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Trajectories of anxiety symptoms and associations with incident cardiovascular disease in adults with type 2 diabetes

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ABSTRACT

Background: Trajectories of anxiety symptoms in people with type 2 diabetes (T2D) and their associations with diabetes health outcomes have not been investigated. This study examined latent longitudinal trajectories of anxiety symptoms in adults with T2D and their associations with incident cardiovascular disease (CVD).

Methods: Data were from the Evaluation of Diabetes Treatment Study, a community-based cohort study of adults aged 40–76 years with T2D. Anxiety and CVD were assessed by self-report at baseline and at four annual follow-up assessments. $N = 832$ participants without cardiovascular disease at baseline and 12-month follow-up were included in the present study. Group-based trajectories of anxiety at baseline, 12-month follow-up, and 24-month follow-up were modelled using latent class growth modeling. Associations between anxiety trajectories and CVD reported at 24-, 36-, or 48-month follow-ups were examined with logistic regression analysis adjusted for sociodemographic and lifestyle characteristics.

Results: Four distinct anxiety trajectories were identified, reflecting chronically low (39.4%), chronically moderate-low (47.4%), chronically moderate-high (11.1%), and chronically high (2.2%) anxiety. The likelihood of CVD was greater for the chronically moderate-low (OR = 2.23, 95% CI = 1.36–3.66), chronically moderate-high (OR = 3.05, 95% CI = 1.54–6.02), and chronically high (OR = 3.61, 95% CI = 1.09–12.00) anxiety trajectory groups compared to the chronically low anxiety group.

Conclusion: The identified latent trajectories reflected three groups with chronic courses of anxiety symptoms at different levels of severity and one group with chronically low levels of anxiety. Chronic anxiety, even at subthreshold levels, was associated with an increased risk of CVD among people with T2D.

1. Introduction

Cardiovascular disease (CVD) is a leading cause of death among adults with type 2 diabetes (T2D) [1,2]. Anxiety symptoms, which tend to be more common in people with T2D than in the general population [3], are associated with cardiovascular mortality [4] and an increased risk of CVD [5] in people with diabetes as well as with functional disability [6,7] and poor glycemic control [8]. However, longitudinal studies on anxiety symptoms and diabetes health outcomes have largely focused on anxiety symptoms measured at a single time-point [4,5,9]. Measurement of anxiety symptoms over repeated assessments can be more informative than a single assessment as it can prospectively capture anxiety chronicity.

Chronic anxiety may be more strongly associated with poor health outcomes compared to non-chronic anxiety or persistently low anxiety. For instance, one study found that chronically high anxiety was associated with an increased risk of diabetes compared to those who were persistently not anxious over the course of 21 years [10]. Recurrent subthreshold depressive episodes were also found to be associated with poor functioning and health-related quality of life in adults with type 2 diabetes [11]. However, whether the temporal course of anxiety symptoms is associated with poor diabetes outcomes such as CVD has not been explored. One strategy to study individual differences in anxiety symptom course is to examine latent temporal trajectories of symptoms [12,13] and their associations with incidence of CVD.

The first goal of the present study was to examine latent trajectories of anxiety symptoms over three years in adults with type 2 diabetes diagnosed within the past 10 years. The second goal of the study was to examine the extent to which latent anxiety symptom trajectories at three time points over two years were associated with the incidence of

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CVD over two years.

2. Method

2.1. Study population

Data were from the Evaluation of Diabetes Treatment (EDIT) Study, a prospective telephone-based community health survey of English- and French-speaking residents of the Canadian province of Quebec between 40 and 76 years of age who had been diagnosed by a physician within the past 10 years and who were insulin-naïve at the time of the baseline assessment. Baseline was completed in the year 2011 and four follow-up assessments were conducted annually. The study protocol was approved by the Douglas Mental Health University Institute Research Ethics Committee and participants provided informed consent. Further information about the EDIT study can be found elsewhere [14].

A total of 2033 participants completed the baseline assessment (n = 1691 agreed to be contacted for a follow-up assessment). Inclusion criteria for the present study were being free of CVD at baseline (n = 620 excluded) and 12-month follow-up (n = 106 excluded) and having complete data on anxiety symptoms at baseline (n = 15 excluded) and at least one follow-up assessment of the 12-month or 24-month follow-up (n = 460 excluded). Thus, 832 participants were included in the trajectory analysis. For the analysis that examined associations between anxiety symptom trajectories and incident CVD, only those with complete data on incident CVD for at least one of the three final follow-up assessments (i.e., 24-month, 36-month, and 48-month follow-up) were included (n = 743).

2.2. Measures

2.2.1. Anxiety symptoms

Anxiety symptoms were assessed with the Generalized Anxiety Disorder Scale (GAD-7) [15], a 7-item questionnaire that assesses the extent to which symptoms of generalized anxiety disorder were endorsed within the past two weeks. Symptoms include feelings of nervousness and anxiety, worry, restlessness, irritability, fear, and difficulty relaxing. Items are rated on a 0–3 scale and are summed to create a total score ranging from 0 to 21, with higher scores reflecting a greater severity of anxiety symptoms. A score of > 10 is indicative moderate to severe anxiety [15]. Internal consistency of the GAD-7 at baseline, 12-month follow-up, and 24-month follow-up in our sample was very good, with αs = 0.81, 0.85, and 0.87, respectively.

2.2.2. Cardiovascular disease

CVD was assessed by combining questions from the Diabetes Complications Index (DCI) [16] and by a self-report question about physician-diagnosed heart diseases. The DCI assesses six common diabetes complications including coronary artery disease and cerebrovascular disease. Coronary artery disease was assessed by questions about having received a diagnosis of coronary artery disease or heart attack by a doctor or having experienced symptoms such as chest pain within the past six months. Cerebrovascular disease was assessed by questions about having previously suffered a stroke or stroke-like symptoms, or having been told by a doctor that they had a transient ischemic attack. Participants also responded to the question "have you ever been diagnosed by a doctor with heart disease?" as part of a series of questions about prevalent chronic conditions. Incidence of CVD was considered if participants had a positive response to the DCI questions about coronary artery disease or cerebrovascular disease or reported having been diagnosed by a physician with heart disease at the 24-month, 36-month, or 48-month follow-up. These questions were also used to determine the exclusion criteria of CVD at baseline and 12-month follow-up.

2.2.3. Covariates

Covariates included age, sex, ethnicity, education (less than secondary school, secondary school graduation, some post-secondary, and post-secondary graduation), marital status (married/living with a partner or single), duration of diabetes in years (0–2, 3–5, 6–8, and 9–10), current smoking status, alcohol use frequency (never, monthly or less, 1–4 times per month, 2–3 times per week, and 4 or more times per week), number of days in the past 30 days having participated in exercise (0–9 days, 10–19, and 20–30), and body mass index (kg/m^2 categorized as normal weight [18.5–24.9]/underweight [18.4 or less]/overweight [25.0–29.9]/obese [30 or more] according to World Health Organization recommendations [17]). Depressive symptoms were assessed with the Patient Health Questionnaire (PHQ-9) [18], a 9-item scale that assesses the extent to which symptoms of depression were endorsed within the past two weeks. Symptoms include feeling depressed or hopeless, anhedonia, sleep problems, fatigue, appetite or eating changes, low self-esteem, difficulty concentrating, moving or speaking slowly or restlessness, and suicidal thoughts. Items are rated on a 0–3 scale and are summed to create a total score ranging from 0 to 27, with higher scores reflecting a greater severity of depressive symptoms. A score of > 10 is indicative moderate to severe depressive symptoms. Internal consistency of the PHQ-9 at baseline was good (α = 0.74). Depressive symptoms were not included as covariates in the statistical analyses given the overlap between symptoms of depression and anxiety assessed by the PHQ-9 and GAD-7, respectively, however anxiety trajectory groups were compared on frequency of high depressive symptoms.

2.3. Statistical analysis

Group-based trajectories with a censored normal distribution were modelled using latent class growth modeling (LCGM), a semi-parametric technique that can estimate categorical latent classes that group together participants with similar anxiety symptom trajectories over time [12,13]. LCGM uses all available data and assumes that data are missing at random, a technique that is advantageous over traditional statistical techniques that exclude missing data by listwise deletion [19]. Continuous GAD-7 scores from baseline, 12-month, and 24-month follow-ups were included in the trajectory analysis. The first step of the analysis was to determine the number of trajectory groups that best fit the data. This was done by an iterative process that estimated a series of quadratic growth models with varying number of classes [13], selected a priori from one class to 6 classes. Model fit was compared on the Bayesian Information Criterion (BIC). The model with the lowest BIC and a log Bayes Factor, calculated as 2 * (BIC of the more complex model − BIC of the simpler model, whereby a simpler model refers to a model with a fewer number of estimated classes), above 6 and was selected [12]. The next step was to refine the model according to the shape of each trajectory, which was based on the statistical significance of the polynomial terms that best described each trajectory group. For each group, non-statistically significant (p > 0.05) quadratic, linear, or intercept terms were removed and only statistically significant polynomial terms per group were retained in the final model. The final model was further tested for model adequacy by examining whether there was good correspondence between the estimated probability of group membership and proportion assigned to that group based on posterior probability of group membership, whether the odds of correct classification (OCC) for each group suggested good assignment accuracy for groups, with greater values suggesting better assignment accuracy and with values > 5.0 indicating high assignment accuracy, and whether there was good internal reliability for each trajectory group based on the average posterior probability of assignment (> 0.7) [13]. Participants were assigned to a trajectory group based on their highest posterior probability of group membership [20].

Associations between anxiety symptom trajectory groups and incident CVD at 24-month, 36-month, or 48-month follow-up were