Diabetes-Related Symptom Distress in Association With Glucose Metabolism and Comorbidity

The Hoorn Study

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OBJECTIVE — The purpose of this study was to determine the associations between diabetes-related symptom distress, glucose metabolism status, and comorbidities of type 2 diabetes.

RESEARCH DESIGN AND METHODS — This was a cross-sectional sample of 281 individuals with normal glucose metabolism (NGM), 181 individuals with impaired glucose metabolism (IGM), and 107 subjects with type 2 diabetes. We used the revised type 2 Diabetes Symptom Checklist (DSC-R) to assess diabetes-related symptom distress.

RESULTS — The total symptom distress score (range 0–100) was relatively low for diabetic subjects (mean ± SD 8.4 ± 9.4), although it was significantly different from that for subjects with IGM (6.5 ± 7.1) and NGM (6.1 ± 7.9) ($F = 3.1$, 2 d.f., $P = 0.046$). Ischemic heart disease was associated with elevated DSC-R scores on three subscales, whereas depression showed higher symptom distress levels across all DSC-R domains.

CONCLUSIONS — Worsening glucose metabolism is associated with increasing diabetes-related symptom distress. This relationship is attenuated by ischemic heart disease and particularly by depression.

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Type 2 diabetes can seriously affect patients' health-related quality of life (1), and symptom distress has been recognized as an important patient-reported outcome (2,3). So far, empirical data about symptom distress in relation to glucose metabolism status and comorbidities are sparse, especially among subjects with impaired glucose metabolism (IGM) (pre-diabetes). Therefore, we analyzed cross-sectional data of the 2000–2001 follow-up examination from the Hoorn Study, a population-based cohort study, to compare levels of diabetes-related symptom distress among groups with different glucose metabolism status (i.e., normal glucose metabolism [NGM], impaired glucose metabolism [IGM], and diabetes) and to examine the moderating effect of complications and comorbidities, including depression.

RESEARCH DESIGN AND METHODS

— The total study sample consisted of 569 subjects, 280 men and 289 women, with a mean ± SD age of 69.8 ± 6.4 years. Details of the 2000–2001 follow-up examination from the Hoorn Study have been described before (4). All subjects gave written informed consent. Information about age and sex was assessed by means of a questionnaire. BMI and blood pressure were measured using standard methods. Hypertension was defined as a diastolic blood pressure ≥90 mmHg and/or a systolic blood pressure ≥140 mmHg and/or taking antihypertensive medication. Glucose metabolism status was based on an oral glucose tolerance test using the World Health Organization 1999 diagnostic criteria (5). Ischemic heart disease was determined from a 12-lead electrocardiogram. Prevalent cardiovascular disease was assessed by the Rose questionnaire (6).

Neuropathy was defined as the presence of impaired foot sensitivity, assessed with Semmes-Weinstein monofilaments. Diabetic retinopathy was defined as Wisconsin grade ≥1.5 (7), based on retinal photography. Microalbuminuria was defined as an albumin-to-creatine ratio of >2.0 mg/mmol (8). Depression was assessed using the 20-item Center for Epidemiologic Studies Depression Scale (CES-D) (score ≥16) (9). Diabetes-related symptom distress was measured with the revised version of the revised type 2 Diabetes Symptom Checklist (DSC-R) (10).

χ^2 tests (percent) and ANOVA were performed to study differences in characteristics, comorbidities, and DSC-R variables for NGM, IGM, and diabetes. Because previous studies suggest that depression is associated with increased levels of symptom distress (11,12), we included depression as a covariate in the ANOVA to sort out the potential interaction between the DSC-R total scores and NGM, IGM, and diabetes. Mann-Whitney *U* tests were performed for between-group comparisons regarding DSC-R, i.e., *1*) diabetes versus IGM and *2*) diabetes versus NGM. Student's *t* tests were used to determine the association between co-

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Table 1—*Mean scores for diabetes-related symptom distress total and subscale scores in subjects with and without comorbidity among all participants*

	DSC-R (0–100) score for comorbidity*											
	Ischemic heart disease†		Prevalent cardiovascular disease‡		Neuropathy		Retinopathy		Microalbuminuria		Depression	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
n	345	202	465	100	215	203	192	24	468	81	440	68
Hyperglycemia	6.1	8.1	7.1	6.6	5.7	8.4§	7.0	10.4	7.0	7.4	5.9	14.2‖
Hypoglycemia	5.1	5.3	5.3	5.3	4.3	5.5	5.2	9.4	5.5	4.4	3.8	15.3‖
Neuropathic pain	4.2	7.0‖	5.4	4.7	4.6	5.4	5.6	11.2§	5.1	6.0	3.9	12.7‖
Sensibility	4.7	5.8	5.0	5.4	4.1	5.4	5.6	5.6	5.0	5.0	3.9	10.5‖
Fatigue	11.5	14.1	13.1	11.1	10.9	12.6	12.8	14.1	12.6	12.7	9.4	31.2‖
Cognitive distress	6.2	8.6‖	7.3	7.3	6.1	7.9	6.9	12.8§	7.3	6.6	5.1	20.6‖
Cardiovascular	5.4	6.7	6.0	6.5	5.4	5.8	4.6	9.6‖	6.2	5.3	4.6	15.4‖
Ophthalmological	4.7	6.6†	5.3	6.2	5.5	5.3	6.5	9.0	5.5	5.1	4.3	11.8‖
DSC-R total score	5.9	7.7‖	6.7	6.6	5.7	6.9	6.7	10.0	6.7	6.5	5.1	16.0‖

*Numbers do not total exactly because of missing values, particularly for retinopathy. †Based on electrocardiogram recording. ‡Assessed by the Rose questionnaire. §$P < 0.05$; ‖$P < 0.01$.

morbidities and DSC-R scores in subjects with and without comorbidity. $P < 0.05$ was considered statistical significant. All analyses were performed using SPSS, version 11.5 for Microsoft Windows.

RESULTS — ANOVA showed that worsening glucose metabolism, represented by NGM (mean ± SD 6.1 ± 7.9), IGM (6.5 ± 7.1), and diabetes (8.4 ± 9.4), was associated with increasing DSC-R total scores ($F = 3.1$, 2 d.f., $P = 0.046$). In addition, we included depression (CES-D score) as a covariate in the ANOVA to sort out the potential interaction. Virtually the same DSC-R scores were found for the subjects with NGM (6.0 ± 7.7), IGM (6.1 ± 7.0), and diabetes (8.5 ± 9.7), although scores were not statistically significant ($F = 0.99$, 2 d.f., $P = 0.245$). Mann-Whitney *U* tests revealed that diabetic patients reported a significantly greater burden of neuropathic pain ($P = 0.033$), sensibility symptoms ($P = 0.004$), and total symptom distress ($P = 0.005$) than subjects with NGM but not those with IGM (supplemental Table A1, available in an online appendix at http://dx.doi.org/10.2337/dc08-1074).

Subjects with ischemic heart disease had a significantly higher total DSC-R score compared with subjects with nonischemic heart disease. Most strikingly, both the DSC-R score total and all subscale scores appeared to be ~3-fold higher for subjects with depression (CES-D score ≥16) than for those without depression at all three stages of glucose metabolism (Table 1).

CONCLUSIONS — This is the first study to demonstrate the association between glucose metabolism status and the level of diabetes-related symptom distress using the DSC-R score. Worsening glucose metabolism is associated with increasing diabetes-related symptom distress. This relationship is attenuated by ischemic heart disease and by depression in particular. The results presented provide supportive evidence of the validity and reliability of the DSC-R.

The fact that subjects with depression reported significantly higher DSC-R levels compared with those without depression suggests that negative affect has a strong amplifying effect on diabetes symptom burden, representing higher illness intrusiveness. The association between diabetes symptoms and depressive mood could also be bidirectional, with diabetes symptoms contributing to the development of depressive symptoms (13). Yet, even after correction for depression we found that diabetic subjects report higher levels of diabetes symptom distress than subjects with NGM or IGM, underscoring the importance of glucose metabolism status.

In individuals screened for type 2 diabetes, relatively high levels of symptom distress may indicate comorbid depression and a need for antidepressant treatment. Likewise, in patients with established diabetes, high symptom distress despite relatively good glycemic control may point to elevated levels of depression. New longitudinal research on this complex relationship is warranted to further understand underlying mechanisms and to develop effective therapeutic strategies.

The strengths of our study are the use of data from a population-based sample, the use of a standard measurement to determine glucose metabolism status (i.e., an oral glucose tolerance test), the availability of information on comorbidities, and the use of the validated DSC-R to determine diabetes-related symptom distress. There are also limitations. This present study has a cross-sectional design. Further prospective research should help to clarify the course of symptom distress over time across different stages of glucose metabolism. In addition, determining the impact of different treatment strategies (i.e., diet, blood glucose–lowering drugs, and insulin) on the DSC-R levels among diabetes patients was beyond the scope of this study. However, given the increasing importance of patient-reported outcomes, future researchers should carefully explore the impact of diabetes medication on symptom distress as a measure of health-related quality of life.

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