Anxiety disorders and onset of cardiovascular disease: The differential impact of panic, phobias and worry

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ABSTRACT

Anxiety has been linked to onset of cardiovascular disease. This study examines the differential impact of types of anxiety (panic, phobia and worry) on 3-year onset of non-fatal cardiovascular disease (CVD). By investigating anxiety disorders as opposed to anxiety symptoms and by using a reliable diagnostic instrument to assess anxiety, limitations of previous studies are considered.

5149 persons at risk for CVD were interviewed using the Composite International Diagnostic Interview. The panic-type included panic disorder and panic attacks; the phobic-type included agoraphobia and social phobia, and the worry-type included generalized anxiety disorder. CVD was self-reported and required treatment or monitoring by a doctor. Analyses were adjusted for sociodemographics, behavioral variables, and comorbid somatic and psychiatric disorders. During follow-up, 62 persons (1.2%) developed CVD. Baseline generalized anxiety disorder was strongly associated with onset of CVD (adjusted OR: 3.39). Further research should replicate findings and focus on biological underpinnings of this association.

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1. Introduction

Anxiety has been found to increase the risk for the onset of cardiovascular disease (CVD) in a recent meta-analysis (Roest, Martens, de Jonge, & Denollet, 2010). This meta-analysis included 20 studies in which nonpsychiatric cohorts of initially healthy adults (total $n = 249,846$) were followed between 2 and 21 years. The presence of anxiety at baseline was associated with a 26% increase in risk of onset of coronary heart disease (95% CI: 1.15–1.38) and 48% increase in risk of cardiac death (95% CI: 1.14–1.92), controlling for demographic variables, biological risk factors and health behaviors (Roest, Martens, de Jonge et al., 2010). These risk estimates implicate that reducing exposure to anxiety by increasing treatment for anxiety might contribute to the prevention of CVD. Any contribution to the prevention of CVD would be more than welcome given that cardiovascular disease is a leading cause of morbidity and mortality worldwide (Mathers & Loncar, 2006) and has a huge economic impact (Roger et al., 2012). Targeting anxiety to prevent the onset of CVD is moreover an appealing option because anxiety is common in the general population (de Graaf, ten Have, van Gool, & van Dorsselaer, 2012; Kessler et al., 2005), effective treatments for anxiety exist (NIHCE, 2011) and given that only a minority of anxiety disorder patients receive treatment (Wang et al., 2005), there is a large potential to increase treatment rates of anxiety.

A major limitation of previous studies assessing the impact of anxiety on onset of CVD concerns the assessment of anxiety. All except one study (i.e. Phillips et al., 2009) investigated anxiety on symptom-level; several studies assessed anxiety symptoms with a single question or by using a subscale with unknown psychometric properties; and most often assessment of anxiety was too global to differentiate between types of anxiety. Anxiety as a concept includes panic, phobias and worry. This distinction is reflected in the DSM-classification in which panic disorder represents panic, agoraphobia and social phobia represent the phobic-type, and generalized anxiety disorder represents the worry-type of anxiety (APA, 1994). The effects of panic, phobias and worry have not been investigated within a single study and many studies investigating one type of anxiety did not control for co-occurring other types of anxiety (see Roest, Martens, de Jonge et al., 2010), even though comorbidity among anxiety disorders is common (Hofmeijer-Sevink et al., 2012). Examining the unique contribution of types of anxiety on cardiovascular risk has been advocated (Laan et al., 2011; Roest, Martens, de Jonge et al., 2010) because it may well be that these types of anxiety have a differential impact on onset of CVD.

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Using data of the Netherlands Mental Health Survey and Incidence Study-2 (NEMESIS-2), it was possible to take previous research one step further by taking the abovementioned limitations into account. We aim to examine the impact of the category of DSM-IV anxiety disorders, and of the panic-type, the phobic-type and the worry-type of anxiety on 3-year onset of non-fatal CVD. Specifying the types of anxiety impacting on cardiovascular function may clarify the association between anxiety and CVD, and may specify target groups for the prevention of CVD. This is utmost importance given the morbidity and mortality associated with CVD.

2. Materials and methods

2.1. Procedures

Data were derived from baseline and three-year follow-up assessment of the Netherlands Health Survey and Incidence Study-2 (NEMESIS-2). Its design and procedures have been more fully described elsewhere (de Graaf, ten Have, & van Dorsselaer, 2010). Briefly, NEMESIS-2 is a prospective psychiatric survey conducted among the adult general population (aged 18–64 years) in the Netherlands. Procedures were approved by a medical ethics committee and participants provided written informed consent after full explanation of the study. A multistage, stratified random sampling procedure was applied, as is more fully described in de Graaf et al. (2010). Baseline data (T0) were gathered between November 2007 and July 2009. The three-year follow-up (T1) assessment was conducted between November 2010 and June 2012. The mean duration between T0 and T1 was 3 years and 7 days (1102 days, SD 64 days). At baseline, 6646 participants were willing to participate (weighted corrected response: 65.1%, see for calculation of response rate, de Graaf et al. (2010)). This sample was representative of the Dutch general population, although younger participants were somewhat underrepresented. Of the 6646 participants at baseline, 5303 were followed up after three years (response rate 80.4%, excluding deaths ($n = 50$)). Attrition was not significantly related to any 12-month disorder, any anxiety, any mood, or any substance use disorder, nor to the separate disorders, while controlling for sociodemographics.

For the present study, we selected respondents who participated in both baseline and follow-up interview ($n = 5303$). Participants with known CVD at baseline ($n = 68$) were excluded, as well as 86 participants who had not received the somatic disorder questionnaire (as they only agreed to participate with a short interview). This resulted in a sample size of 5149 adults at risk for onset of CVD.

2.2. Measurements

2.2.1. Anxiety disorders

Anxiety disorders, as well as panic attacks (PAs), were diagnosed according to DSM-IV criteria (APA, 1994) using the Composite International Diagnostic Interview (CIDI) version 3.0, which was adapted for the Dutch population (Alonso et al., 2004; de Graaf et al., 2008). The CIDI is a fully structured interview for diagnosing DSM-IV mental disorders to be administered by trained lay interviewers (Robins et al., 1988). The CIDI version 3.0 and earlier versions have good psychometric properties when assessing anxiety disorders and depressive disorders (Haro et al., 2006; Wittchen, 1994). Anxiety disorders included 12-month panic disorder (with or without agoraphobia), agoraphobia, social phobia and generalized anxiety disorder, and panic attacks according to DSM-IV criteria (see below). To study the differential impact of panic, phobia and worry on onset of CVD, three groups were defined. The

'Panic' group included participants with 12-month panic disorder with or without agoraphobia, and 12-month PAs. Respondents with subclinical panic disorder (i.e. PAs) were included because of the clinical relevance of PAs (Batelaan et al., 2007, 2010, 2012; Kessler et al., 2006) and to achieve sufficient statistical power to study the impact of panic on onset of CVD. The 'Phobia' group included participants with 12-month social phobia and/or agoraphobia. The 'Worry' group included participants with 12-month GAD. Thus, groups were defined irrespective of the presence of comorbid anxiety disorders (see Section 2.3).

2.2.2. Cardiovascular disease

Cardiovascular disease was assessed by means of self-report, using a 32-item questionnaire including common chronic somatic disorders. This questionnaire is used in various large scale cohort studies (de Graaf et al., 2010; Penninx et al., 2008). In the questionnaire, CVD was described as 'a severe cardiac disease or myocardial infarction'. CVD was only regarded present if treatment or monitoring by a medical doctor for this condition had been present in the year preceding the interview. In general, comparisons between self-reports of chronic somatic disorders and medical records show moderate to good concordance (Baker, 2001; Knight, Stewart-Brown, & Fletcher, 2001; NCHS, 1994).

2.2.3. Covariates

Covariates were included on the basis of their relation with CVD and anxiety disorders. These are sociodemographics (Roger et al., 2012; Thurston, Kubzansky, Kawachi, & Berkman, 2006; WHO, 2011) behavioral variables (Pate et al., 1995; Roger et al., 2012; USDHHS, 2010; WHO, 2011; Yusuf et al., 2004), somatic conditions (Franco, Peeters, Bonneux, & de Laet, 2005; Roger et al., 2012; Seshasai et al., 2011; WHO, 2011; Yusuf et al., 2004) and comorbid psychiatric disorders (Nicholson, Kuper, & Hemingway, 2006; Yusuf et al., 2004). All were assessed at baseline by means of self-report. *Sociodemographics* included gender, age (in years), partner status (yes/no), and educational level (4 categories). *Behavioral variables* included smoking, excessive alcohol use, physical inactivity and Body Mass Index (BMI). Smoking was defined as smoking in the past four weeks. Excessive alcohol use was assessed using the CIDI 3.0 and defined as >21 drinks weekly for males and >14 for females. Physical inactivity was assessed using the International Physical Activity Questionnaire (IPAQ; Craig et al., 2003) and defined as less than 5 days per week of moderate-intensity activity at least 30 min a day. Body Mass Index (BMI) was defined as the respondent's body mass divided by the square of his or her height (kg/m^2).

Comorbid somatic conditions included 12-month hypertension and 12-month diabetes mellitus. Both were assessed by means of the somatic disorder questionnaire described above and required monitoring or treatment by a medical doctor for these conditions. *Comorbid psychiatric disorders* included 12-month other type of anxiety disorder (see statistical analysis) and 12-month depressive disorder, all assessed by means of the CIDI. Comorbid depressive disorder included major depressive disorder and dysthymia.

2.3. Statistical analysis

Descriptive statistics were used for the characterization of the sample under study. To examine the association between any anxiety disorder and the anxiety groups (panic, phobia, worry), and onset of CVD, univariate logistic regression models were performed. In logistic regression analyses with a low prevalence of the independent variable and with limited events to predict, the number of events per predictor variable should be considered (Vittinghoff & McCulloch, 2006). To limit the number of covariates,