Anxiety does not predict mortality. A population-based study

Anxiety has been associated with excess mortality in the past decade, but results are inconsistent (1-6). One important concern, which precludes the generalizability of findings from these studies, is the inconsistency in methods. Some studies have used questionnaires assessing symptoms of anxiety, while others have used semi-structured or structured interviews to diagnose DSM anxiety disorders. Moreover, the significant overlap between the symptoms of anxiety and depression makes it imperative to examine confounding or effect-modification by depression, but most existing studies did not address this problem. Finally, the short follow-up of many studies bears the chance of reverse causality, and the follow-up in the literature has rarely exceeded 10 years.

In the population-based Rotterdam Study (7), we identified two sub-cohorts: one, consisting of 2,977 participants (1993-1995), in which there was an assessment of anxiety symptoms, and the other, consisting of 3,079 participants (2002-2004), in which there was an assessment of anxiety disorders. These sub-cohorts were followed for all-cause mortality till 2013. Anxiety symptoms were evaluated by the Hospital Anxiety and Depression Scale – Anxiety (HADS-A), whereas anxiety disorders (generalized anxiety disorder, panic disorder, agoraphobia, social phobia, and specific phobia) were assessed by the Composite International Diagnostic Interview, and diagnosed according to DSM-IV-TR criteria.

We excluded participants with dementia at baseline. We considered depression as a fundamental covariate and adjusted for depressive symptoms (assessed by HADS – Depression) in the analyses of anxiety symptoms, and for DSM depressive disorders (assessed by the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) interview) in the analyses of anxiety disorders. We used anxiety and depressive symptoms continuously in analyses, and also dichotomized them using the accepted cutoffs to define clinically relevant symptoms, and to assess the overlap between clinically relevant symptoms of anxiety and depression.

The cohort with anxiety symptoms assessment, whose mean age was 68.7 ± 8.5 years and which included 55% females, had 1,451 deaths during 19.3 years (13.2 ± 5.5 years). The cohort with anxiety disorders assessment, whose mean age was 75.5 ± 6.2 years and which included 59% females, had 1,138 deaths during 11.3 years (7.4 ± 2.5 years). Anxiety symptoms but not disorders were associated with an increased risk of mortality: hazard ratio (HR) per standard deviation (SD)=1.10 (95% CI: 1.02-1.14). This attenuated after adjusting for cardiovascular confounders: HR per SD= 1.04 (95% CI: 1.00-1.10). Neither anxiety symptoms (HR per SD=0.99; 95% CI: 0.92-1.07) nor anxiety disorders (HR per SD=0.99; 95% CI: 0.77-1.29) were associated with an increased risk of mortality

after additionally adjusting for depression. There was no evidence of effect modification by gender.

Interestingly, we found an association between anxiety symptoms and excess mortality during a short follow-up of 3 years in men (HR per SD 1.77; 95% CI: 1.28-2.44). This short-term association which disappears with a longer follow-up points to reverse causality (anxiety was possibly secondary to existing morbidities which caused mortality in a short follow-up).

The marginally increased risk of mortality observed with anxiety symptoms was largely explained by the presence of comorbid depressive symptoms. The correlation between symptoms of anxiety and depression was 0.66. Of the 362 (13.3%) participants who had clinically relevant anxiety symptoms, and the 238 (8.8%) who had clinically relevant depressive symptoms, 151 (5.6%) had comorbid depression and anxiety. In contrast, the overlap was much less marked for the disorders: of the 252 (8.2%) participants with anxiety disorders and 81 (2.6%) with depressive disorders, only 36 (1.2%) overlapped. Symptoms of anxiety and depression assessed by items in a self-administered questionnaire such as the HADS-A, e.g., "worrying thoughts go through my mind", may be less specific than those covered in a clinical interview.

In conclusion, anxiety symptoms and anxiety disorders were not associated with excess mortality in our population-based study. The previously observed associations between anxiety symptoms and increased mortality may be largely explained by the presence of comorbid depression, or due to a short follow-up.

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