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Research report

Clinical and course characteristics of depression and all-cause mortality: A prospective population-based study

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ABSTRACT

Background: Given the large heterogeneity of depressive disorders (DD), studying depression characteristics according to clinical manifestations and course is a more promising approach than studying depression as a whole. The purpose of this study was to determine the association between clinical and course characteristics of DD and incident all-cause mortality.

Methods: CoLaus|PsyCoLaus is a prospective cohort study (mean follow-up duration=5.2 years) including 35–66 year-old randomly selected residents of an urban area in Switzerland. A total of 3668 subjects (mean age 50.9 years, 53.0% women) underwent physical and psychiatric baseline evaluations and had a known vital status at follow-up (98.8% of the baseline sample). Clinical (diagnostic severity, atypical features) and course characteristics (recency, recurrence, duration, onset) of DD according to the DSM-5 were elicited using a semi-structured interview.

Results: Compared to participants who had never experienced DD, participants with current but not remitted DD were more than three times as likely to die (Hazard Ratio: 3.2, 95% CI: 1.1–10.0) after adjustment for socio-demographic and lifestyle characteristics, comorbid anxiety disorders, antidepressant use, and cardiovascular risk factors and diseases. There was no evidence for associations between other depression characteristics and all-cause mortality.

Limitations: The small proportion of deceased subjects impeded statistical analyses of cause-specific mortality.

Conclusions: A current but not remitted DD is a strong predictor of all-cause mortality, independently of cardiovascular or lifestyle factors, which suggests that the effect of depression on mortality diminishes after remission and further emphasizes the need to adequately treat current depressive episodes.

1. Introduction

The high mortality associated with mental disorders has been studied for several decades (Harris and Barraclough, 1998). An association between depression and mortality has also been observed in various studies (Cuijpers and Smit, 2002; Cuijpers et al., 2013, 2014; Harris and Barraclough, 1998; Schulz et al., 2002; Van den Akker et al., 2003; Wulsin et al., 1999). Indeed, a meta-analysis of community studies (Cuijpers and Smit, 2002) found a 1.8 times elevated mortality in depressed compared to non-depressed subjects. However, the results varied largely across studies, which was also reflected by a review of clinical and community studies (Wulsin et al., 1999) that documented 29 studies providing evidence for a positive association, 13 revealing no association and 15 providing a positive association only in subgroups.

The authors of previous reviews (Schulz et al., 2002; Wulsin et al., 1999) and meta-analyses (Cuijpers and Smit, 2002; Van den Akker et al., 2003) suggested that future research should measure covariates other than demographics, in particular lifestyle factors and physical comorbidity in order to better understand the possible mechanisms underlying the association between depression and mortality. Moreover, the review of Schulz et al. (2002) also showed that the type of instrument used to assess depression is an

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important source of variance across studies. Compared with negative studies, those that revealed a positive association between depression and mortality relied more frequently on a formal interview procedure than on depression rating scales. Indeed, depression rating scales are only rough indicators of clinical depression (Roberts and Vernon, 1983), hardly allow characterization into depression subtypes and do not take into account the frequent occurrence of comorbid mental disorders or past psychopathology. Given the large heterogeneity of depression in terms of symptom manifestations, course and response to pharmacological treatment (Antonijevic, 2006; Ghaemi and Vohringer, 2011), studying characteristics of depression according to clinical manifestations and course is likely to be a more promising approach than studying depression as a whole and could also help to better understand the partially inconsistent results of previous research regarding the association between depression and all-cause mortality. However, up to this date the association between course characteristics, such as the age of onset (Ferentinos et al., 2015) or the time spent in episodes has hardly been studied, whereas a recent community study showed the recency of depression to be associated with mortality due to ischemic heart disease mortality (Surtees et al., 2008). Moreover, although the results of recent studies suggest that among the depression subtypes the atypical one was most strongly associated with cardiovascular risk factors (Glaus et al., 2013; Lamers et al., 2013; Lasserre et al., 2014), the association between this subtype and mortality has not yet been examined.

The present prospective population-based cohort study designed to determine the association between depressive disorders (DD) and incident all-cause mortality over a 5-year follow-up period attempted to overcome a series of limitations of previous research by (1) the use of a semi-structured diagnostic interview that also assessed clinical (diagnostic severity level, atypical features) and course characteristics (recency, recurrence, time spent in episodes, age of onset) of (DD) and (2) the assessment of a large array of other risk factors including socio-demographic and lifestyle (smoking, alcohol use and inactivity) characteristics, comorbid anxiety disorders, antidepressant use as well as preexistent cardiovascular diseases and cardio-metabolic risk factors (obesity, hypertension, dyslipidemia and diabetes mellitus). Accordingly, the established association between DD and all-cause mortality with adjustment restricted to demographic characteristics only of the present study should be comparable with findings of previous research that also relied on formal depression diagnoses. However, in contrast to previous research the present study also allowed us to test whether this association was independent of a series of other risk factors such as lifestyle characteristics, antidepressant use and physical conditions. Similarly, we could determine the influence of clinical and course characteristics of DD on the risk of dying.

2. Methods

2.1. Study design and participants

The present paper used data from CoLaus|PsyCoLaus, a prospective cohort study designed to assess the associations between mental disorders and cardiovascular diseases (CVD) or cardiovascular risk factors in the community. The sample was randomly selected from the residents of the city of Lausanne (Switzerland) in 2003 according to the civil register (Firmann et al., 2008). Sixty-seven percent of the 35–66 year-old subjects who underwent the physical exam (CoLaus; $n=5535$) between 2003 and 2006 also accepted the psychiatric evaluation (PsyCoLaus) (Preisig et al., 2009), which resulted in a sample of 3720 individuals who had both the somatic and psychiatric evaluation. The sex distribution of the PsyCoLaus sample did not differ significantly from that of the general population in the same age range (Preisig et al., 2009). Although the youngest 5-year band of the cohort was underrepresented and the oldest 5-year band overrepresented, participants of PsyCoLaus and individuals who refused to participate revealed comparable scores on the General Health Questionnaire (GHQ-12 (Goldberg, 1972), French translation (Bettschart and Bolognini, 1996)), completed during the somatic exam. Six subjects needed to be excluded from the present analyses because of incomplete information on depressive episodes.

All subjects who participated at baseline were invited to a first follow-up evaluation between April 1st, 2009 and July 31, 2012, which allowed us to assess the vital status of 3668 out of the 3714 subjects (98.8%) who had valid information on depressive episodes at the psychiatric baseline evaluation. The reminders (46 subjects) had all moved away from Switzerland. These subjects were more likely to be physically inactive (62.2% vs. 44.2%) and to have a history of CVD (8.7% vs. 2.5%). The median follow-up period of the cohort was 5.2 years (s.d.: 0.8 years) corresponding to 19,143 person-years.

2.2. Assessments

Diagnostic information on mental disorders was collected using the semi-structured Diagnostic Interview for Genetic Studies (DIGS), which was developed and extensively validated by the NIMH Molecular Genetics Initiative (Nurnberger et al., 1994). The French translation (Leboyer et al., 1995) also revealed excellent inter-rater reliability for major DSM-IV disorders (Berney et al., 2002; Preisig et al., 1999) and minor depression (Vandeleur et al., 2014), whereas the 6-week test-retest reliability was slightly lower (Berney et al., 2002; Preisig et al., 1999). The DIGS was completed with anxiety disorder sections of the Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L) (Endicott and Spitzer, 1978). Major Depressive Disorders (MDD) and Other Specified Depressive Disorders (OSDD) including short-duration depressive episodes (4–13 days) and depressive episodes with insufficient symptoms (depressed affect and at least one of the other eight symptoms of a major depressive episode) were diagnosed according to the DSM-5. According to the suggestions of Angst and colleagues (Angst et al., 2002) a depressive disorder was considered as atypical if one or more episodes met at least 3 out of the 5 criteria of the DSM specifier for atypical features (the specifier is identical for DSM-IV and DSM-5): (1) mood reactivity, (2) significant weight gain or increase in appetite, (3) hypersomnia, (4) leaden paralysis and (5) interpersonal rejection sensitivity). Given the ongoing controversy regarding the definition of atypical features (Parker et al., 2002; Thase, 2009), we have chosen the none-hierarchical approach recommended by Angst et al. (2002), which in contrast to DSM-IV and DSM-5, does not require the presence of mood-reactivity. A DD was considered as current if the criteria for a depressive episode were met at the time of the baseline interview and remitted if the lifetime criteria for DD were fulfilled but the criteria for a current depressive episode were not met at the baseline assessment. The time spent in episodes was assessed by adding up the duration of all depressive episodes that the participants had reported. Age of onset was the age of onset of the first recalled episode of the DD. The two latter variables were dichotomized at the median (one year and 33 years, respectively). A lifetime anxiety disorder was diagnosed if the participant fulfilled the criteria for generalized anxiety disorder, social phobia, panic disorder or agoraphobia. Interviewers were required to be master-level psychologists, who were trained over a two month-period. They received ongoing supervision throughout the study by an experienced senior psychologist.