory background (12.8 vs. 8.6%; $P < 0.01$). Forty-six T1DM patients without ED (27 males and 19 females) died, whereas in patients with ED, no case of death was documented.

Current BMI-SDS (no ED vs. AN, BN, or EDNOS, respectively: median 0.25 [quartile 1; quartile 3 −0.34; 0.83] vs. −0.48 [1.32; 0.25], 0.40 [−0.03; 0.87], or 0.42 [−0.17; 1.13]) and BMI-SDS$_{min}$ (−0.29 [−0.94; 0.34] vs. −1.58 [−2.55; −0.73], −0.32 [−1.03; 0.46], or −0.36 [−1.16; 0.47]) were lowest in T1DM with AN.

Demographic and ED-specific data for the study population classified by sex and type of ED are given in Table 1. Male patients with AN (n = 8) or BN (n = 6) are not shown owing to the low number.

Table 1—Demographics and ED characteristics for study population classified by sex and type of ED

	Female T1DM patients				Male T1DM patients	
	No ED	AN	BN	EDNOS	No ED	EDNOS
Patients, *n* (%)	24,283 (98.44)	133 (0.54)	56 (0.23)	196 (0.79)	27,465 (99.70)	68 (0.25)
Migratory background, %	13.1	6.8	8.9	9.2	12.5	10.3
Age (years)	15.6 (12.5; 17.5)	16.7 (15.4; 18.3)	17.7 (16.3; 21.0)	16.8 (14.9; 17.7)	15.9 (12.9; 17.5)	15.7 (13.5; 17.4)
Age at diabetes onset (years)	9.3 (6.1; 12.1)	11.4 (8.2; 13.5)	9.8 (6.6; 12.6)	10.0 (6.4; 12.5)	9.9 (6.3; 13.1)	7.3 (4.2; 10.2)
Duration of diabetes (years)	5.5 (2.4; 9.0)	5.4 (2.8; 9.4)	8.5 (4.9; 13.8)	6.3 (3.5; 10.2)	4.9 (2.0; 8.6)	7.6 (4.5; 11.5)
BMI (kg/m^2)	21.9 (19.2; 24.7)	19.5 (18.0; 22.0)	23.9 (21.4; 25.1)	23.0 (21.0; 26.0)	21.1 (18.8; 23.6)	21.4 (18.2; 25.0)
BMI-SDS	0.39 (−0.21; 0.96)	−0.50 (−1.33; 0.21)	0.44 (−0.02; 0.94)	0.53 (−0.11; 1.16)	0.12 (−0.45; 0.70)	0.27 (−0.39; 1.00)
BMI-SDS$_{min}$	−0.21 (−0.87; 0.44)	−1.58 (−2.55; −0.73)	−0.24 (−1.00; 0.51)	−0.37 (−1.17; 0.47)	−0.36 (−0.99; 0.26)	−0.32 (−1.10; 0.48)
Lanugo, %	0.03	0.75	0.00	0.00	0.01	0.00
Amenorrhea, %	0.5	13.5	7.1	4.1	—	—

Data are median (quartiles) unless otherwise indicated. Male patients with AN (n = 8, 0.03%) or BN (n = 6, 0.02%) are not shown owing to the low number of patients.

Diabetes-Related Outcome Variables

Clinical Variables

Hypertension and dyslipidemia were both more common in T1DM with EDNOS or BN than in T1DM without ED (after demographical adjustment [Table 2]). For T1DM with EDNOS, differences were significant. Patients with AN had lower frequencies (nonsignificant) compared with patients without ED (Table 2).

Diabetes Treatment and Metabolic Control

HbA_{1c} was significantly higher in patients with ED than in patients without ED (Table 2). Additional adjustment for SMBG and interaction between SMBG and ED did not alter this finding (means ± SEM: 8.26 ± 0.01% [66.8 ± 0.1 mmol/mol] vs. 8.67 ± 0.15% [71.2 ± 1.6 mmol/mol], 9.15 ± 0.23% [76.5 ± 2.5 mmol/mol], or 9.03 ± 0.11% [75.2 ± 1.2 mmol/mol]; no ED vs. AN, BN, or EDNOS: P = 0.007, $P < 0.001$, and $P < 0.001$). On average, $HbA_{1c\ max}$ during the course of diabetes was highest in T1DM with BN (median 9.03% [quartiles 7.88; 10.67] vs. 9.34% [8.14; 12.53], 10.91% [8.78; 13.22], or 10.76% [9.00; 12.96]; 75.2 mmol/mol [62.6; 93.1] vs. 78.6 mmol/mol [65.4; 113.5], 95.7 mmol/mol [72.4; 120.9], or 94.1 mmol/mol [74.9; 118.1]).

Reported daily frequency of SMBG was comparable between groups (4.79 ± 0.01 vs. 4.83 ± 0.13, 5.12 ± 0.20, or 4.66 ± 0.10 measurements per day). In T1DM without ED, a daily frequency of SMBG of more than four was related to a −0.7% (−7.5 mmol/mol) lower HbA_{1c} compared with patients measuring blood glucose four or fewer times daily. The corresponding figures for patients with AN, BN, and EDNOS were −0.9% (−10.0 mmol/mol), −1.3% (−13.9 mmol/mol), and −0.7% (−7.4 mmol/mol).

Daily insulin dosage per kilogram body weight was reported lowest in BN patients (Table 2). However, patients with AN must have a body weight below normal in order to meet diagnostic criteria. Therefore, we assumed that square meter BS will be a better reference basis for daily insulin dosage than kilogram body weight. Insulin dosage per square meter BS was reported significantly lower in patients with AN or BN than in patients with no ED (Table 2). Between T1DM with EDNOS and without ED, no clinically relevant difference was observed.

Pathological insulin injection sites (e.g., lipohypertrophy) were significantly more common in patients with ED (Table 2). Completeness of examination of injection sites did not differ between groups (89.2 vs. 91.4, 87.7, or 90.5%; each $P > 0.05$).

Patients with ED had a lower frequency of continuous subcutaneous insulin infusion (CSII) than patients without ED. In T1DM with AN, frequency was lowest and significantly different (Table 2).

Diabetes Complications

Rate of severe hypoglycemia was higher in T1DM with ED (Table 2). For patients with AN or EDNOS, the difference was significant. Hypoglycemia with coma was also more common in T1DM with ED; however, no statistical significance was reached (3.9 ± 0.1 vs. 5.8 ± 1.5, 6.4 ± 2.6, or 5.4 ± 1.1 events per 100 person-years). In patients with ED, diabetic ketoacidosis occurred significantly more often than in patients without ED (Table 2).

All patients with ED required hospitalization significantly more often than patients without ED (Table 2). Duration of hospital stay was also significantly longer in patients with any type of ED (Table 2).

Table 2—Diabetes-related outcome variables for pediatric and young-adult T1DM patients with and without comorbid ED

				P			*P*		*P*
Adjusted estimates	No ED	AN	BN	No ED vs. AN	No ED vs. BN	EDNOS	No ED vs. EDNOS
n	51,748	141	62			264	
Clinical variable, %							
Hypertension	20.6	16.9	20.9	NS	NS	27.5	0.005
Dyslipidemia	37.4	32.8	41.8	NS	NS	56.0	<0.001
Treatment and metabolic control							
HbA_{1c} (%)	8.29 ± 0.01 (*n* = 51,084)	8.61 ± 0.15 (*n* = 139)	9.11 ± 0.23	0.043	<0.001	9.00 ± 0.11 (*n* = 262)	<0.001
HbA_{1c} (mmol/mol)	67.1 ± 0.1 (*n* = 51,084)	70.6 ± 1.7 (*n* = 139)	76.1 ± 2.5	0.043	<0.001	74.9 ± 1.2 (*n* = 262)	<0.001
Daily insulin dosage (units/kg)	0.838 ± 0.001	0.815 ± 0.025	0.729 ± 0.038	NS	0.004	0.845 ± 0.018	NS
Daily insulin dosage (units/BS)	29.93 ± 0.05	27.30 ± 0.92	25.86 ± 1.38	0.004	0.003	30.61 ± 0.67	NS
CSII, %	19.5	13.1	15.1	0.037	NS	17.6	NS
Pathological insulin injection sites, %	48.4 (*n* = 48,327)	64.3 (*n* = 138)	64.1 (*n* = 55)	<0.001	0.024	62.1 (*n* = 254)	<0.001
Complications and comorbidities							
Severe hypoglycemia per 100 person-years	18.6 ± 0.2	24.8 ± 3.2	26.5 ± 5.3	0.024	NS	24.3 ± 2.2	0.004
Diabetic ketoacidosis per 100 person-years	5.7 ± 0.1	12.1 ± 2.1	18.0 ± 4.1	<0.001	<0.001	12.9 ± 1.6	<0.001
Hospitalization per 100 person-years	54.9 ± 0.3	89.3 ± 6.0	132.0 ± 12.7	<0.001	<0.001	91.0 ± 4.4	<0.001
Duration of stay (days per year)	4.81 ± 0.01	11.31 ± 0.21	18.05 ± 0.48	<0.001	<0.001	8.44 ± 0.13	<0.001

Data are means ± SEM unless otherwise indicated. Estimates are based on multivariable regression models and are adjusted for age, sex, and duration of diabetes. Only parameters with at least one significant difference between groups are shown in the table. *P* values are given for the comparison with no ED. Some variables were not documented in all patients; in this case, the number studied is given in parentheses. NS, not significant.

Fig. 2 summarizes results of Cox proportional hazard models for retinopathy and microalbuminuria. Patients with BN had a 2.5-fold higher risk for retinopathy than patients with no ED (P = 0.007). Patients with EDNOS also had a higher risk but without statistical significance. In contrast, patients with AN had no increased risk for retinopathy. For the occurrence of microalbuminuria in T1DM with any type of ED, risk was comparable with risk for patients with no ED. Earlier onset of diabetes was protective for both microvascular complications.

Sex Differences in Diabetes-Related Outcome Variables

A sex-specific analysis of diabetes-related outcome variables was feasible for T1DM with EDNOS compared with T1DM without ED. For most variables studied, no sex differences were found after adjustment for age and duration of diabetes. The only exceptions were rates of severe hypoglycemia and hypoglycemia with coma, frequency of CSII, and risk for retinopathy. In females with EDNOS, severe hypoglycemia and hypoglycemia with coma were both significantly more common (no ED vs. EDNOS: 19.0 ± 0.2 vs. 24.9 ± 2.7 and 3.6 ± 0.1 vs. 5.5 ± 1.2 events per 100 person-years; P = 0.012 and P = 0.047). Also, the frequency of CSII was lower (23.0 vs. 19.6%; P = 0.255) and the risk for retinopathy higher (HR 1.51 [95% CI 0.87–2.62]). In contrast, in males with EDNOS and without ED, rate of severe hypoglycemia did not differ significantly (18.2 ± 0.2 vs. 23.1 ± 4.2 events per 100 person-years; P = 0.192), and occurrence of hypoglycemia with coma (4.3 ± 0.1 vs. 4.5 ± 1.8 events per 100 person-years; P = 0.920) as well as frequency of CSII (16.8 vs. 17.6%; P = 0.834) was comparable. In addition, males with EDNOS had no increased risk for retinopathy (0.87 [0.22–3.50]).

CONCLUSIONS

This is the first large study aiming to describe differences between young T1DM patients with and without comorbid ED, as diagnosed in clinical practice. The additional diagnosis of AN, BN, or EDNOS had physiological consequences. Metabolic control was significantly worse; lipodystrophy at injection site, diabetic ketoacidosis, and hospitalization were significantly more common; and duration of hospital stay was significantly longer than in T1DM without ED. Interestingly, a significantly elevated risk for retinopathy was only present in T1DM with BN.

Higher HbA_{1c} levels in patients with ED have been reported previously (2,20–22). Reasons could be blood glucose fluctuations due to overeating or binge eating, insulin omission or under dosing (23), and lack of adherence to treatment regimen. In addition, in patients with BN or BED, nonlinearity of insulin-to-carbohydrate ratio and glucose excursion due to meals with large protein/fat content may play a role.

Ziegler et al. (24) showed in pediatric T1DM patients an inverse association between the frequency of SMBG and HbA_{1c}. This association was also present in our T1DM patients with ED. However, reasons for SMBG in patients with and without ED may differ. In patients with ED, SMBG could serve as control tool to prevent ketoacidosis. Hence, patients with ED may tend to skip the documentation of high blood glucose measurements.

A unique tool to reduce weight in T1DM is "insulin purging." Beside the catabolism of lipids, the induced glycosuria results in excretion of calories with urine and contributes to weight loss. For females withholding insulin, a higher morbidity and an earlier mortality were reported (21,23,25). Nevertheless, up to 47.9% of T1DM patients with ED withhold insulin (26). In our study, the lower

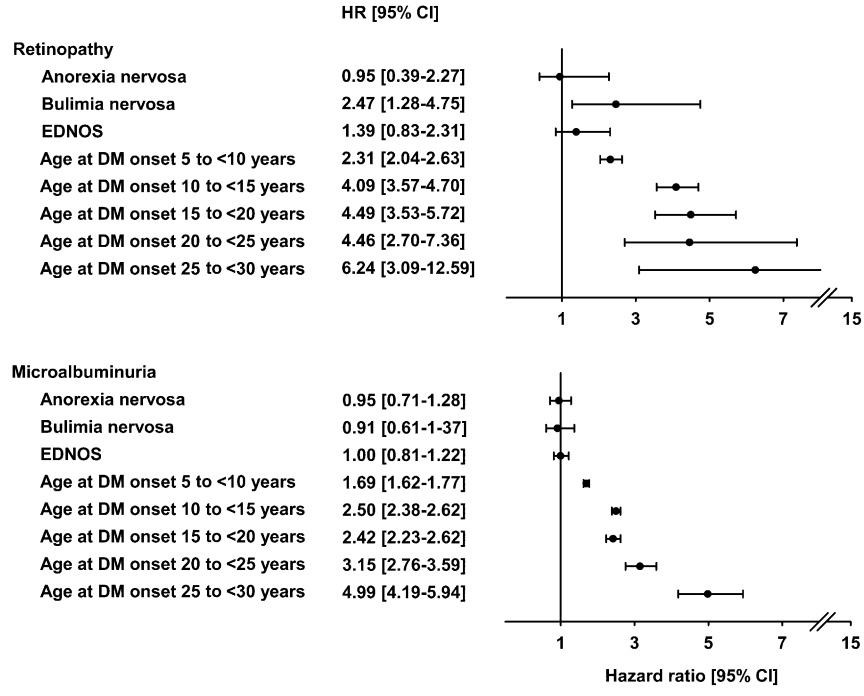

Figure 2—Cox proportional HRs with 95% CIs for the occurrence of retinopathy and microalbuminuria. Shown is the risk for retinopathy and microalbuminuria depending on the presence and type of ED and age at diabetes onset. HR >1 is associated with an increased risk compared with patients with no ED/age at diabetes (DM) onset <5 years.

reported insulin dosage in patients with AN or BN indicates insulin omission, under dosing, or under reporting. Another explanation might be enhanced insulin sensitivity due to excessive physical activity or, in patients with AN, due to empty glycogen storages. For anorectic women, increased insulin sensitivity was previously reported (27).

Avoidance of their own body sight in patients with ED may lead to incorrect insulin injections and cause tissue damage and thereby contribute to the higher frequency of pathological insulin injection sites in T1DM patients with ED. In anorectic patients, other possible reasons could be the lean body shape and the low amount of fat mass.

In our study, insulin pump treatment tended to be less frequent in T1DM with ED. A previous small study also reported insulin pump therapy in 25% of cases only (26).

Microvascular damage is a logical consequence of higher HbA_{1c} levels. Small previous studies among females with T1DM reported a strong association of disturbed eating habits with the occurrence of microvascular complications (21), especially retinopathy (22). In a meta-analysis, risk for retinopathy among T1DM females with BN was increased threefold (28). Our study also revealed a 2.5-fold increased risk for retinopathy in T1DM with BN. Additionally, our data indicate an increased risk for retinopathy in T1DM with EDNOS and no increased risk for retinopathy in T1DM with AN. The latter may be explained by delayed puberty and lower levels of IGF-I in AN patients (29,30). For both, an association with a lower prevalence of retinopathy was reported (31,32). The comparable risk for microalbuminuria between T1DM with and without comorbid ED confirms findings from Rydall et al. (22). They found in 71 women with T1DM no significant association between disordered eating and microalbuminuria (22). In AN patients, low protein intake and low blood pressure may counterbalance the effect of high HbA_{1c} values on the risk of microalbuminuria. Earlier onset of diabetes was associated with a lower risk for retinopathy and microalbuminuria in our study. This is similar to findings in T1DM without ED (17).

Rates of severe hypoglycemia and diabetic ketoacidosis were higher in T1DM patients with ED. Severe caloric restriction may lead to higher rates of hypoglycemia (33) and insulin restriction to more frequent episodes of diabetic ketoacidosis (23).

As expected, dyslipidemia and hypertension were more common in T1DM with BN or EDNOS than in patients without ED. In patients with AN, frequencies tended to be lower. Previous findings in 16 nondiabetic women with AN revealed higher cholesterol, triglyceride, LDL, and HDL levels compared with 25 healthy females (34). These discrepancies may be attributed to the lifetime diagnosis of ED in our study. Patients identified with ED may not have pronounced symptoms of ED during the last 2 years of care. Clinical remission under therapy is possible. However, remission of psychological disturbances is doubtful.

Due to the complexity of both diseases, a higher rate of hospitalization and a longer duration of hospital stay in T1DM with ED were expected and confirm previous findings of a higher need for inpatient care in ED patients with T1DM compared with patients without T1DM (26). Reasons could be failure to take medications, ketoacidosis, refeeding in case of severe cachexia, reestablishing metabolic control, or insulin purging (23).

Sex-specific comparisons between T1DM with EDNOS and without ED revealed few differences. The discrepancies found might be explained by the low number of male patients with EDNOS.

A total of 0.9% of our T1DM patients had a clinical diagnosis of ED. In studies from Jones et al. (2) and Grylli et al. (20), 10% and 11.5% of the investigated patients with T1DM had ED based on DSM-IV criteria. Recently, ED prevalence among adolescents with T1DM was estimated to 7.0% (35). In a meta-analysis of T1DM females, prevalence of AN was not significantly higher compared with nondiabetic control subjects; however, BN was reported significantly more often (5). Most previous studies were screening studies targeted for the detection of EDs. This might be one reason for the lower number of comorbid EDs in our cohort of T1DM patients based on a clinical diabetes registry. Moreover, the documentation of the comorbid diagnosis was made by diabetologists and not by psychiatrists. Disordered eating is often denied or downplayed by patients. A clinical diagnosis of ED might not always be reported to diabetologists by patients or their psychologists. However, one of the clinically most obvious signs of AN is underweight and has possibly contributed to a higher number of T1DM patients identified with AN compared with other EDs in our study. Not all our patients with AN were underweight at the time of evaluation. However, the lowest BMI-SDS_{min} since start of documentation clearly indicates underweight. The median BMI-SDS_{min} of -1.58 corresponds to the 5.7th BMI percentile for age and sex.

Contrary to many previous studies, male T1DM patients were also included in our analysis. Clinically serious psychiatric disorders like AN or BN were rarely recognized in males. However, a clinical diagnosis of EDNOS was not uncommon. The burden of diabetes and of the associated therapy with a major focus on food and eating pattern may contribute to this type of disordered eating in T1DM males. Previous small studies indicated also a level of disturbed eating (e.g., insulin restriction or skipping, higher drive for thinness) in male T1DM patients (4,20,36). However, in small studies from Austria and Sweden, no male with T1DM had an ED based on DSM-IV criteria (4,20).

The strength of the current study is its large number of patients. To our best knowledge, this is the first extensive report in English on demographics and clinical characteristics of T1DM patients with clinically recognized comorbid AN, BN, or EDNOS compared with T1DM without ED. One limitation is the potential underreporting of EDs in the database. Patients allowing only the documentation of diabetes and not the diagnosis of ED were classified as T1DM patients only. Additionally, subclinical EDs could not be considered. Because DSM-IV or ICD-10 codes used by diabetologists at each site were used to subclassify patients with ED, it is possible that DSM-IV criteria used for classification have not been met in the strictest sense. Hence, there could be an overlap in the diagnostic categories.

In summary, our study revealed that the comorbid clinical diagnosis of ED in pediatric and young adult T1DM patients is associated with worse

metabolic control and a negative effect on the course of diabetes. Even if no patient with ED died in our series, a 10-year follow-up study by Nielsen et al. (37) indicated that the comorbidity of AN increased mortality dramatically in T1DM females. Therefore, early recognition and adequate treatment of EDs in T1DM is essential. Furthermore, the low prevalence of clinically recognized EDs observed in our study indicated that a high proportion of pediatric and young-adult T1DM patients with EDs are still undiagnosed in German/Austrian specialized diabetes care centers. Specific validated and reliable screening tools (e.g., DiabEss [38], Diabetes Eating Problem Survey-Revised (DEPS-R) [39]) should be considered by diabetologists. In addition, they should be aware of comorbid EDs in T1DM in order to involve specialized clinical psychologists early.

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