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

The Hoorn Study

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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morbidity and DSC-R scores in subjects with and without comorbidity. $P < 0.05$ was considered statistically 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 ($P = 0.004$), sensitivity 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 non-ischemic heart disease. Most strikingly, both the DSC-R score total and all subscale scores appeared to be $\sim3$-fold higher for subjects with depression (CES-D score $\geq 16$) 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.

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

|                | Ischemic heart disease† | Prevalent cardiovascular disease‡ | Neuropathy | Retinopathy | Microalbuminuria | Depression |
|----------------|-------------------------|----------------------------------|------------|-------------|------------------|------------|
|                | No | Yes | 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 | 8.48 | 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 | 11.28 | 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.

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