

CLINICAL STUDY

Depression, obesity, and smoking were independently associated with inadequate glycemic control in patients with type 1 diabetes

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Abstract

Objective: The aim of this study was to explore the associations between inadequate glycemic control of diabetes and psychological, anthropometric, and lifestyle variables in a population-based cohort of type 1 diabetes patients.

Design: Cross-sectional study.

Methods: In this study, 292 patients with type 1 diabetes, aged 18–59 years, participated. Psychological data were assessed by self-report instruments: Hospital Anxiety and Depression Scale and Toronto Alexithymia Scale-20. Anthropometrics, blood analyses, data from medical records, and data from the Swedish National Diabetes Registry were collected.

Results: Self-reported depression (adjusted odds ratio (AOR) 4.8), obesity (AOR 4.3), and smoking (AOR 3.0) were independently associated with inadequate glycemic control of diabetes (HbA1c > 8.6%). Gender-stratified analyses showed that self-reported depression (AOR 19.8) and obesity (AOR 7.0) in women and smoking in men (AOR 4.2) were associated with HbA1c > 8.6%. Alexithymia, antidepressant medication, and physical inactivity were associated with HbA1c > 8.6% only in bivariate analyses. Alexithymia, self-rated anxiety, physical inactivity, and absence of abdominal obesity were associated with self-reported depression.

Conclusions: Depression was the only psychological factor independently associated with HbA1c > 8.6%. The association was of comparable importance as obesity and smoking, well-known risk factors for inadequate glycemic control and diabetes complications. The association between depression and HbA1c > 8.6% was particularly strong for women. Alexithymia, which is a relatively stable personality trait, was associated with depression. In the future care of patients with diabetes, psychological aspects should be considered alongside anthropometrics and lifestyle factors in order to achieve the goals for HbA1c.

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Introduction

Patients with diabetes have an increased prevalence of depression (1, 2, 3). Depression in diabetes is associated with low quality of life (3), impaired glycemic control (3), increased frequency of complications (4, 5, 6), and all-cause mortality (6). Depressive symptoms are associated with poor diet (3, 7, 8), smoking habits (9), less exercise (7), low adherence to medication (3, 7, 8), and higher health care costs (3, 8). There are suggested overlapping biological links between depression and autoimmune diabetes indicated by high levels of circulating cytokines associated with both conditions, insulin deficiency impairing neurogenesis and neurotransmitter metabolism, a chronic hyperglycemic state and hypoglycemia episodes, and hyperactivity of the

hypothalamic–pituitary–adrenal axis. All these factors may induce or worsen depression (1).

Affects are signals to the individual of one's inner state. Affect dysregulation and absence of conscious awareness of affects have health implications (10, 11, 12). Alexithymia is defined by four factors: difficulty identifying feelings, difficulty describing feelings, externally oriented thinking (low degree of introspection and reflection), and constricted imaginative processes (10). A deficit in the awareness of affects results in abnormal physiological reactions, a propensity for impulsive behavior, and an impaired capacity for self-care and self-regulation (10). Inadequate metabolic control of diabetes (13), altered immune function (14), altered cortisol responses (15), and changes of C-reactive protein and serum lipid levels (16) are associated with

alexithymia, which in turn has been linked with depression, anxiety, stress-related disorders, diabetes, and obesity (11, 17, 18, 19, 20). Alexithymia has also been associated with reduced social support, which negatively affects the prognosis of disease and health problems (11, 21).

Poor glycemic control is associated with smoking in patients with diabetes (22, 23). Abdominal obesity is associated with dyslipidemia and increased risk of cardiovascular disease (24, 25). Physical inactivity is associated with insulin resistance, dyslipidemia, increased blood pressure, and microvascular dysfunction (26, 27).

The hypotheses of this study are that psychological factors, particularly depression, are important variables associated with inadequate glycemic control and that the associations are underestimated compared with smoking, physical inactivity, and obesity. The aim of this population-based study of adult patients with type 1 diabetes was to explore whether glycemic control measured as HbA1c was associated with psychological and anthropometric variables and lifestyle factors.

Materials and methods

Participants and procedures

Between March and December 2009, 292 patients with type 1 diabetes were recruited consecutively at a specialist diabetes outpatient clinic at a central hospital with a catchment population of 125 000 in Southern Sweden. They were enrolled by a specialist nurse or physician. Inclusion criteria were age 18–59 years and diabetes duration for at least 1 year. Exclusion criteria were severe somatic comorbidities (cancer, hepatic failure, end-stage renal disease, and social blindness), severe mental disorder (psychotic disorder, bipolar disorder, severe personality disorder, severe substance abuse, mental retardation, or other severe cognitive deficiency), or inadequate knowledge of Swedish.

Psychological data were assessed by self-report instruments. Blood analyses and anthropometric measurements were performed by nurses. Information regarding general diabetes-related data, clinical psychiatric diagnoses, and antidepressant medication was collected from the Swedish National Diabetes Registry (S-NDR) and computerized medical records. All patients provided written informed consent, and the study was approved by the Regional Ethical Review Board of Linköping University: Dnr M120-07, T89 - 08. Clinical Trials Registry: NCT01498614.

Self-report psychological instruments

Hospital Anxiety and Depression Scale Anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS) (11, 28, 29, 30). HADS

consists of two subscales with seven items reflecting depression (HADS-D) and seven items reflecting anxiety (HADS-A). Each statement has four response alternatives with scores from 0 to 3. The recommended cutoff level was used for both subscales: ≥ 8 points. A major characteristic of HADS is that potential symptoms from somatic diseases are not included, and it allows identification of cases of anxiety disorders and depression in patients from non-psychiatric hospital clinics (28). In a Swedish population sample, mean (s.d.) for HADS-D was 4.0 (± 3.5) and for HADS-A 4.6 (± 3.7) (29). The validity of the HADS-D was controlled by analyzing the associations between HADS-D and clinical psychiatric diagnosis and use of antidepressant medication.

Toronto Alexithymia Scale-20 Alexithymia was assessed by the 20-item Toronto Alexithymia Scale-20 (TAS-20) (11, 14, 15, 16, 18, 19, 20, 21, 31, 32, 33) based on three subscales: 'difficulty identifying feelings', 'difficulty describing feelings', and 'externally oriented thinking'. TAS-20 consists of 20 statements rated from 1 to 5. The recommended cutoff point was used: ≥ 61 points, which in a Swedish normative sample of 137 persons yielded a prevalence of alexithymia of 2% (20).

Blood analyses and anthropometric measurements

HbA1c Venous samples for analyses of HbA1c were analyzed with high-pressure liquid chromatography, HPLC – variant II, Turbo analyzer (Bio-Rad) (34). The results were converted from Mono-S HbA1c % to HbA1c % according to the National Glycohemoglobin Standardization Program (NGSP) (35). HbA1c (NGSP) was dichotomized at the third quartile (HbA1c $> 8.6\%$), which was defined as inadequate glycemic control of diabetes. HbA1c was analyzed at the Department of Clinical Chemistry, Växjö Central Hospital.

Anthropometrics WC, weight and length were measured by a nurse according to standard procedures. Abdominal obesity was defined for men as WC ≥ 1.02 m and for women as WC ≥ 0.88 m (36). General obesity was defined as BMI ≥ 30 kg/m² for both genders.

Data collected from the S-NDR and medical records

Data were collected from both the S-NDR and the medical records regarding diabetes type, diabetes duration, age, psychiatric and somatic diagnoses, medication, number of severe hypoglycemic episodes, smoking habits, and physical activity. Computerized medical record data collected from the Departments of Internal Medicine and Ophthalmology, and Primary

Care, including primary care psychological counseling, also served as a validation of the S-NDR data. Comprehensive computerized drug prescription data (including prescription data from the Department of Psychiatry) were studied as well.

Hypoglycemia A severe hypoglycemic episode was defined as a patient needing help from another person.

Smoking Patients were defined as smokers if they had smoked any amount of tobacco during the last year.

Physical inactivity In the S-NDR, physical activity is categorized into four groups, < 1/week, 1–2 times/week, 3–5 times/week, or daily activities. Patients were defined as physically active if they performed moderate activities such as 30 min of walking at least once a week.

Foot complications These were defined as neuropathy, angiopathy, earlier or present diabetes foot ulcer, foot infection, foot deformity, arthropathy, or amputation of the lower limb.

Retinopathy Diabetes retinopathy was defined as non-proliferative or proliferative retinopathy with microangiopathy changes as viewed by fundus photography through a dilated pupil.

Macrovascular complications Macrovascular complications were defined as ischemic heart disease, stroke, or transient ischemic attack (TIA). Ischemic heart disease was defined as angina pectoris, previous myocardial infarction, percutaneous transluminal coronary angioplasty (PTCA), or coronary artery bypass graft (CABG) surgery.

AITD Due to the association of type 1 diabetes with an increased risk of additional autoimmune diseases, special care was given to identify patients with an autoimmune thyroid disease (37). Patients diagnosed with hypothyroidism or hyperthyroidism were considered suffering from autoimmune thyroid diseases (AITD), though all were not tested for specific antibodies.

Statistical analysis

Frequencies of psychological factors, metabolic and lifestyle variables, and diabetes complications were calculated using ordinary descriptive measures. Fisher's exact test was used to analyze differences of prevalence. After checking for normality, all continuous variables were analyzed using Student's *t*-test. Crude odds ratios (CORs) were calculated for the associations between self-reported depression (HADS-D ≥ 8) and the four variables: antidepressant medication, clinical psychiatric diagnosis, macrovascular complications, and AITD. CORs were calculated for the associations between HbA1c > 8.6% and each variable in the study. CORs

were calculated for the associations between alexithymia and the two variables: smoking and abdominal obesity. In a backward elimination multiple logistic regression analysis, abdominal obesity showed a higher association with HbA1c > 8.6% than general obesity and was therefore chosen in the subsequent multiple regression models.

Multiple logistic regression analyses (Backward: Wald) were performed with HbA1c > 8.6% and self-reported depression as dependent variables and were controlled for gender, age, and diabetes duration. Patients with macrovascular complications were excluded from the multiple logistic regression analyses as they all had multiple complications. When HbA1c > 8.6% was used as dependent variable, the following factors were used as independent variables: the psychological factors, antidepressant medication, abdominal obesity, and lifestyle variables. When self-reported depression was used as dependent variable, the two variables, diabetes retinopathy and foot complications, were added to the variables previously mentioned, and antidepressant medication was excluded. The Hosmer and Lemeshow test for goodness-of-fit and Nagelkerke R^2 were used to evaluate each regression analyses model. $P \leq 0.05$ was considered statistically significant. CIs of 95% were used.

In the self-report instruments, missing values were imputed using regression on the other variables in the same subgroup. Multinomial regression was used as there were a limited number of possible answers. Imputation for patients with type 1 diabetes was done in 1/292 cases of HADS-D and in 2/292 cases of TAS-20. SPSS version 18 (IBM), was used for statistical analyses.

Results

Characteristics of the participants

In this study, 292 patients with type 1 diabetes participated. Data regarding age, anthropometrics, complications, diabetes duration, lifestyle, metabolic factors, and self-reported psychological variables are presented for all and gender stratified in Table 1. Women had higher prevalence rates of self-reported anxiety and obesity, and men had a higher prevalence of foot complications. There were no gender differences in mean HbA1c, diabetes duration, or age.

According to medical records, 41 (14%) patients had a history of clinical psychiatric diagnoses; 19 had clinical depression, eight had clinical anxiety disorders, and 14 had stress-related disorders, substance abuse, anorexia nervosa, or attention deficit hyperactivity disorder. Twenty-three patients (8%) used antidepressant medication. Thirty-three patients (11%) had AITD.

Macrovascular complications were present in ten patients (3%) and their HbA1c mean (s.d.) was 8.3% (± 1.7). Three patients had stroke or TIA, five had

Table 1 Characteristics of participants. Data are *n* (%), and Fisher's exact test was used unless otherwise indicated.

	All	Men	Women	<i>P</i>
Number (%)	292	162 (55)	130 (45)	
Age range (years)	18–59	19–59	18–59	
Age mean (s.d.) (years)	41.0 (±11.6)	42.0 (±11.8)	39.7 (±11.4)	0.10 ^a
Diabetes duration range (years)	1–55	2–53	1–55	
Diabetes duration mean (s.d.) (years)	21.1 (±12.1)	22.0 (±12.7)	19.9 (±11.2)	0.16 ^a
Psychological variables				
Depression ^b	30 (10)	16 (10)	14 (11)	0.84
Alexithymia ^b	44 (15)	20 (12)	24 (18)	0.18
Anxiety ^b	101 (35)	40 (25)	61 (47)	<0.001
Metabolic factors				
HbA1c (%) mean (s.d.)	8.0 (±1.2)	7.9 (±1.1)	8.0 (±1.3)	0.33 ^a
HbA1c > 8.6%	80 (27)	41 (24)	39 (32)	0.19
Hypoglycemia ^c	13 (4)	7 (4)	6 (5)	1.0
Anthropometric variables				
General obesity ^d	36 (12)	12 (7)	24 (19)	0.004
Abdominal obesity ^e	49 (17)	13 (8)	36 (29)	<0.001
Lifestyle variables				
Smoking ^f	28 (10)	18 (12)	10 (8)	0.42
Physical inactivity ^g	36 (13)	19 (12)	17 (14)	0.85
Complications				
Diabetes retinopathy	209 (72)	118 (73)	91 (70)	0.69
Foot complications	47 (17)	34 (22)	13 (11)	0.016
Macrovascular complications ^h	10 (3)	6 (4)	4 (3)	1.0

^aStudent's *t*-test.^bSelf-reported.^cDefinition: ≥ 1 severe episode last year.^dDefinition: BMI ≥ 30 kg/m².^eDefinition: WC for men ≥ 1.02 m, WC for women ≥ 0.88 m.^fAny amount of tobacco during the last year.^gLess than 30 min of physical activity/week.^hStroke/TIA and/or ischemic heart disease.

ischemic heart disease, and two had both types of complications. These ten patients had retinopathy, seven had foot complications, four had self-reported depression, four had self-reported anxiety, and three had alexithymia. Macrovascular complications were associated with depression (COR = 6.6 (1.7–24.8), *P* = 0.005) but not with HbA1c > 8.6% (COR = 1.1 (0.3–4.5), *P* = 0.85).

Associations between clinical psychiatric diagnoses, antidepressant medication, and HADS

Of the 41 patients with a clinical psychiatric diagnosis, 26 (63%) scored positive on at least one of the two HAD subscales compared with 30% for patients without known clinical psychiatric diagnoses. For patients with a clinical psychiatric diagnosis, the COR (CI) for scoring positive on HADS-D was 10.8 (4.7–24.8), *P* < 0.001. For the 23 patients using antidepressant medication, the COR (CI) for scoring positive on HADS-D was 9.6 (3.7–24.6), *P* < 0.001.

Glycemic control

Mean HbA1c levels for patients with and without depression, alexithymia, anxiety, severe hypoglycemia episodes, obesity, physical inactivity, smoking, retinopathy, foot, and macrovascular complications are

presented gender stratified in Table 2. Mean HbA1c levels were higher for men who were smoking or physically inactive than for non-smoking or physically active. Mean HbA1c levels were higher for women with self-rated depression, alexithymia, obesity, smoking, retinopathy, foot complications, and macrovascular complications than for women without these factors (Table 2).

There were 80 (27%) patients with HbA1c > 8.6%: 41 men (24%) and 39 women (32%). Age (*P* = 0.27) and diabetes duration (*P* = 0.80) were not associated with HbA1c > 8.6%.

In bivariate analyses, the following variables were associated with HbA1c > 8.6%: abdominal obesity (COR 3.3 (1.7–6.2), *P* < 0.001), general obesity (COR 3.6 (1.8–7.4), *P* < 0.001), alexithymia (COR 2.6 (1.3–5.1), *P* = 0.004), self-reported depression (COR 2.6 (1.2–5.6), *P* = 0.015), smoking (COR 2.8 (1.2–6.1), *P* = 0.013), antidepressant medication (COR 2.7 (1.1–6.3), *P* = 0.026), physical inactivity (COR 2.2 (1.0–4.7), *P* = 0.049), and retinopathy (COR 2.7 (1.4–5.5), *P* = 0.003).

The following variables were not associated with HbA1c > 8.6%: self-reported anxiety (COR 1.2 (0.70–2.0), *P* = 0.52), macrovascular complications (COR 1.1 (0.3–4.5), *P* = 0.85), AITD (COR 1.8 (0.9–3.9), *P* = 0.11), and foot complications (COR 1.1 (0.6–2.3), *P* = 0.74). In multiple logistic regression analysis, abdominal obesity (adjusted odds ratio (AOR) 4.3), self-reported

Table 2 Gender-stratified mean levels of HbA1c for positive and negative findings for the variables in the study. Data are *n* (%) and mean (s.d.).

	Men			Women		
	<i>n</i> (%)	HbA1c %	<i>P</i> ^a	<i>n</i> (%)	HbA1c %	<i>P</i> ^a
Gender	162 (55%)	7.9 (±1.1)		130 (45%)	8.0 (±1.3)	
Psychological factors						
Depression ^b						
Yes	16 (10)	7.9 (±1.0)	0.90	14 (11)	9.0 (±1.3)	0.004
No	146 (90)	7.9 (±1.1)		116 (89)	7.9 (±1.3)	
Alexithymia						
Yes	20 (12)	8.1 (±1.4)	0.34	24 (18)	8.8 (±1.5)	0.002
No	142 (88)	7.9 (±1.1)		106 (82)	7.9 (±1.3)	
Anxiety						
Yes	40 (25)	7.8 (±1.0)	0.41	61 (47)	8.3 (±1.5)	0.088
No	122 (75)	8.0 (±1.2)		69 (53)	7.9 (±1.2)	
Metabolic factor						
Hypoglycemia						
Yes	7 (4)	8.4 (±1.0)	0.26	6 (5)	7.7 (±1.0)	0.50
No	155 (96)	7.9 (±1.1)		124 (95)	8.1 (±1.4)	
Anthropometric variables						
General obesity						
Yes	12 (7)	8.0 (±1.4)	0.69	24 (19)	8.7 (±1.1)	0.010
No	150 (93)	7.9 (±1.1)		104 (81)	7.9 (±1.3)	
Abdominal obesity						
Yes	13 (8)	8.5 (±0.9)	0.07	36 (29)	8.7 (±1.2)	0.001
No	146 (92)	7.9 (±1.1)		89 (71)	7.8 (±1.3)	
Lifestyle variables						
Smoking ^c						
Yes	18 (12)	8.4 (±0.9)	0.046	10 (8)	9.2 (±1.9)	0.004
No	136 (88)	7.8 (±1.1)		111 (92)	7.9 (±1.2)	
Physical inactivity						
Yes	18 (12)	8.5 (±1.3)	0.007	13 (11)	8.5 (±0.8)	0.20
No	136 (88)	7.8 (±1.0)		108 (89)	8.0 (±1.4)	
Complications						
Diabetes retinopathy						
Yes	118 (73)	8.0 (±1.1)	0.17	91 (70)	8.4 (±1.3)	<0.001
No	43 (27)	7.7 (±1.2)		38 (30)	7.3 (±1.0)	
Foot complications						
Yes	34 (22)	7.9 (±1.1)	0.9	13 (11)	8.9 (±1.4)	0.006
No	123 (78)	7.9 (±1.1)		110 (89)	7.9 (±1.3)	
Macrovascular complications						
Yes	6 (4)	7.4 (±1.1)	0.29	4 (3)	9.5 (±1.9)	0.028
No	156 (96)	7.9 (±1.1)		126 (97)	8.0 (±1.3)	

^aStudent's *t*-test.^bSelf-reported.^cDefinitions of the variables are the same as presented earlier.

depression (AOR 4.8), and smoking (AOR 3.0) were associated with HbA1c > 8.6%. Gender sub-analyses showed that the associations between self-reported depression (AOR 19.8), abdominal obesity (AOR 7.0), and HbA1c > 8.6% remained significant for women and smoking (AOR 4.2) for men (Table 3).

Associations with self-reported depression

In patients with self-reported depression, the alexithymia prevalence was 50% and the self-reported anxiety prevalence was 83%. In patients without self-reported depression, the alexithymia prevalence was 11% and the self-reported anxiety prevalence was 29%. In multiple logistic regression analysis, alexithymia (AOR 14.8), self-reported anxiety (AOR 31.1), HbA1c > 8.6% (AOR 11.0), physical inactivity (AOR 8.2), and absence of

abdominal obesity (AOR 0.04) were associated with self-reported depression (Table 4); smoking, retinopathy, and foot complications were not associated with self-reported depression (Table 4). AITD was not associated with depression (COR 0.8 (0.2–2.9), *P* = 0.76).

Associations between smoking, obesity, and alexithymia

Alexithymia was associated with abdominal obesity (COR 2.2 (1.1–4.8), *P* = 0.037) but not with smoking (COR 1.7 (0.6–4.5), *P* = 0.28).

Patients not included in the study

The 141 patients who chose not to participate had a mean HbA1c of 8.0%. Thirty-eight patients were

Table 3 Factors associated with inadequate glycemic control. Patients with macrovascular complications were not included. Data are controlled for age, diabetes duration, and gender. The values from the last step in the model are presented for the nonsignificant results. Nagelkerke R²: ^a0.162; ^b0.115; and ^c0.309. Hosmer and Lemeshow test: ^a0.153; ^b0.218; and ^c0.902.

	HbA1c > 8.6%					
	All ^a		Men ^b		Women ^c	
	AOR (95% CI)	P ^d	AOR (95% CI)	P ^d	AOR (95% CI)	P ^d
Abdominal obesity	4.3 (2.0–9.3)	<0.001	3.3 (0.9–12.2)	0.07	7.0 (2.5–19.7)	<0.001
Depression ^e	4.8 (1.9–11.9)	0.001	2.0 (0.5–7.5)	0.29	19.8 (3.9–99.7)	<0.001
Smoking	3.0 (1.2–7.2)	0.017	4.2 (1.5–11.9)	0.008	1.5 (0.2–9.5)	0.66
Antidepressants	2.0 (0.7–6.2)	0.22	2.0 (0.4–11.7)	0.43	1.7 (0.3–9.8)	0.59
Anxiety ^d	0.6 (0.3–1.3)	0.24	0.4 (0.1–1.2)	0.10	0.9 (0.3–2.5)	0.82
Alexithymia	1.3 (0.5–3.2)	0.62	1.1 (0.2–4.9)	0.95	2.3 (0.6–8.0)	0.23
Physical inactivity	1.0 (0.4–2.5)	0.96	2.1 (0.7–6.6)	0.21	0.2 (0.04–1.3)	0.09

^an=257.

^bn=145.

^cn=112.

^dMultiple logistic regression (Backward: Wald).

^eSelf-reported.

non-eligible: seven patients had severe somatic comorbidity (mean HbA1c 7.8%); 21 patients had severe mental disorder, mental retardation, or other cognitive deficiency (mean HbA1c 8.9%); and ten had inadequate knowledge of Swedish (mean HbA1c 7.9%).

Discussion

In this population-based study of self-reported depression, alexithymia, and self-reported anxiety in 292 patients with type 1 diabetes, we found that self-reported depression was the only psychological factor that was independently associated with inadequate glycemic control of diabetes (HbA1c > 8.6%). With an AOR of 4.8, the association was of comparable importance as abdominal obesity (AOR 4.3) and smoking (AOR 3.0). Gender analyses showed that self-reported depression was particularly associated with inadequate glycemic control in women (AOR 19.8). Abdominal obesity (25) and smoking (22) are well-known risk factors for poor glycemic control and have been associated with dysfunction of the cortisol metabolism (38, 39), which is also the case for depression (1). This shared underlying mechanism should be further explored. Physical inactivity was associated with self-reported depression, but in contrast to earlier research, smoking and abdominal obesity were not (7, 8, 9, 40). Previous research (4, 5), as opposed to data in this study, has shown associations between depression and diabetes retinopathy and foot complications. Associations between the severity of these complications and depression were not investigated in this study. This is an appeal for future research. Macrovascular complications were associated with self-reported depression in bivariate analyses, but we did not enter them in the regression analyses as these patients had many other complications with spurious interactions. Treated AITD was not associated with HbA1c > 8.6% or with

self-reported depression. TSH is controlled every other year in these patients, so the risk for undiagnosed AITD is low.

Alexithymia, a relatively stable personality trait and a risk factor for depression, but often enhanced during depressive periods (17), was strongly associated with self-reported depression in this study. The prevalence of alexithymia among patients with self-reported depression was 25 times higher, and among patients without self-reported depression, five times higher than in a Swedish normative sample (20). Alexithymia was associated with abdominal obesity but not with smoking. Both findings are consistent with previous research (20, 41). Alexithymia showed stronger association with depression than retinopathy and foot complications. It is remarkable that retinopathy and foot complications were not associated with depression in logistic regression analyses as it could be assumed that these conditions would eventually cause secondary depression. There was a high frequency of comorbidity between self-reported anxiety and self-reported

Table 4 Factors associated with self-reported depression. n=246. Logistic regression (Backward: Wald). Patients with macrovascular complications were not included. Data are controlled for age, diabetes duration, and gender. For the nonsignificant results, the values from the last step in the model are presented. Nagelkerke R²: 0.533. Hosmer and Lemeshow test: 0.142.

	Self-reported depression ^a	
	AOR (95% CI)	P
Alexithymia	14.8 (3.5–62.4)	<0.001
Anxiety ^a	31.1 (5.9–164)	<0.001
HbA1c > 8.6%	11.0 (2.8–44.1)	0.001
Abdominal obesity	0.04 (0.004–0.3)	0.003
Physical inactivity	8.2 (1.3–51.1)	0.025
Foot complications	3.3 (0.6–17.6)	0.16
Retinopathy	3.1 (0.6–17.6)	0.24
Smoking	0.8 (0.1–5.9)	0.80

^aSelf-reported.

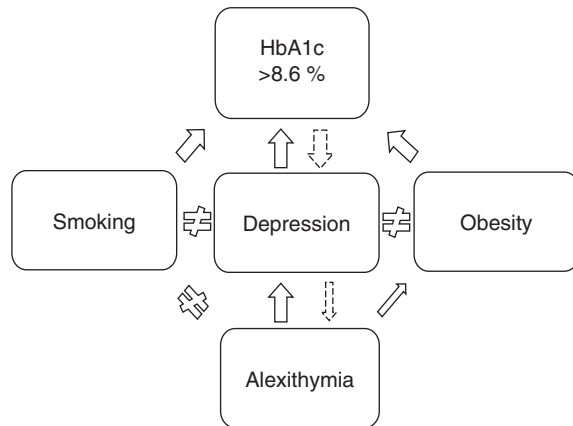


Figure 1 Probable directions of the most important associations discussed in the article.

depression. Anxiety affects quality of life but was not associated with high HbA1c in this study.

There are limitations to this cross-sectional study. The diagnosis of depression was not confirmed by a diagnostic interview. On the other hand, the use of antidepressant medication (COR 9.6) and a clinical psychiatric diagnosis (COR 10.8) were significantly associated with HADS-D ≥ 8 , which supports that the test is adequate for testing depression. HADS-A does not differentiate between different anxiety syndromes, so for further analyses of the role of anxiety in diabetes, more specific diagnostic tools must be used. HbA1c was only measured once. As this was a cross-sectional study, it was necessary to measure HbA1c at the same time as the patients answered the self-report instruments. Yet, had we asked for venous samples 2 days in a row, fewer patients would eventually have accepted to participate.

Whether depression is primary or secondary to poor metabolic control of diabetes, or bidirectional, cannot be clarified by this study. The same can be concluded for the association between alexithymia and depression. Alexithymia can be a risk factor for depression but can also be a symptom of reduced overall cognition associated with diabetes or depression (1). The probable directions of the associations discussed here are shown in Fig. 1.

To summarize, in this study, it is clearly shown that self-reported depression was of similar importance for glycemic control as obesity and smoking. It is important to pay attention to the personality trait alexithymia – a risk factor for both depression and obesity. Much attention in the care of patients with diabetes is focused on physical factors; however, in this study, it is clearly demonstrated that psychological factors are related to glycemic control as well. An AOR of 4.8 for the association between self-reported depression and poor metabolic control of diabetes should not be neglected. For the future care of patients with type 1 diabetes, it may be valuable to consider both depression and

alexithymia to achieve an adequate HbA1c and optimize the patients' self-care abilities. Despite the efforts we spend on reducing risk factors such as obesity and smoking, we still do not reach the goals for HbA1c. This could be due to an undiagnosed or inadequately treated depressive disorder. Future suggestions for managing patients with unacceptable high levels of HbA1c are to test them for depression (30) and alexithymia (31, 32). If test results are positive, clinical exploration and decisions regarding treatment should be made. Antidepressant medication (3) and/or psychotherapy can be used, either as cognitive behavioral therapy (42), and in case of alexithymia emotion focused therapy (43), or psycho-educational methods (11, 44).

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

E O Melin, M Thunander, H O Thulesius, R Svensson, and M Landin-Olsson participated as investigators and reviewed and edited the manuscript. E O Melin, M Thunander, and R Svensson contributed to the study design and implementation. E O Melin, H O Thulesius, and M Landin-Olsson contributed to the analysis and wrote the statistical methods. E O Melin 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.

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